A New Design Process Intervention to Promote Efficient, Evidenced, and Safe Development of Patient-Specific Implants and Guides

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Sean Adam Peel

BA (Hons.) Industrial Design and Technology – with Diploma in Professional Studies

Director of Studies: Dr. Dominic Eggbeer
Head of Surgical and Prosthetic Design
PDR – International Centre for Design and Research
Cardiff Metropolitan University

Supervisor: Dr. Peter Dorrington
Senior Lecturer
College of Engineering
Swansea University

Supervisor: Prof. Andrew Walters
Director of Research
PDR – International Centre for Design and Research
Cardiff Metropolitan University

Awarding Body: Cardiff Metropolitan University

This research was undertaken under the auspices of Cardiff Metropolitan University.

Declaration

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

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Abstract

This research identified drivers and barriers to routine National Health Service (NHS) adoption of Computer Aided Design (CAD) and Additive Manufacturing (AM) for the production of patient-specific devices. It proposed and verified a design process intervention, which aimed to overcome the most important barriers and better exploit the drivers. The data generated and recorded in this work spanned qualitative and quantitative findings from fourteen real-world clinical case studies, a fully-realised structure for a Quality Management System (QMS), prototyping of a design intervention in a paper-based format, and verification of its intended impacts with three users across commercial and clinical contexts.

Key barriers to routine adoption were identified as being the nature of existing publications, evolving regulatory requirements, poor awareness of design or design control, and inconsistent approaches to procuring custom devices. The literature featured necessarily short clinical follow-up, and often reported on design and fabrication methods in very poor detail – to the detriment of reproducibility. Health economics evidence was scarce. In the short to medium term future, new regulatory requirements will compel all institutions, including hospitals, to implement a Quality Management System for the design of medical devices. As such, generalisable procedures, forms, and records for compliance with the BS EN ISO 13485 quality standard were devised, and used as the foundation of the design intervention.

The QMS-led design intervention form aimed to: create fully-populated product requirements lists before commencing modelling; introduce project management, identification, traceability, review, verification, and feedback activities; improve the confidence and experience of the designer or acting designer; and prompt record keeping in-line with the requirements of ISO 13485. It achieved all of these aims, at least as far as could be ascertained within the research constraints. Further expansion and verification of the framework is required in future – across different specific surgeries and across more users.

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Glossary of Terms

Term	Definition
Additive Manufacturing	Processes whereby components are created by adding material in layers
Accura ClearVue	Brand name for a transparent SLA material
Alloplastic	Synthetic tissue replacement
Anatomical Model / Medical Model	(Usually) a polymer AM model of a patient's anatomy – used for communication and planning
Anterior / Posterior	Front / back
Autologous	Patient's own tissue
CAM	Computer Aided Manufacturing – fully or semi-automated subtractive milling of (in this research) titanium or PEEK
Cancellous Bone	Deeper, more porous bone
Computer Aided Design (CAD)	Software tools for the creation of virtual geometries
Coronal approach / flap	Surgical technique for creating access to the bones of the upper face and skull. Scar hidden in hairline.
Coronal view	Scan data view from anterior to posterior aspect.
Cortical Bone	Denser, more superficial bone
Craniofacial surgery	Concerning congenital and acquired deformity of the skull
Cranium	The non-facial bones of the skull
CT	Computed Tomography – a 3D scanning process based on X-rays
Dermatochalasis	Excess / sagging eyelid tissue
DCIA free flap	Deep Circumflex Iliac Artery – a bone graft from the hip
DICOM	Digital Imaging COmmunications in Medicine – standard scan data format
Diplopia	Double vision
EBM	Electron Beam Melting – a metal AM process
Enopthalmos	Sunken eye
Exopthalmos	Protruding eye
Fibrous Dysplasia	Benign bone lesion(s)
Fibula free flap	Bone graft from the smaller of the two main bones in the lower leg
Free Flap	Harvested tissue graft including a blood supply which is re-connected at the point of implantation
FreeForm Plus	Haptic input CAD software
Frontal Bone	Forehead portion of cranium
Globe	Eye-ball
Guide	Transient-use surgical device for controlling drilling angles, drilling depths, saw vectors, bone positioning, or implant placement
Hounsfield Units	Pixel density measurement in scan-data
Implant	Fixation or reconstructive device for long term use in the body
In-lay	An implant design approach where the contours of the implant achieve tangency with the edge of the defect
Jig	Alternative term – guide
Kirschner Wire (K-Wire)	Sharpened pins frequently used in orthopaedic surgery

Magics	STL file editing and repair software
Mandible	Lower jaw
Maxilla	Upper jaw
Maxillofacial surgery	Concerning the hard and soft tissues of the head and neck
Medial / Lateral	Towards the midline of the patient / away
Medpor	Brand name for an implantable porous polyethylene material
Meningioma	Cancer – mostly benign, but occasionally malignant
Midface	Upper jaw, zygomatic complex, orbits
Mimics	Software tool for selecting desired tissue densities in scan data
MRI	Magnetic Resonance Imaging – scanning process based on a magnetic
Neurosurgical	Concerning the nervous system, usually the brain
On-lay	An implant design approach where the device overlaps the defect edge
Opthalmology	Concerning the eye and visual system
Orbit	Eye-socket
Osteoinduction	Process by which bone growth is induced
Osseointegration	On-growth or in-growth of bone to an implant
Osteotomise / osteotomy	Cutting bone
Patient-Specific Instrument	Alternative term – guide / implant
PEEK	PolyEther Ether Ketone – medical grade polymer
PMMA	PolyMethyl MethAcrylate – medical grade polymer (Acrylic)
Pretracheal	Surgical technique for accessing the facial bones, with the scar hidden.
Prosthesis	Artificial anatomy – usually for rehabilitation
Proximal / Distal	Towards the trunk / away
Scapula free flap	Bone graft from the shoulder blade
Seroma	Pocket of fluid build-up post-surgery
Skull	Cranium, plus midface, plus mandible
SLA	StereoLithography Apparatus – a polymer AM process
SLM	Selective Laser Melting – a metal AM process
STL	STereoLithography (3D) file format
Stock implants	Off the shelf implants – sometimes modifiable to suit the patient through cutting and bending
Stress-shielding	Reduced bone density caused by an implant artificially lowering stress – can result in bone resorption (breakdown) and implant loosening
Sulfonation	Process producing an etching action on PEEK to create surface porosity
Superficial / deep	Towards the surface / away from the surface
Superior / Inferior	Towards the top of the head / towards the feet
Swaged	A cold metal-shaping process using dies
Temporal Bone	Bone in the temporal region of the cranium (between forehead and ear)
Temporalis	Muscle in the temporal region of the cranium (between forehead and ear)
Temporomandibular joint (TMJ)	Joint between mandible and midface
Ti6Al4V ELI	Medical grade alloy – used in AM process to fabricate implants
Voxels	A value on a regular grid in 3D; the 3D equivalent of a pixel
Z-Corp	Legacy term for a powder-binding AM process
Zygoma	Cheekbone

1. Introduction

This research developed a novel design control intervention for the patient-specific device design process. It aimed to accomplish this by generating a conceptual framework, new quantitative data, and new rich qualitative insights into maxillofacial implant and surgical guide design practice. Crucially, this was in the context of a semi-commercial, standalone design consultancy and research institute (hereafter 'the institute') which has been using Computer Aided Design (CAD) and Additive Manufacturing (AM) to solve surgical challenges since 1998. The research was undertaken on a part-time basis; alongside the author's commercial implant design work and business development commitments. So, this work was grounded in real-world service delivery. It sought to bring a critical eye to bear on a rapidly growing field with substantial investment from industry (Wohlers, 2018); significant clinical drivers (Bibb et al., 2015); and generous media attention (Griffith, 2014); but which is still not fully matured for routine use (Peel and Eggbeer, 2016). This chapter provides background information on factors which are fundamental to this work (Chapters 1.3-1.7), before introducing the research aim (1.8), objectives (1.9), and scope (1.10).

Surgeons, clinical technicians, and biomedical designers (or design engineers) are the immediate target audiences for this work. However, that does not rule-out potential relevance for other professionals seeking to understand more about how CAD, and AM or Computer Numerically Controlled (CNC) machining can be used *effectively* to improve patient care. Therefore, the utility of this research for surgeons, design researchers, software engineers, production engineers, and healthcare economists is certainly not precluded. Efficacy and efficiency were motivating factors at the heart of the research; particularly in suggesting when and how cutting-edge techniques are best used in terms of costs and benefits. This is especially pertinent given the media hype surrounding AM in medicine (which has with full disclosure, benefitted the institute too). The institute has witnessed a trend for hospital units to invest in AM machines which do not necessarily best suit their needs, at least when compared to the more comprehensive services delivered to them previously. Informal discussions suggested troublingly, that a significant motivation was just to keep pace with contemporary fashion. There are however, competing arguments involving improved speed of delivery for AM anatomical models.

To be clear, the researcher's values aligned with the institute's commercial and academic aims in developing this thesis, and should be acknowledged early. As will become clear, the

existing published literature *and* the new data from this work, pointed unambiguously towards better clinical outcomes in the majority of cases when CAD and AM (or CNC) devices are used. It is the researcher's opinion that where appropriate, these benefits should be available to all doctors and patients in the UK National Health Service (NHS); which is the contextual focus for these studies. The institute, of course, stands to benefit from any potential increase in CAD device consultancy demand. To this end, the research project was structured to make a positive contribution to the institute's professional practice and therefore enterprise income. Along the way to defining and then designing methods to realise this goal, it is believed that important academic contributions were made; from characterising current practice in new ways, to establishing a standard design process, and in verifying the performance of a proposed new design intervention. It offered a way to better structure and control design, in a field with no prominent existing structures or service models to enable flexible working across different software tools, stakeholders, and political drivers. In short, this research sought to make it easier for more people (designers or clinicians) to design better patient-specific devices (implants and guides), more often (daily or weekly – as a matter of routine).

1.1. Thesis and Research Structure

This document is divided into nine main Chapters as shown by the overview in Figure 1. This was inductive research in an area where widely accepted existing theories or hypotheses did not exist. As such, the research questions were developed through framing the research scope, identifying themes in the clinical, technical, regulatory, and commercial contexts, reviewing the published literature, conceptualising the findings, and identifying weaknesses or assumptions.

Each Chapter, contains sub-Chapters divided by subject. Generally, the thesis structure works to focus from a top-level contextual frame, to granular, tangible contributions to knowledge. Chapter 2 – Research Context provides an overview of the patient-specific device stakeholders, their environments, and their unique requirements. It describes this through institute and collaborator experience, and through making reference to news reports and the academic literature. Indeed, it identifies key themes for proper consideration in the literature. Chapter 3 reviews that literature on a pragmatic narrative basis, organised by those themes. It establishes strengths and weaknesses of previous work, and identifies specific gaps which can be, and are addressed by this and future

research. Chapter 4 describes and justifies the research methods – from a philosophical level, down through conceptual frameworks, research questions, data collection tools, procedural details, and ethics precautions. Chapters 5-7 present the results from the data collection activities prescribed by Chapter 4. These are mostly from primary investigations, though Chapter 6 does include a crucial supplementary systematic literature review amongst its contents. Chapter 8 discusses and synthesises the findings through the frames of intervention success, research validity, and then presents an updated conceptual framework. Chapter 9 summarises conclusions from this research – and points towards specific future work which is desirable for enhancing and expanding both the conceptual framework, and the intervention itself.

1.2. Centre for Applied Reconstructive Technologies In Surgery (CARTIS)

A formalised research partnership exists between PDR (the institute) and the two largest local hospitals. The Centre for Applied Reconstructive Technologies In Surgery (CARTIS) was established in 2006 with the aim of generating world-class research outputs and improvements in clinical practice. It combines the technical, design, and academic research expertise of the institute; with the clinical, artistic, and prosthetic expertise of the Maxillofacial Laboratory at Morriston Hospital (Swansea, UK) and the department of Oral and Maxillofacial Surgery at the University Hospital of Wales (UHW) (Cardiff, UK).

This collaboration has several benefits for the partner organisations: formal and informal knowledge exchange and consultancy; grounding research activity in pragmatic real-world scenarios (Whitaker, 2014); mutual dedication of resources to developing funding bids and dissemination; and reciprocal access to observe clinical and design engineering contexts respectively (Figure 2). The latter point was strengthened at the beginning of this research with honorary employment for institute staff at Morriston Hospital and, by extension, in the Welsh NHS (Appendix 12). This was significant – it provided, at a procedural level at least, unrestricted access to laboratory and surgical observation (and the associated clinical staff). As such, the majority of the data collection for this research was carried out with local clinicians and local facilities. This was in line with the resource and time constraints of this work, though wider UK and global contexts were identified as being highly desirable routes to developing the content and validity of this work in the future.

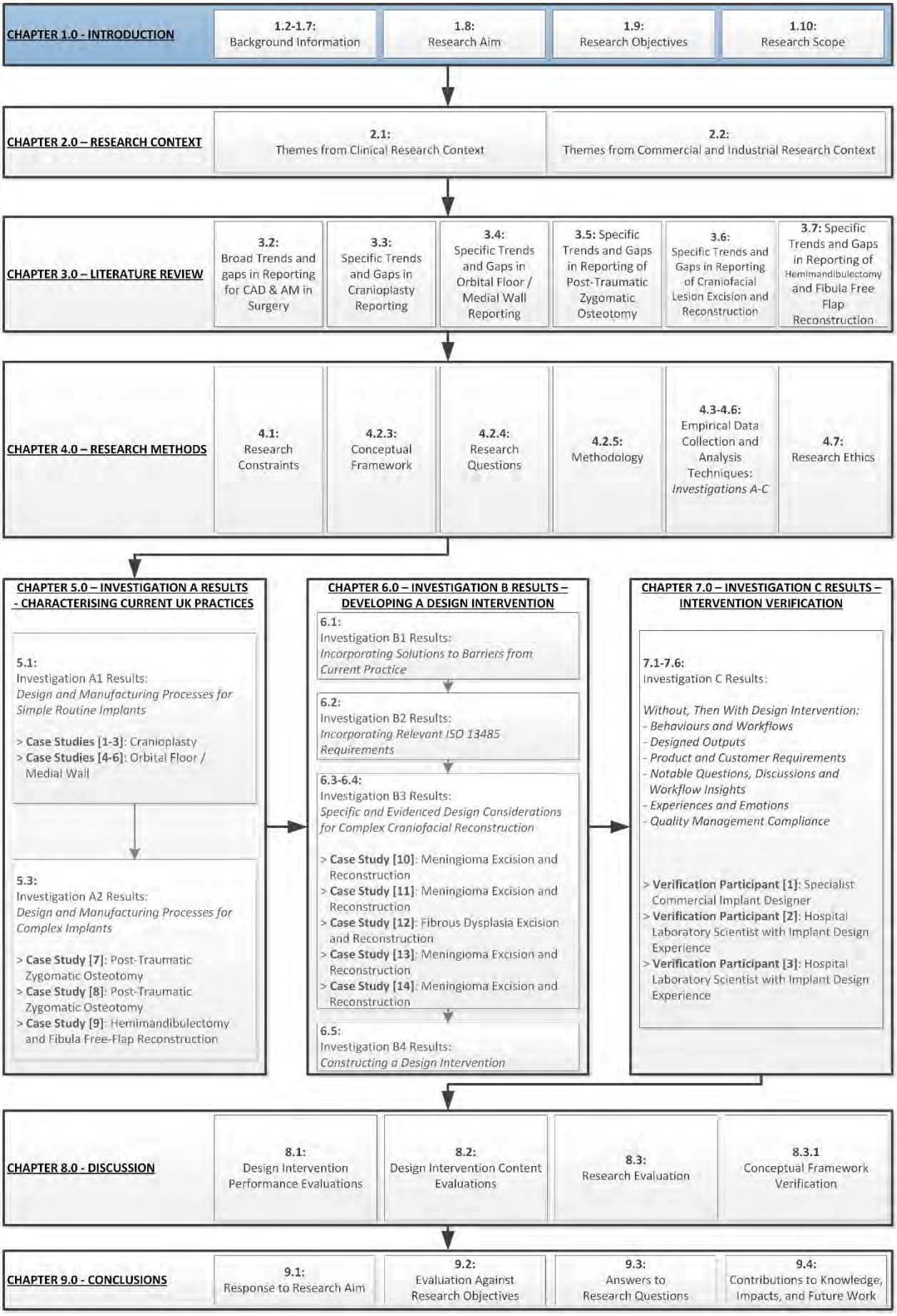


Figure 1 - Thesis Overview, With Current Location Highlighted (Chapter 1)

Figure 2 - CARTIS Collaboration In-Theatre at Morriston Hospital

1.3. Additive Manufacturing (AM)

AM has, over its lifetime, also been known as Rapid Prototyping (RP), 3 Dimensional Printing (3D Printing), and Solid Freeform Fabrication (SFF) as catch-all terms for the technique. Said technique encompasses a wide range of established, obsolete, and emerging sub-processes based on different methods of adding material to a platform in a layer-by-layer fashion to produce prototype or end-use parts. Qualities of each AM subset are easiest to describe in relation to one another. Generally, the major sub-categories represented over the institute's history and in the medical device design literature were, for polymers: vat polymerisation; material jetting; powder bed fusion; and material extrusion; and for metals: Selective Laser Melting (SLM); and Electron Beam Melting (EBM). Both of which are types of powder bed fusion with different energy sources. A range of alternative proprietary names exist for these over-arching processes; and competing manufacturers offer variants of each process (with the exception of EBM which is exclusive to ARCAM, Sweden). However, for clarity, this

work always related proprietary variants and names back to the headline terms listed above. Furthermore, many other AM processes exist and are occasionally featured in the literature – including brand-new, potentially transformative processes like CLIP (Carbon, 2017) but they did not have the same vast bodies of evidence for technical and clinical efficacy as the long-established processes identified above.

Each of these processes works by slicing a virtual model of the designed part into many layers, before depositing, hardening, or melting physical material in sections matching those layers. Support is provided to the structure as building progresses by either a scaffold-like structure of the same material, or by enveloping the part in a dissimilar material with a view to subsequent removal. Repeating this process on successive layers builds-up a solid artefact replete with any internal details and features which could not otherwise be fabricated economically – such as undercuts. This unique ability, in parallel with eliminating the need for expensive tooling, makes AM well-suited to producing one-off patient-specific surgical devices (Bibb et al., 2015). Rehabilitative and protective custom devices have also explored these characteristics – with promising outcomes for wrist splinting (Paterson, 2013, Paterson et al., 2015), protective face masks (Cazon et al., 2014), sports gloves (Harte and Paterson, 2017), orthoses (Pallari et al., 2010), and prosthetic limb sockets (Rogers et al., 2000).

AM's remarkable ability to produce complex geometries can sometimes lead to an underestimation of the role of design for manufacture. Careful consideration is still required, even in the absence of traditional factors like positioning casting split lines. For AM, important design factors centre on optimising build orientation and support structures for accuracy, build volume efficiency, and surface finish (Bibb et al., 2015). However, the term 'rapid prototyping' is misleading – especially compared to casting or moulding; AM is relatively slow on a per-part basis. Production timeframes relative to off-the-shelf implant availability was a notable theme in the literature review.

Many parameters determine the properties of the finished solid part: such as the thickness of a single layer; and the rate of deposition, extrusion, hardening, or melting across each individual layer. Further specific technical parameters must be fine-tuned for any given process – but they are not the focus of this research, as previously discussed. This sub-Chapter briefly characterises pertinent AM processes to the degree necessary for contextualising the work. In general, technical efficacy was, reasonably, taken as a pre-

requisite for consideration of a technology. In day-to-day operation, all industrial machines, office-based machines, and consumer-grade machines require careful supervision and regular maintenance. Maintenance costs and proprietary material costs are critical factors in determining the viability of an AM service, and can be overlooked without thorough consideration (Pucci et al., 2017, Christensen and Rybicki, 2017).

1.3.1. Application of AM to Surgery

The technical efficacy and clinical benefits of fabricating medical models from Computed Tomography (CT) scan data were recognised in the 1990's (Mankovich et al., 1990). Models have since been used for communication with patients (Petzold et al., 1999), for planning and rehearsing surgical procedures (Kermer et al., 1998), as jigs forming the basis of manually carved reconstructions in wax or clay (Hughes et al., 2003) and for pre-shaping off-the-shelf reconstructive plates (Kernan and Wimsatt III, 2000). They are regularly used, widely accepted and have been integrated as essential elements into modified versions of conventional device workflows such as for cranioplasty implant fabrication (Bartlett et al., 2009).

As an extension to medical modelling, CAD tools have been used to manipulate and correct virtual models of defective bony anatomy, with the resulting physical models regularly used as jigs for lab-based implant fabrication (Winder et al., 1999). Additionally, their use has extended to directly designing mould tools for soft-tissue prostheses to shorten the patient's time in-clinic and reduce costs (Eggbeer et al., 2012).

Olszewski et al. (2010) used computer software programs to successfully define optimal bone, cut and fixation positions; increase the predictability and accuracy of surgical outcomes; and reduce the duration of theatre time. Anticipating pitfalls, optimising plans and sequences through multiple iterations, and mentally preparing the surgeon through imagery, were all key results of planning likely to contribute to that theatre efficiency metric (Steinbacher, 2015). Taken together, these factors represented the sum of typically cited virtual planning benefits, with some authors going further and justifying their claims by validating the accuracy of surgical results against planned intent (Metzger et al., 2007). The high degree of process complexity

(from evaluating scan data, integrating multiple components, and choosing from continuous repositioning alternatives) suited the CAD-driven approach well. Drawbacks almost always revolved around high costs (Li et al., 2016, Ganry et al., 2017, Tarsitano et al., 2016, Mazzoni et al., 2015) and extended planning and delivery times (Kirke et al., 2016, Mazzoni et al., 2015, Martelli et al., 2016).

Translation of those plans to the physical reality of the operating theatre has been achieved via patient-specific surgical guides (referred to as Patient-Specific Instruments (PSI's) at times). Guides interface with both the patient's anatomy and the surgeon's tools or hands to control: drilling location (Bibb et al., 2010); drilling angles (Vrielinck et al., 2003); saw cutting vectors (Bibb et al., 2009, Foley et al., 2013); the repositioning of bones (Herlin et al., 2011); the stability of residual bones following resection but prior to grafting (Reiser et al., 2015); and the shape of auto-grafts themselves (Soleman et al., 2015).

Usually following-on from digital surgical planning, those documented benefits enabled by printing (or occasionally still machining) patient-specific implants, were numerous, significant, and well-established. Relative to conventional custom or batch produced stock implants, they have been shown to have: achieved a more accurate fit with better stability (Kim et al., 2017); resulted in better functional outcomes (Sanna et al., 2017); resulted in better aesthetic outcomes despite extra constraints (Goodson et al., 2017); reduced theatre time (Shuang et al., 2016); reduced the likelihood of needing surgical revisions (Singare et al., 2009); decreased stress shielding (artificially lowered stresses around the implant site leading to bone remodelling) (Harrysson et al., 2008); avoided limb amputations (Hsu and Ellington, 2015); increased the safety of procedures for theatre staff (Rana et al., 2015b); incorporated tailored mechanical properties (Parthasarathy et al., 2011); resolved the most complex and non-standard defects (Wyatt, 2015); and improved osseointegration where desired (Palmquist et al., 2011). Additionally, positive secondary effects could be reasonably inferred; such as reduced infection risks and blood loss (Lethaus et al., 2012a), and accelerated recovery (Levine et al., 2013).

1.3.2. Specific Characteristics of Relevant Technologies

1.3.2.1. Polymer – Vat Polymerisation (SLA)

The standardised term for this process is vat polymerisation (British Standards Institution, 2017a). However, it is more commonly known in the clinical design literature by its commercial name of StereoLithography Apparatus SLA (Figure 3). It was developed in the 1980's and represented the first commercial AM technology (3D Systems, 2017). It builds parts by using a laser to harden layered profiles on a metallic bed submerged slightly in a vat of photo-sensitive epoxy-based resin. Its support structures are built from the same material and must be removed manually following build completion (Figure 4). There are a vast array of materials available for this process – including those which have been tested and validated by the FDA as being suitable for producing intra-operative transient use devices (Bibb et al., 2015).

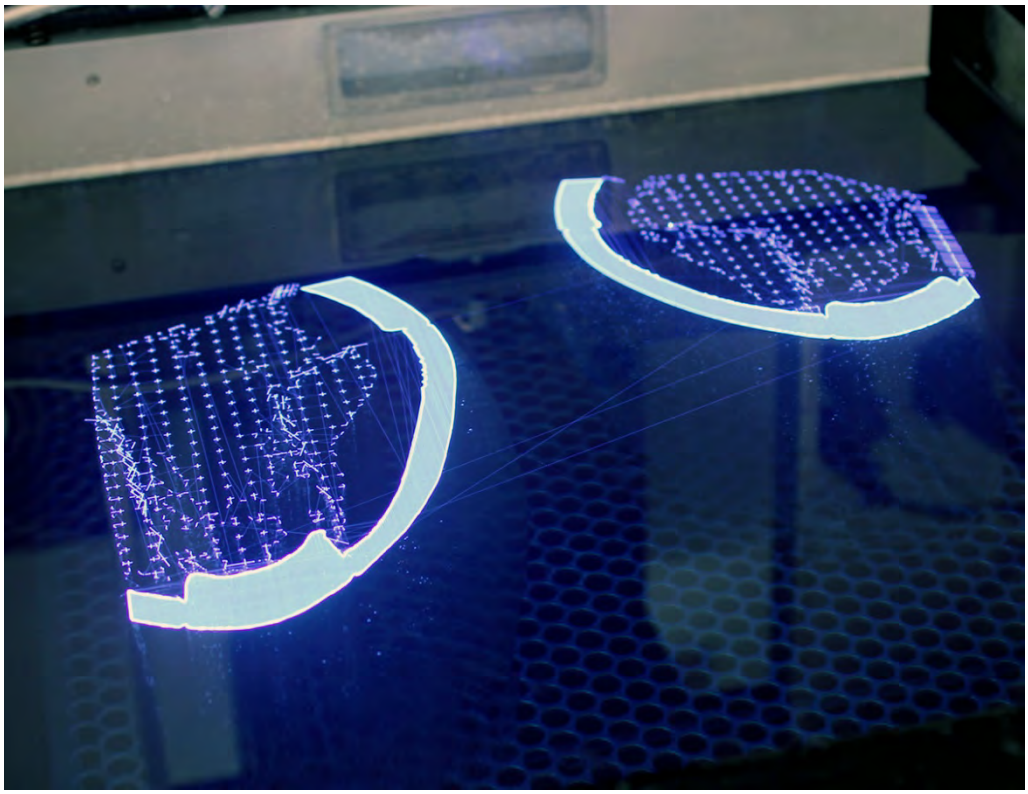


Figure 3 - Institute SLA Mid-Build

Of further benefit to clinical applications is the availability of transparent materials – which allow clear views of internal anatomical structures in models, or the underlying anatomy in guides, and which can be precisely and selectively coloured (by scanning the laser across the resin multiple times) to highlight critical features (Erickson et al., 1999). However, SLA is usually an expensive, industrial, relatively messy process – not easily situated in an office or otherwise sensitive environment. Finished parts require washing clean of any excess resin with isopropanol. The latest generation of consumer grade machines feature small-format vat polymerisation amongst their ranks (Formlabs, 2017b) which may serve to lower some of these hurdles.

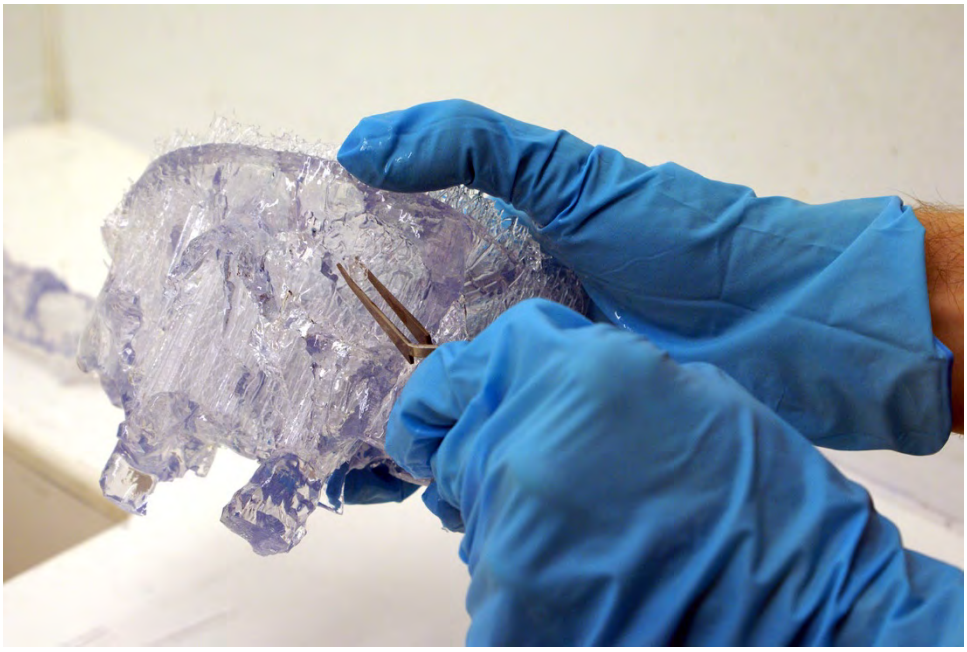


Figure 4 - Manual Removal of SLA Supports

1.3.2.2. Polymer – Powder Bed Fusion (SLS)

The standardised term for this process is powder bed fusion (British Standards Institution, 2017a). However, it is more commonly known in the clinical design literature by its commercial name of Selective Laser Sintering (SLS). SLS has been applied to surgical guide production (Leiggener et al., 2009) and to build medical models (Mazzoli, 2013). It works by using a laser to bind together polymer powder substrate on top of a build plate (ibid). Parts are supported during fabrication by the un-sintered build material which envelops the emerging

part as the build platform lowers through the chamber. While this means that support structure removal is eliminated as a post-processing step, special care must be taken to remove all of the un-sintered powder from the part.

SLS limitations focus mainly on build times – it is a process which requires significant warming of the build chamber prior to fabrication and subsequent cooling upon completion (Bibb et al., 2015). It is usually a comprehensively industrial and expensive process without the ability to selectively colour areas like with SLA, and with a more limited feature resolution. However, like SLA, some lower price (though not quite consumer-level) machines are beginning to emerge (Formlabs, 2017a). Materials range from polyamide, to polystyrene, polypropylene and polycarbonate (Mazzoli, 2013). Transparent materials and selective colouring are not an option for SLS.

1.3.2.3. Polymer – Material Jetting

Material jetting works much like a 2D printer – using a print-head to selectively jet liquid droplets of material across a flat profile. The platform then moves down, or the print-head up, to commence the next layer – but not before UV lamps solidify the previous slice (Bibb et al., 2015). The process can deliver multiple materials across one build – including mixing some basic components in the print head to vary the colour or the shore hardness of the part (ibid). This material variability is primarily exploited for support structure purposes – with either a jelly-like substance, or a wax-like substance used to envelop the part while it builds (Figure 5). Those support materials must be water jetted or melted away, respectively, before the finished part can be used.

Materials suitable for transient surgical use are an option, however they are not necessarily the cleanest materials when compared to other AM processes (O'Malley et al., 2016). This might be attributable to contamination from the dissimilar support material. This is pertinent – because mid-range, office-based machines with medium to large build envelopes are, along with low-end consumer-grade material extrusion machines, one of the technologies most often purchased by hospital laboratories (at least in the experience of the institute).

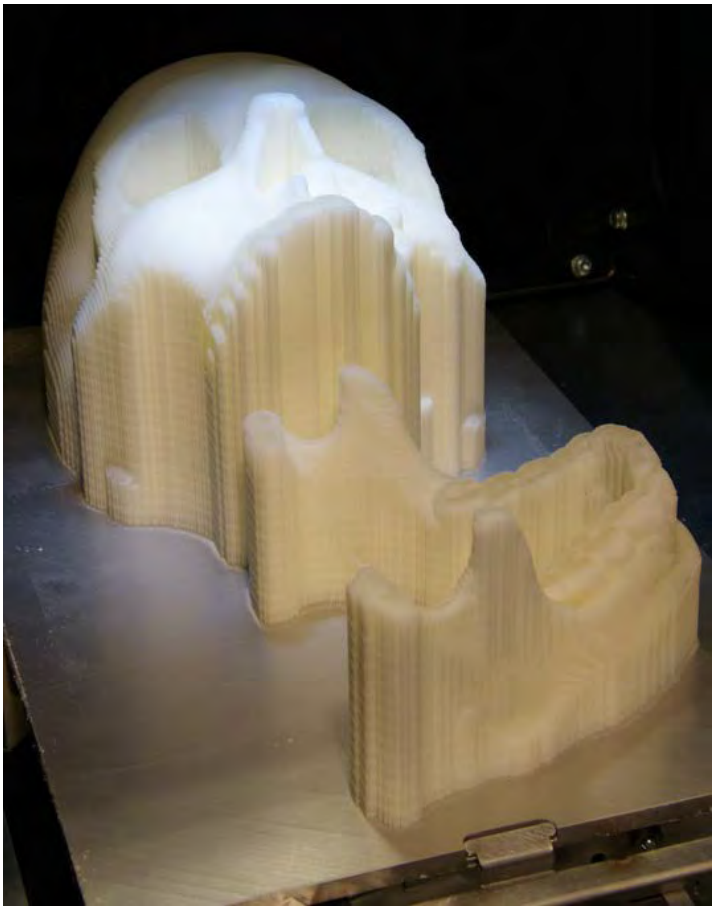


Figure 5 - Wax Support Structure on ProJet (3D Systems, USA) MJP Printer

1.3.2.4. Polymer – Material Extrusion (FDM)

The standardised term for this process is material extrusion (British Standards Institution, 2017a). However, it is more commonly known in the clinical design literature by its commercial name of Fused Deposition Modelling (FDM). FDM has been used to produce models and surgical guides (Sohmura et al., 2009) using materials which are validated for transient surgical use – such as ABS. The process works by extruding a bead of polymer material across a platform to draw a given layer of a part. The build platform then moves down, or the extruder head up, before commencing with the next layer of the artefact. Support structures can be of the same build material or of a soluble material from a separate extruder head. They are removed manually, sometimes after being softened by soaking where the latter applies. Intra-layer strength can be lower than the other highlighted processes in this sub-Chapter and the surface finish compromised by a relatively large 'stair-step' effect (Bibb et al., 2015).

Patents on the industrial FDM process were amongst the first to expire – yielding an influx of the very first consumer-grade AM machines in recent years. These have been used to produce patient-specific surgical devices (Huang et al., 2015) but it is not clear if this was undertaken responsibly, by adhering to regulatory requirements and appropriate quality standards. For basic anatomical models, low-cost consumer-grade FDM machines can be entirely appropriate tools based in a hospital unit (Chae et al., 2015, Eley, 2017). However, in the institute's experience, albeit with a limited number of the myriad available options, these low end machines can be less reliable and require greater supervision than industrial printers. These factors must be weighed against the lower machine costs and very-low material costs.

1.3.2.5. Metal – Powder Bed Fusion (SLM)

The standardised top-level term for this process is powder bed fusion (British Standards Institution, 2017a). However, it is more commonly known in the clinical design literature by its commercial name of Selective Laser Melting (SLM). SLM is a metal AM process – most often using Ti6Al4V ELI powder as the build material, where the production of implantable devices is concerned. Titanium is an inert material, long-established as being biocompatible (Breitbart and Ablaza, 1997). The SLM process works by using a laser to melt metallic powder grains together in an inert atmosphere. Like the other processes, profiles are created on a layer-by-layer basis. The build plate moves down by one layer – and fresh powder is automatically deposited across the existing partial structure by a sweeper blade. Support structures are constructed using the same material as the main body of the part – and must be designed with extra care because of the high temperatures involved in the melting action. Dissipating that heat in a controlled and deliberate way through the structure is essential for preventing cracks and deformations resulting from concentrated thermal stresses, such as in Figure 6. Support structures (Figure 7) are removed manually – using cutting discs because of the strength of the material relative to polymer scaffold-style supports which can often be snapped away by hand.

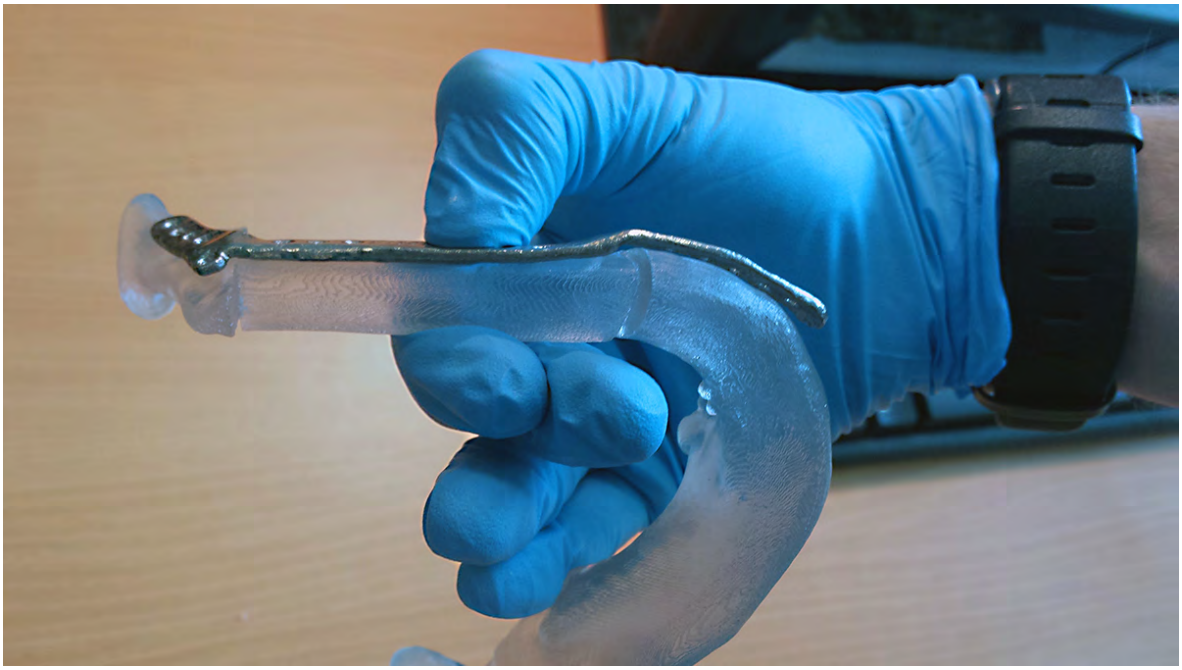


Figure 6 - Deformed Mandible Implant

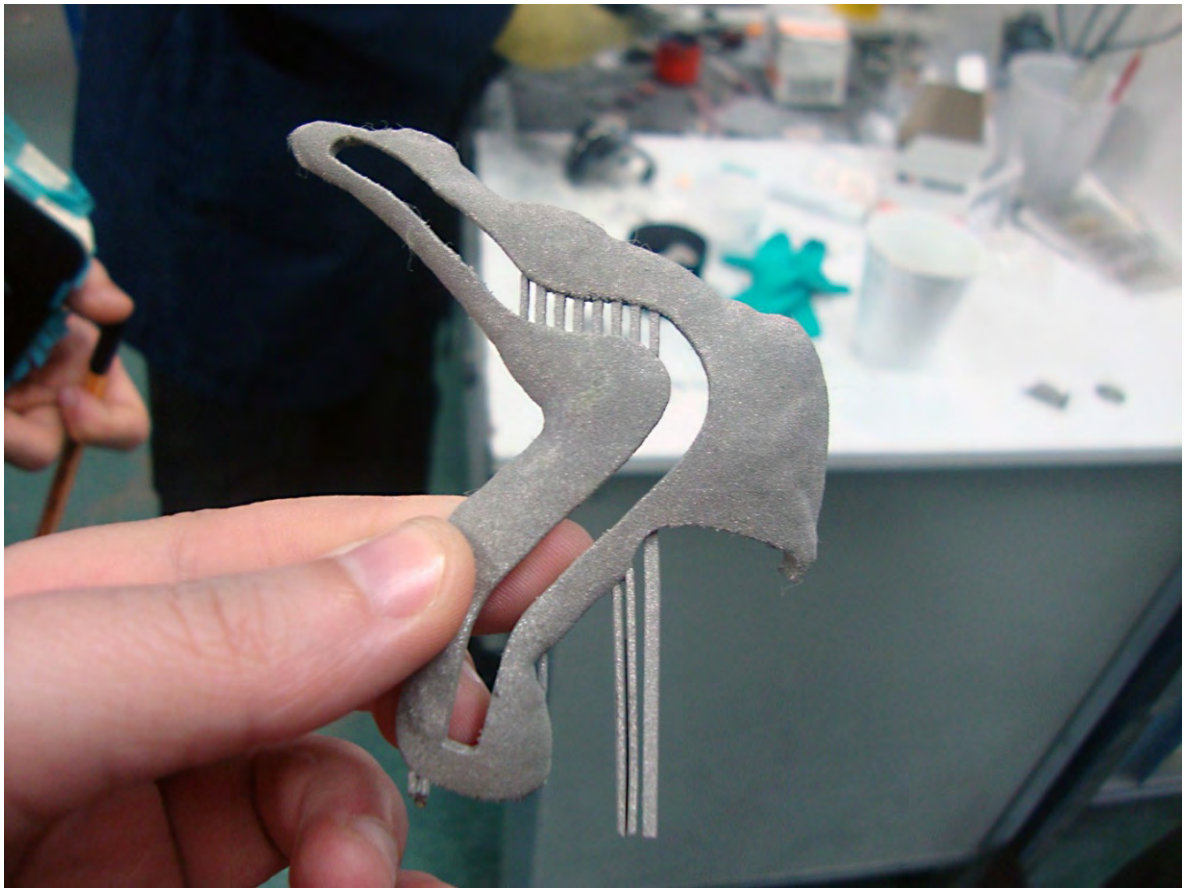


Figure 7 - SLM Part with Residual Supports

Relative to EBM (summarised below), SLM is generally better suited to producing parts with fine details and which require smoother surface finishes (Bibb et al., 2015). This is mostly attributed to SLM's smaller minimum strut thickness feasibility. This potentially gives SLM another advantage over EBM in the production of porous lattice architectures; where implants incorporate a deliberately manipulated macro porosity to improve osseointegration. Being able to build smaller individual cells comprising intricate cross-struts as part of their architecture can increase design freedoms in scenarios where they have been narrowed, by a choice to pursue stretch-dominated cell designs, like tetrahedron and octet topologies (Arabnejad et al., 2016). Macroporosity and microporosity, in parallel with osseointegration and osseoinduction were notable themes in the literature – as highlighted in Chapter 3. These themes are usually most relevant for orthopaedic applications – so consideration was also given to transferrable findings from those specialties.

Grit blasting can be used to provide an intermediate finish between 'as-built' and highly polished. It represents one method of creating a microporosity, alongside etching and plasma coating with hydroxyapetite (HA) (Perez and Mestres, 2016). Conversely, high speed manual polishing tools (Figure 8) are deployed, where a mirror-like surface finish is desired; this can be a slow process, and care must be taken not to polish away too much material – particularly in thin areas. The institute and collaborators often thicken part geometries by a uniform amount prior to building, to allow for material loss during polishing. Implants built using SLM require heat-treatment to achieve suitable toughness for implantable applications (Facchini et al., 2010). Post-processing then, is time-consuming and labour intensive.

Where industrial polymer printers can be prohibitively expensive for achieving routine use, depending on the machines in question, industrial metal AM machines, are uniformly more expensive by an order of magnitude. Moreover, infrastructure requirements for safe material handling and effective part post-processing are significant, and again, demand major investment. The marketplace is expanding, with the very recent emergence of office-based meal AM machines like the Metal X (Markforged, 2018) and the Desktop Metal Studio

System (Desktop Metal Inc., 2018). However, they have not been validated for surgical applications.

Figure 8 - Manual Polishing Set-up at Renishaw PLC

1.3.2.6. Metal – Powder Bed Fusion (EBM)

The standardised top-level term for this process is powder bed fusion (British Standards Institution, 2017a). However, it is more commonly known in the clinical design literature by its commercial name of Electron Beam Melting (EBM). EBM works on a similar basis to SLM but with two major differences. An electron beam is used in place of a laser for melting the powder grains together, and it takes place in a build chamber which is pre-heated to 80% of the build material's melting temperature (Moiduddin et al., 2017). A drawback of this is longer warm-up and build cooling times relative to SLM, but the major benefits come from increased build speeds and lower thermal stresses in the parts (Luca et al., 2009). As such, EBM is better suited to producing larger parts than SLM. Likewise, heat-treatment is not required as a post-processing stage in order

to achieve sufficient strength and toughness for implantable components. This has, in the institute's experience, saved up to a day of post-processing time. EBM surface finishes are though, as highlighted above, considerably rougher than SLM – with features (such as screw holes) requiring more intensive post machining to ensure functional requirements are met (Bibb et al., 2015).

1.4. Subtractive Machining

The PolyEther Ether Ketone (PEEK) implants designed by the institute (and those offered by major international companies) are fabricated by conventional subtractive Computer Numerically Controlled (CNC) machining. This can also apply to patient-specific titanium implants; including some from KLS Martin (KLS Martin Group, 2017). CNC machining as a general manufacturing process has a longer history than the still-developing applications of AM. This is despite its application to maxillofacial implants being first reported by Scolozzi et al. (2007). This relative lack of modernity for the process, if not the application, may partially account for the use CNC fabrication being unreported. Instead, this fact must be inferred from clinical reports; by looking at the material choice and the shape of the implant. For example, CNC fabrication in (Scolozzi, 2012) is the logical deduction from the use of PEEK and the relatively complex geometries involved. More surprisingly, Rudman et al. (2011) incorrectly stated that PEEK implants were able to be produced using the SLA process.

In light of this sparse reporting, it is unsurprising that there were no mentions found of precise technical details in the clinical literature; such as machine type, cutting tool choices, work piece dimensions, feed rates, cutting speeds, or use of specific lubricants. However, some universal considerations can be discussed based on general principles.

This fabrication process adds design constraints to the creation of implant geometries. It requires the consideration of cutting tool access to the work piece for machining features (van Noort, 2012), meaning that unlike AM, internal void details or highly complex surface forms are not achievable (Bibb et al., 2015). The minimum achievable thickness of the patient specific device is larger. For example, whereas the minimum implant thickness in the institute's practice for AM titanium is 0.3mm, the minimum thickness for PEEK is 3.0mm; with both of those design rules based on guidelines from

manufacturing and marketing entities for the respective materials. Other fundamental CNC factors for consideration include: using chamfers where possible in place of radii; ensuring the work piece can be clamped to the machine bed; complexity limitations related to standardised cutter profiles and sizes; and similar limitations resulting from restrictions on work piece orientation (Swift and Booker, 2003). Some of these limitations can be mitigated by the most sophisticated CNC machines which operate in five or six axes (as opposed to the more usual 3). These machines can achieve a greater degree of complexity, by introducing multi-directional tool access via additional rotational axes (Jywe et al., 2012, Cheng et al., 2005). These extra dimensions can be incorporated through the table to which the work piece is clamped, through the spindle head, through the column to which the spindle head is attached, or through a combination of these (ibid). However, this comes at the cost of more complexity in toolpath planning and setup (Zhao et al., 2013a) and high machine costs

By virtue of the use of PEEK, rather than the process of machining, design freedoms are also curtailed regarding the relative ease with which tailored macroporosities can be incorporated into parts. PEEK can accept sprayed surface finishes which create surface microporosities to improve osseointegration (Walsh et al., 2015), but have a reduced range of possibilities for novel unique surface features (such as those demonstrated by Harrison et al. (2014)) to achieve the same purpose.

Though they were not the primary focus of this research, the additional factors arising from the comparisons between digitally designed AM implants, and digitally designed CNC machined implants, were important to note. Of similar importance is the issue of cost. PEEK implants are more expensive than similarly sized titanium equivalents (Peel et al., 2017). This is to be expected because of the higher cost of the PEEK material relative to titanium. Additionally, the process is material inefficient – with significant waste (Swift and Booker, 2003, Bibb et al., 2015) and more labour-intensive machine setup for more complex shapes (Bibb et al., 2015). These factors generally outweigh the benefits of lower capital expenditure on machines, and smaller post-processing burdens (Swift and Booker, 2003).

1.5. Medical Imaging

Three imaging modalities were of relevance to this research. Of those, two were key and were involved directly: Computed Tomography (CT) and Cone Beam Computed Tomography (CBCT). Magnetic Resonance Imaging (MRI) was only a peripheral issue, because of its occasional appearance in publications relating to this field. MRI data were not used in this research. Other imaging modalities feature very rarely in the published literature relating to CAD, AM, and surgical applications, such as: optical surface scanning (Kittur et al., 2012); X-rays (Shapií et al., 2012); and ultrasound (Vaezi et al., 2012). However, they are not commonplace because of, respectively: being restricted to capturing skin contours; being in two dimensions; and being of a low resolution. Accordingly, these and any other scanning or imaging tools were deemed not relevant to this work.

1.5.1. Computed Tomography (CT)

CT scans have been used in medical modelling since the origins of the technique which exploited subtractive machining (Mankovich et al., 1990). CT scans are essentially a series of consecutive X-rays taken at pre-defined increments through the anatomical region of interest (Bibb et al., 2015). Individual scan slices generally have a resolution of 512x512 pixels and is stored in the Digital Imaging Communication in Medicine (DICOM) format (ibid). Scans show greyscale pixels – with bright white being the densest tissue, and black being air. CT is more effective at capturing hard tissues than MRI and is the modality most often encountered by the institute.

Scan-data processing software works by allowing the user to threshold pixels according to their density (measured in Hounsfield Units) and then copy all adjoining pixels to a new mask or layer. In this way, through pre-set default values, manual adjustment, and editing individual data slices, particular structures and tissues of interest can be segmented. This can be assisted by, or be prior to, volumetrically rendering those attached 2D pixels into 3D pixel-based (voxel) representations of the underlying data. From that stage, STereoLithography (STL) format files can be

exported for transferring virtual models of segmented scan-data to surgical planning or design software tools.

Drawbacks of CT scans centre mainly on potential harm to patients. CT scans deliver radiation doses which are substantially higher than conventional radiography – and can contribute to the development of cancers (Smith-Bindman et al., 2009). As such, they must be used selectively, in line with ethical considerations. This has impacted some institute projects in the past – when compromised scans (comprising a low number of slices, a too-large slice distance, or with only partial coverage of the region of interest) have had to be used in place of re-scanning. Another critical drawback is related to NHS funding issues as addressed by sub-Chapter 2.1. This factor can manifest as limited scanner capacity and therefore delays. Finally, soft-tissue definition is poor and a CT dataset can require supplementary MRI information where good definition for all tissues is required.

1.5.2. Cone Beam Computed Tomography (CBCT)

CBCT scans work on the same general basis as CT scans, but with a smaller field of view, and lower radiation doses (Ludlow and Ivanovic, 2008). They are physically smaller machines and are becoming increasingly prevalent in NHS oral and maxillofacial surgery units – including in CARTIS partner institutions - because of their lower costs relative to full size CT scanners. Generally, they are used to capture information about the tissues of the head and neck. However, there are significant drawbacks to CBCT scans – related to scan-data processing. The greyscale values vary across the slices of an individual scan (Bibb et al., 2015). This can lead to much longer segmentation times at the institute – as global Hounsfield unit thresholding values must be manually adjusted locally throughout the scan. Noise artefacts are the other major barrier to speedy segmentation – requiring similar local thresholding activities to mitigate (ibid).

1.5.3. Magnetic Resonance Imaging (MRI)

As mentioned, MRI scans are rarely encountered by the institute, and do not feature in the new data presented in this thesis. However, its applications are occasionally relevant to this research and are highlighted by the literature review in Chapter 3. MRI imaging works by detecting the energy which is released by atoms in the body after they have been temporarily re-aligned by radio waves affecting their magnetic field (Bibb et al., 2015). The resulting images are greyscale, with bone and air being black, and fat being bright white because of high water content (ibid).

Whilst generally being poor at imaging bone, specific research into custom algorithms has been undertaken to obtain usable results (Eley et al., 2014) though this is not the norm in the maxillofacial field. The MRI scans processed by the institute have contained a small number of slices, with a large distance between those slices making accurate bone contour representation difficult. MRI does not deliver a radiation dose but is not compatible with some patients who have existing metallic implants – due (obviously) to the magnetic field. Images can be co-registered with CT datasets to create fuller, more accurate virtual models of more tissue densities (Daisne et al., 2003).

1.6. Relevant Bodies, Regulations, and Standards

For the UK NHS and its procurement of medical devices, the key regulatory stakeholders are the European Commission, the Medicines and Healthcare products Regulatory Agency (MHRA), the International Organization for Standardization (ISO), the British Standards Institution (BSI), and the National Institute for Health and Care Excellence (NICE) – at least in an advisory capacity on best practice. The European Commission (EC) proposes and enforces legislation, including regulations, via its political leadership and its permanent staff which is arranged into specific policy areas (European Union, 2018a). After adoption as European Union (EU) laws via the European Parliament and the Council of the EU (European Union, 2018b), the regulations are enforced in the UK by the MHRA (Medicines and Healthcare products Regulatory Agency, 2018a). Regulatory compliance is legally mandatory and aims to ensure safety. On the other hand, international standards – the adherence to which can in some instances be a

component of regulatory compliance, are nonetheless themselves voluntary (Standardization, 2018). They are formulated by the membership of the ISO, which comprises 161 national standards bodies, to ensure globally consistent quality and efficiency in addition to safety (ibid). BSI represent the UK at the ISO, and are appointed by the UK government as the national standards body – responsible for publishing standards in the UK (British Standards Institution, 2018). Separately, and non-exclusively, BSI provide assessment and certification services to organisations as a notified body (Medicines and Healthcare products Regulatory Agency, 2018b).

Consequently, medical devices marketed in the UK must meet the requirements of the Medical Device Directive (The Council of European Communities, 1993). The critical relevant factor for this research is the requirement to produce devices under a suitable recognised Quality Management System (QMS). ISO 13485:2016 is the most recent relevant international quality standard for medical device design and production (International Organization for Standardization, 2016). It should be noted that patient specific devices and services are classed as custom devices – and do not need to be CE-marked as they are intended for single use on a named patient. The following sub-Chapters provide an overview of quality management issues and requirements – relevant to this research.

1.6.1. Key Standard - ISO 13485 Quality Management

ISO 13485 demands a risk-based approach to determining, planning, documenting, deploying, monitoring, and controlling procedures. It aims for continuous improvement of an organisation's processes and products. The institute and this research is focused on the design stages of device development – and as such, will focus on the design-related clauses from the summary of the entire standard provided below in Table 1. An expanded list of requirements can be found (Appendix 1).

This is not to say that design occurs in isolation, given that appropriate constraints must be accommodated from the outset, for either AM or CAM production limitations. Table 1 summarises the relevant aspects of the thirty-six page international standard. Any design intervention must address these requirements, or at least avoid being in conflict with them, to have relevance across different design

contexts - outside of NHS hospitals. The significance of these requirements – even for in-hospital design work – is likely to grow quickly in the short term.

Table 1 - Overview of Relevant Requirements Extracted and Summarised from BS EN ISO 13485:2016

Section of Standard	(Summarised) QMS Requirements
4 – QMS	Document: a quality policy and quality manual. Document: determined procedures; determined forms, and determined records. Establish and maintain a medical device file. Control all documents. Control and maintain records.
5 – Management Responsibility	Evidence top management's commitment. Provide a framework for reviewing quality objectives. Define responsibilities and authorities. Appoint a management representative. Implement management review.
6 – Resource Management	Document process(es) for staff competence and training. Document infrastructure requirements. Document work environment requirements.
7 – Product Realisation	Document process(es) for, and record risk management. Determine and review requirements specified by the customer. Determine product requirements not stated by the customer. Document plans for customer and regulatory authority communications. Document stages including: reviews; verification; validation; and responsibilities assignments. Produce outputs which are verifiable and approved prior to release. Document systematic design and development review. Document appropriate design verification plans. Document procedures for design transfer.

	Document procedures to control design and development changes. Maintain a design and development file for each medical device. Document procedures to ensure purchased product conformity. Create purchasing information template. Document procedures for production. Document procedures for validating processes. Document procedures for product identification and segregation. Document processes for product traceability.
8 – Measurement, Analysis & Improvement	Document procedures for feedback. Document procedures for timely complaints handling. Document procedures for notifying regulatory authorities of complaints. Document a procedure for internal audits. Monitor the QMS processes for effectiveness. Monitor and measure product characteristics. Document a procedure for issuing advisory notices. Document procedures for rework. Document procedures to determine QMS effectiveness. Document procedures for reviewing and correcting nonconformities. Document a procedure for determining and preventing potential nonconformities.

1.6.2. Key Regulation - Medical Device Regulation

Commercial and other non-hospital providers of patient specific devices must adhere to the quality requirements identified above, as a pre-requisite for regulatory compliance. Hospitals in the UK are currently able to design and fabricate devices for their own patients without meeting the requirements of the MDD or being certified to ISO 13485, so long as they are designing and fabricating devices for their own patients. Crucially, this is scheduled to change with the proposed introduction of the Medical Device Regulation (MDR) which is due to supersede the MDD (following a transition period) in 2020 (Medicines and Healthcare products

Regulatory Agency, 2017). The MDR is expected to apply to health institutions as well as manufacturers. Conditional waivers from the requirements may apply, however these conditions include establishing an appropriate QMS (ibid).

As hospitals increasingly adopt digital tools and techniques themselves, they will be required to meet the same standards as external device suppliers. Furthermore, manufacturers cannot rely on customer prescription alone to justify design decision-making. Clinical evidence, generated through post market clinical follow-up is required to support design approaches, either through clinical evaluations or clinical investigations (European Council, 2017). Those evaluations must be ongoing and are subject to review by notified bodies (ibid). The extent and fidelity of clinical evidence for (or against) patient-specific AM or CAM devices, will therefore be of increased significance in the short term and beyond.

1.6.3. Other AM Standards

At the time of writing, there were seven other *current and published* international standards related to AM more generally (International Organization for Standardization, 2018). Their UK implementation and publication is addressed by the British Standards Institution (BSI). They are identical to, but supersede the numbering of, the international standards. Briefly, they address:

- use of terminology for AM, via BS EN ISO/ASTM 52900:2017 (British Standards Institution, 2017a);
- use of terminology for AM with co-ordinate systems and test methodologies, via BS EN ISO/ASTM 52921:2016 (British Standards Institution, 2016d);
- AM file format, via BS EN ISO/ASTM 52915:2017 (British Standards Institution, 2017c);
- requirements for purchased AM parts, via BS EN ISO/ASTM 52901:2017(British Standards Institution, 2017b);
- process categories and feedstock, via BS EN ISO 17296-2:2016 (British Standards Institution, 2016a);
- main characteristics and corresponding test methods, via BS EN ISO 17296-3:2016 (British Standards Institution, 2016b);

- and data processing, via BS EN ISO 17296-4:2016 (British Standards Institution, 2016c).

This research is focused on the design workflow for patient-specific surgical devices. As such, the findings do not address compliance with these more general AM standards directly. Crucially however, they would be relevant to manufacturing and marketing entities (which may in the future include hospitals themselves); when fabricating and selling designs which might be produced as a result of the conclusions from this research.

1.7. The Design Process

The design process as conventionally characterised is driven, constrained, and measured by an iteratively developed product design specification; which is formulated from the design brief – a statement of need (Pugh, 1991). The core design stages progress through: market analysis; specification development; concept design; detail design; manufacturing; and selling (ibid).

A product design specification constrains and justifies factors including performance, material choices, safety, time scales, size, installation, market constraints, adherence to established standards, and ergonomics (Pugh, 1991). Increasingly, requirements are formulated on the basis of user-centred design which can include ethnographic studies of end-users to develop a more sensitive understanding of the subject and context (Shove et al., 2007). Indeed, Jordan (2000) advocates the inclusion of formal *and* experiential properties to contribute towards a product benefits specification; with the aim of enhancing the pleasure of the end-user.

Despite these well-established models for the design process, as applied by practicing designers to their specific contexts, it has been under explored in the patient-specific device design context. This is perhaps related to increasingly blurred lines between roles; as surgeons or other clinical staff incorporate the role of product designer into their everyday practice with in-hospital capabilities; such as in Goodson et al. (2017).

1.8. Research Aim

The aim of this research was to identify limitations in patient-specific device design processes, and to evaluate effective routes to overcoming them, towards enabling routine adoption of digitally designed devices.

1.9. Research Objectives

1) To establish an overview of the UK NHS maxillofacial surgery context specifically, and the existing literature more broadly, regarding the clinical, regulatory, technical, social, economic, and political drivers and barriers related to the design and use of patient-specific guides and implants.

2) To identify the predominant methods of maxillofacial patient-specific device design and fabrication in the UK NHS. To characterise them in terms of their practical, economical, and clinical strengths and weaknesses; using observation, reflection on professional industrial practice, and conceptualisation.

3) To specify and prototype a new design process intervention which overcomes the key barriers identified in objectives (1) and (2); towards promoting routine and safe deployment of digitally designed implants and guides.

4) To test and verify the effectiveness of that intervention against current design processes through empirical testing and appropriate research methods. To analyse the extent to which the new or enhanced intervention has been successful and to make recommendations for its future development.

1.10. Research Scope

The wider CAD and AM (or CAM) custom device context includes a multitude of contributing factors which potentially affect the holistic success of this work against its

ultimate over-arching long-term aim; fully enabling routine use of digital techniques in the NHS. This research sought to contribute to this effort, which remains a medium to long-term goal. That goal is likely to be impacted by many non-design-process factors: managerial decisions; structural considerations; the political climate; new clinical drivers and barriers; the evolution of clinician training, and budget constraints. This research however, was strictly focused on effectively intervening into the design process for patient-specific AM or CAM devices. It was concerned with structuring the decision-making of the acting designers; and with the collection, verification, and accommodation of device design requirements.

Although the potential arose for investigating the best routes for users to interact with that design process intervention, factors like software programming, underlying mathematical software functions, or user interface development, were not within the research scope. Their inclusion would not have been practical or reasonable within the constraints of this doctoral thesis and were, in any case, not modifiable for the tools in question. The same rationale was applied to excluding: technical factors or parameters in AM processes; materials science; and specialised design verification routes (like Finite Element Analysis (FEA)) from the research scope.

Naturally then, given that the expertise and experience of the institute and the researcher were concentrated on maxillofacial applications; the scope of this work was deliberately constrained to patient-specific, additively manufactured (with some involvement of CAM), maxillofacial guides and implants. Both 'routine-simple', and 'unusual-complex' surgical procedures were included in the scope for intervention. Those technical and societal factors discounted above were, nonetheless, mentioned in contextual commentary and in the literature review - where they were occasionally relevant to factors which *were* within scope.

Similarly, the case studies presented in this research relied on the software tools and associated hardware available to the institute and to those clinical settings which were observed. This, for example, resulted in a recurrence of reporting on the use of the same CAD software with a novel haptic interface in place of a standard computer mouse input. As will become clear, assuming they were replaced with alternative tools with the same general capabilities, the specific design tools were independent of the phenomena being studied (i.e. the design processes and the designer's role(s) in them).

1.11. Chapter 1 Summary

In summary, Chapter 1 has:

- introduced the researcher and the institute at which this work was based (Chapters 1.0);
- introduced the structure for this document and this research (Chapter 1.1);
- described the relevant research partnership which impacted on the scope and resources of this work (Chapter 1.2);
- described key background information about the fundamental technical issues on which this work is built (Chapter 1.3 - 1.7), and in doing so has contributed to meeting objective 1 from Chapter 1.9;
- stated the overarching research aim (Chapter 1.8) and those research objectives in full (Chapter 1.9);
- and finally, has explicitly defined the research scope, and its exclusions (Chapter 1.10).

2. Research Context

This Chapter (Figure 9) highlights relevant background information about the political, institutional, commercial, and clinical contexts which affected this research - and which influenced the methods selected. It did this in order to identify the key themes from the academic literature which required pragmatic narrative review. Crucially, this step also provided an opportunity to demonstrate, and to explicitly acknowledge the nature of, key background knowledge and assumptions based on the institutes' collective, and the researcher's individual, professional experience. This chapter contributes to meeting objective 1 from Chapter 1.9.

2.1. Clinical Research Context

2.1.1. UK National Health Service (NHS)

An overwhelming majority of patient-specific device design work undertaken by the institute is directly or indirectly for clinicians working within the UK NHS. It was a reasonable constraint to place on the focus of this research. The NHS, as the state provider of socialised healthcare in the UK, is therefore the largest provider of care in the country with only limited uptake of health insurance at a national level (Office for National Statistics, 2017). This health service is one of the single largest employers in the world (Alexander, 2012) and had an annual budget in 2017-18 of £123.7 billion (The King's Fund, 2017b). As a result it has enormous purchasing power, and so when a treatment method, a medical product, or a service is adopted by even a part of this most significant of providers, a barrier to achieving routine adoption is logically removed.

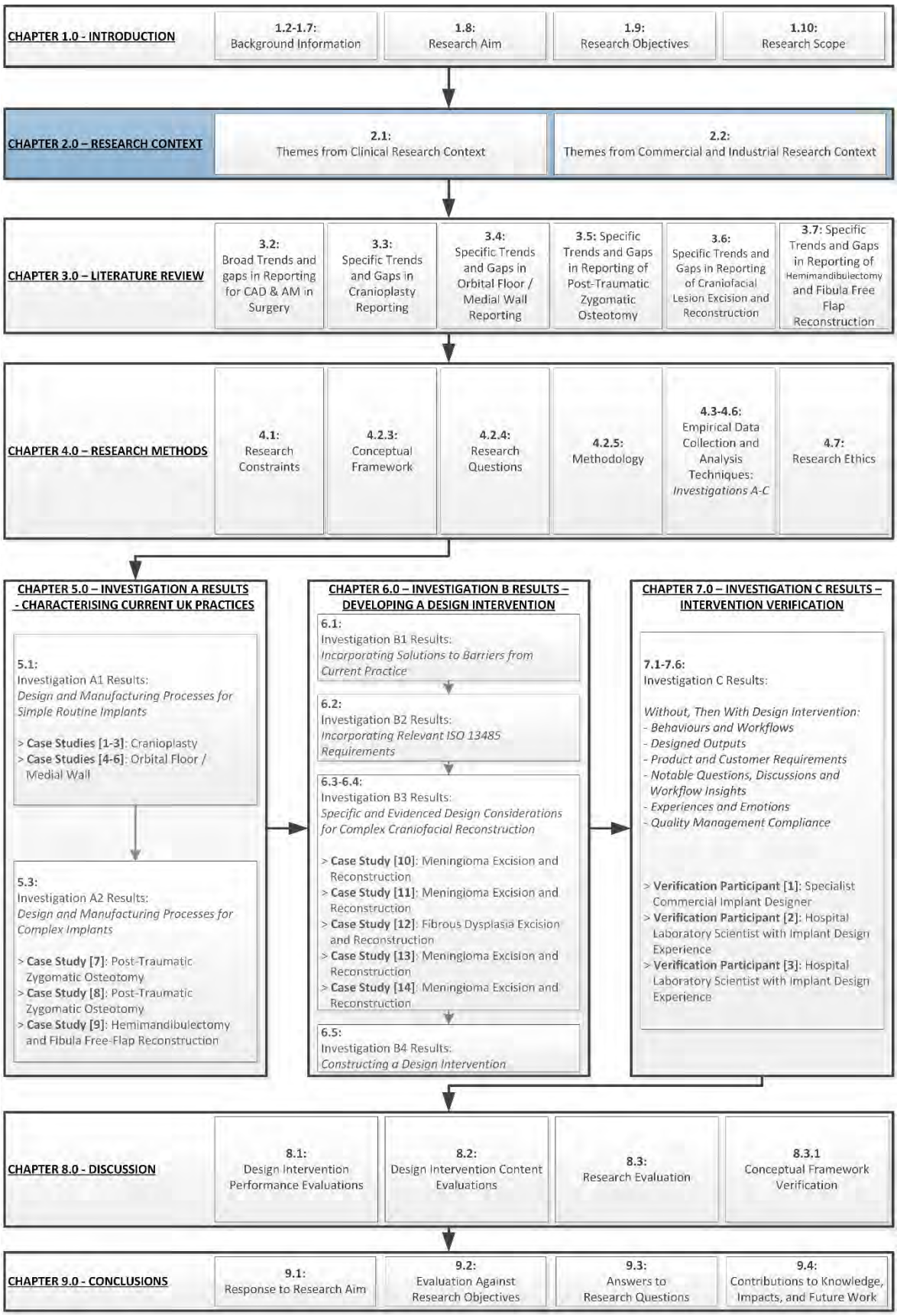


Figure 9 - Thesis Overview, With Current Location Highlighted (Chapter 2)

In 2010, the NHS had its highest public satisfaction rating of 70% - a figure which declined to 63% in 2016 (Robertson, 2017). It has been ranked repeatedly amongst the top ten healthcare systems in the world – in safety, affordability and efficiency (Triggle, 2017). However, it fares poorly in health outcomes (ibid) and is frequently criticised for long waiting times (Robertson, 2017), a burdensome target-meeting culture (The King's Fund, 2010), with underpaid, and stressed staff (Limb, 2015). Many criticisms stem from funding restrictions (The King's Fund, 2017b) which are described in sub-Chapter 2.1.1.2 below. Cost pressures are the major theme in NHS analyses, and in many academic studies about barriers to increased use of CAD and AM / CNC devices.

2.1.1.1. Origins and Development

The NHS was founded by the post-war Atlee government of 1948. It was built on the principle of healthcare being delivered free, at the point of use, to anybody in the population who required it (Campbell, 2016). Indeed, the secretary of state for health had, until 2011 reforms, a legal responsibility for ensuring these provisions were delivered (Pollock and Price, 2011). This was in contrast to the former for-profit insurance-based, or charitable approaches which created barriers to care through personal debt (Campbell, 2016).

Service delivery aside, the advent of the NHS also saw significant infrastructure developments – with new district hospitals, opening at a steady rate (NHS, 2015). In recent years, with many of these older structures being dilapidated or otherwise outgrown, a dramatic increase in infrastructure developments has resulted in several brand-new, state-of-the-art hospitals. Unlike those original developments though, political capital for increases in spending of that kind was compromised. This resulted in the embracing of Private Finance Initiatives (PFI); in which private firms or consortia paid for the building work up-front, but who were (and continue to be) paid back by the state – with significant interest charges (Khadaroo and Abdullah, 2015). Ultimately, this decision faithfully reflects one of the major themes in this research context – a general, medium-term trend of downward pressure on NHS budgets. Funding constraints, and in the case of

some evidence, short-sighted constraints at that (Sorenson et al., 2013), create major barriers to the routine adoption of digitally designed devices. The wider socioeconomic impacts of investments in medical technology are often overlooked, but should be considered in light of their overall value for money and not just their up-front price (ibid).

2.1.1.2. Reforms

Since its inception, the NHS has been the subject of several pragmatic and ideological reforms. Generally these have, since the 1980's, equated to a gradual increase in the amount of private sector involvement in the health service (BBC News, 1999, BMA, 2017). General practice, dentistry, and optometry have, for example, been long delivered by NHS procurement of private practices (The King's Fund, 2017a) Famously, the trend for wider privatisation began with the tendering of services for some support staff; before moving through to the creation of an internal market (BBC News, 1999); the creation of financially and executively independent foundation hospitals (NHS, 2016); and most recently through to the devolution of care commissioning - which has resulted in outsourcing of some major primary care services, and even entire hospitals to for-profit companies (The King's Fund, 2017a). Generally, reforms have been promoted to the public on the basis of providing routes to improved efficiency. The legitimacy of such claims is cast into doubt when the drawbacks of other private health care systems is considered. They include high administration costs and, overall, higher spending on health per capita than the UK (McKenna et al., 2017). Marketisation and ideology aside, a controversial trend for austerity government budgets since the 2008 financial crisis (Reeves et al., 2013) and consequently, an unprecedented reduction in the growth of health service funding (The King's Fund, 2017b), has stressed the system from another angle. Taken together, the politically imposed downward pressures on the NHS budget have peaked at a time when demographic change means that NHS capacity is under massive strain. Put simply, more people are living in the UK, and are living for longer than ever before (Office for National Statistics, 2015).

2.1.1.3. Procurement

Aside from a gradual slide towards the privatisation of NHS human resources and infrastructure, the health service has, quite logically in a mixed economy, always procured devices, equipment, and raw-materials from external suppliers. Major multi-national conglomerates, such as Johnson & Johnson incorporate multiple subsidiaries which specialise in supplying individual device niches. Most pertinently, this includes theatre consumables like surgical kits which might contain screwdrivers, reaming tools, screws, and mini-plates for example (Figure 10). It also includes stock, conventional, and partially customisable implants which represent off-the-shelf alternatives to CAD and AM or CAM implants for certain common procedures (Cohen et al., 2009, Lee et al., 2014). Such devices are, wherever possible, manually pre-bent against a medical model of the patient's defective anatomy so as to save time in theatre (Clijmans, 2007).

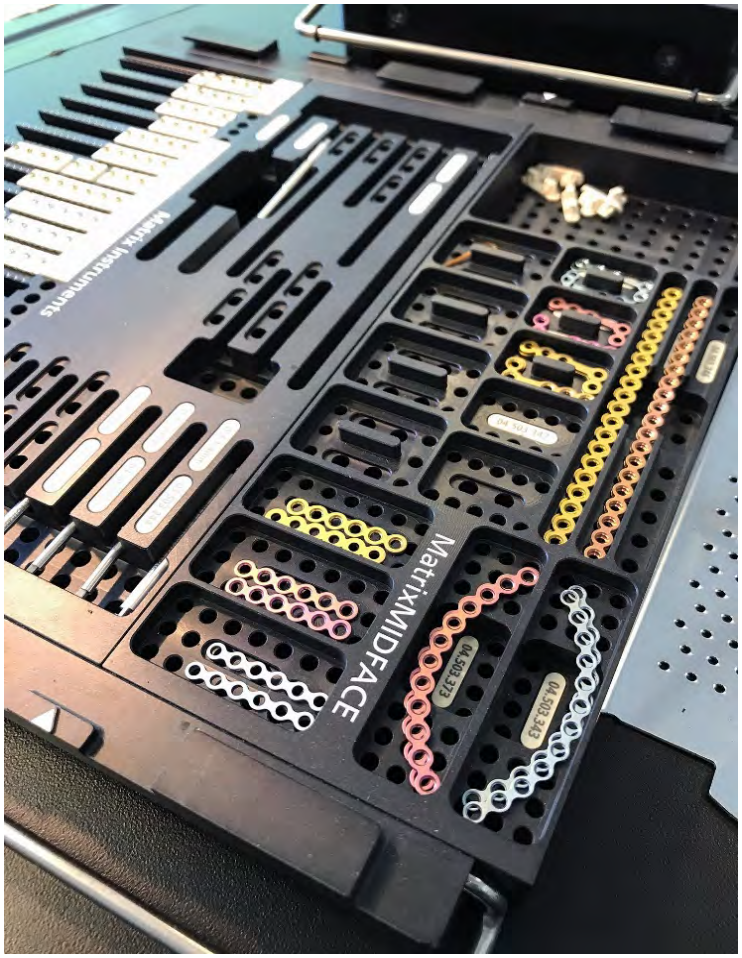


Figure 10 - Partial Synthes Matrix Midface Surgical Kit

Comparisons of costs for routine theatre resources like these are difficult to make on the basis that sales prices are adjusted according to the contract agreed with any given hospital – based on volume of cases and the value of purchases (Macario, 2010). Although this research focused on fully unique patient-specific devices, and not on partially-customisable stock implants, this discrepancy in charging models would have created a significant barrier. The institute's experience of fully-custom device procurement is one of an ad-hoc process dealt-with on a per-case basis. Generally, the institute's collaborators and customers (clinicians) seek approval for a design (and ultimately fabrication) service on the basis of more conventional routes being sub-optimal for patient care. Specifically, this has referred to device geometries which would have been extremely difficult or impossible to produce in a laboratory, and to devices which simply did not exist. The institute has also experienced customers struggling to obtain approval for design and fabrication services on the basis of cost. It is an ever-present concern.

When new drugs, techniques, or technologies are seeking to enter the NHS market, the major gatekeeper is value. Clinical outcomes, and their value judgement counterparts, are assessed for efficacy, efficiency, and quality-of-life by the National Institute for health and Care Excellence (NICE) (National Institute for Health and Care Excellence, 2017). Currently, NICE offers limited advice to clinicians about digitally designed implants specifically; focusing on customised implants as a whole (NICE, 2013b, NICE, 2013a). This situation in the UK mirrors more urgent concerns from clinicians and researchers in the USA (Christensen and Rybicki, 2017) and Australia (Choy et al., 2017, Phan et al., 2016) with regulatory and health-insurance billing vacuums, respectively. These gaps in conventional wisdom and in official guidelines, may create even larger opportunities than usual for exploitative practices by sales representatives, and for potentially misleading marketing to clinicians; as analysed at length by Goldacre (2013). As the literature review in this research observed (Chapter 3), higher quality and quantities of evidence are required to support clinicians, managers, and regulators in their decision-making and lobbying.

2.1.2. NHS Maxillofacial Surgery

In the UK, there are 153 oral and maxillofacial surgery units (British Association of Oral and Maxillofacial Surgeons, 2012). Their remit covers the diagnosis and treatment of diseases and disorders of the mouth, jaws, face, and neck (British Association of Oral and Maxillofacial Surgeons, 2017). As a specialty, it uniquely combines expertise in medicine and dentistry (ibid) such are the morphological and functional relationships between those fields. Most UK consultants have dual qualifications in medicine and dentistry, unlike those in the USA for example, who normally have dentistry alone (Harrison and O'Regan, 2011). In 2016, there were 338 consultants and 189 registrars in NHS England, with 6.33 applicants for every position in specialty training and 2.53 applicants via the core surgical training route (Health Education England, 2018). This was in spite of a marked lack of awareness and exposure to the specialty amongst medical undergraduate students (Goodson et al., 2013). 11% of oral and maxillofacial surgeons are women (Health Education England, 2018).

In the UK, the training pathway comprises two undergraduate degrees, foundation training and/or core surgical training, and specialty training (General Medical Council, 2018). The entire pathway can take 15-17 years (ibid). Crucially, these training routes do not guarantee any theoretical or vocational training in the creation-of, or deployment-of, CAD and AM or CAM patient specific devices. Some experience may be garnered through elective short courses or via the tutelage of an enthusiastic consultant surgeon during placements or job rotations, but it is not consistent.

While this might be expected, given the critically important nature of a surgeon's vocational training in clinical matters, these discrepancies in technical knowledge play a critical role in determining how institute staff members interact with them. A knowledge gap often exists between clinicians and institute designers; and with that, often follows an acceptance gap in terms of how open a clinician-customer is to exploring the use of digitally designed devices. In the institute's experience, this knowledge-gap trend is larger for more experienced clinicians who are further from

their training years and hold more firmly established habits and beliefs. This is an important theme for consideration in the literature review.

2.1.2.1. Procedures Overview

National statistics on maxillofacial procedures are limited. This can be attributed to a lack of detail on a national level about specific surgical techniques employed. Hospital episodes statistics, available from NHS Digital (2016), report on key performance indicators, anatomical sites, and on the general aims of procedures. Detailed audits such as those by Lethaus et al. (2014), which are relevant to the particular focus of this research, are rare and resource intensive. This relative scarcity, and partial picture, highlighted important themes for the proper investigation of digitally designed custom devices – including feedback, record keeping, and quality control.

Typical surgical procedures for the specialty could however, be identified by reviewing the institute's records. These records showed typical simpler procedures to include: impacted tooth removal; orbital trauma repair (Sugar et al., 1992, Hughes et al., 2003); placement of retentive implants for soft-tissue prostheses (Daniel and Eggbeer, 2016); genioplasty; and other facial recontouring (Bibb et al., 2015). Complex procedures typically include: tumour removal and defect reconstruction in (amongst other structures) the upper and lower jaws (ibid); mandibular (and other) distractions (ibid); cleft lip and palate repair; corrective osteotomies (Peel et al., 2016, Bibb et al., 2015); and temporomandibular joint (TMJ) replacement or repair.

2.1.2.2. NHS Maxillofacial Procedure Costs

Like the problems with obtaining complete statistics on the nature of maxillofacial procedures, ascertaining the precise costs of those surgical procedures is extremely difficult. Many authors cite a reduction in theatre time as resulting in cost benefits, such as Salmi et al. (2012), Gil et al. (2015), and

Modabber et al. (2012), but a precise figure is difficult to reach and no definitive figures exist in the literature. Indeed, even hospitals engaged by the institute (and other partners) as part of funded research projects, have been entirely unable to properly source or justify figures used for internal accounting. This is important, precisely because it is a major gap in the argument for wider use of digitally designed patient-specific devices. There are occasional, context-specific estimates for theatre costs such as 16 Euros per minute (Lethaus et al., 2012a) but the calculations are vague and are thus far from generalisable.

Macario (2010) casts doubt on the very concept of calculating theatre (Figure 11) time value as a standalone figure. He cites difficulties in even defining what that figure would be; depending as it does on: fixed costs or overheads, including buildings, equipment, security, depreciation, computer systems, insurance, housekeeping, and salaried labour - which are paid regardless of whether a procedure finishes early or not; variable costs, including disposable supplies which differ according to the volume of activity, including any staff who are paid on an hourly basis; lags in proper updates to hospital 'charge-master' lists - from which internal charges are levied; and, on the increased staff and software costs associated with extra accounting and analyses necessary for producing accurate figures in the first place. Macario's caveats echo anecdotal warnings from surgeons who are customers of the institute; about how shortening surgical procedures does not necessarily guarantee a higher theatre efficiency. This is because time savings would need to be significant to accommodate an extra procedure or procedures in a given day, and if this is not the case, fixed cost overheads still apply. Budgets were a recurring theme in this research, but as this sub-Chapter shows, much broader, holistic studies of patient treatment pathways by health economists will be required in the future to validate (or otherwise) routine use of patient-specific devices.

Figure 11 - Typical Maxillofacial Theatre Setup

Given the myriad difficulties in quantifying immediate financial impacts from reducing surgery durations, even for large-scale organisations and research projects, other themes and metrics for validating digitally designed surgical outcomes were considered in this research. The first was financial, but with a longer term view – towards reducing the number of operations required. As is addressed thoroughly in the literature review, the improved accuracy and improved predictability resulting from CAD and AM or CAM devices (Patel and Duckworth, 2015) increases the number of viable single-stage procedures (Levine et al., 2013), and reduces the need for secondary revisions (Alonso-Rodriguez et al., 2015). The other non-financial themes and metrics highlighted for in-depth literature review were related to: aesthetic outcomes when using digitally designed devices (Mertens et al., 2013); and functional outcomes (Peel et al., 2016). Ultimately, the non-cost measures all relate to quality of life. While it can be argued that downward cost-pressures on the NHS often result in a blind focus on cost and efficiency when evaluating digitally designed devices, institute experience has encountered universal empathy and intensive attention-to-detail on the part of surgeons for their patients. This impression suffers from being a self-selecting sample of surgeons who are engaged with accuracy and outcome measures, but it was nonetheless an important frame for literature searches.

2.1.2.3. Key Pathology Focus – Cranioplasty

When medical management (including temperature control, sedation, and coma) fails to relieve elevated intracranial pressure following a traumatic brain injury, a surgical intervention may be made in the form of a decompressive craniectomy (Lauerman and Stein, 2015). After removing a portion of the cranium, and creating extra space for the brain to swell into, the bone flap can be replaced immediately (craniotomy) or left off (with only the soft tissues covering the brain) pending further recovery (ibid). Other indications for craniectomy (or procedures resulting in similar defects) include resections of cranial lesions (Eufinger et al., 1998); together with benign bone pathologies such as fibrous dysplasia (Rosen et al., 2008), and requiring access to the brain to remove tumours (Dujovny et al., 1997).

Reconstruction of the cranium is primarily undertaken to restore its protective and cosmetic functions (Coulter et al., 2014). Further benefits involve the relief of neurological symptoms – potentially caused by atmospheric pressure acting upon the dura and brain via the skin flap (Dujovny et al., 1997). To minimise infection risk, cranioplasty should be undertaken at least six months after craniectomy (Thavarajah et al., 2012) with up to 14 months reported by Cabraja et al. (2009). In this way, the production period for designing and fabricating digital implants is well accounted for. However, the defect shape can change over time – which can be problematic for pre-fabricated implants based on older scans (Bibb et al., 2015). Soft tissues can also change during this time and have been shown to obstruct the successful insertion of implants fabricated in materials which are difficult to modify in-theatre.

2.1.2.4. Key Pathology Focus – Orbital Floor and Medial Wall Fractures

Enopthalmos caused by a blowout fracture of the orbital floor is the most frequent result of a traumatic impact to the orbit (Deveci et al., 2000). Complications like

hypoglobus (inferior displacement) and diplopia can also follow this increase in orbital cavity volume (van Leeuwen et al., 2012). The major aim of reconstructive surgery is to repair the anatomy to reduce the orbital volume to its original state (Deveci et al., 2000, van Leeuwen et al., 2012), which should correct the projection of the globe (Markiewicz et al., 2012). This can be difficult, when the surgeon's visibility is limited, and placement verification options are limited (ibid). Displacement of the zygoma can compound this difficulty by removing a major adjoining landmark (Jaquiéry et al., 2007). Special attention should be given to the vertical height of the orbital floor at the transition to the medial orbital wall in anatomical restoration (Schmelzeisen et al., 2004). Relapse occurs regularly after enopthalmos correction, so some initial overcorrection is recommended by Gellrich et al. (2002).

With such numerous and intricate considerations, it is unsurprising that conservative management is recommended by Kunz et al. (2013) in scenarios where: the defect is less than 3cm^2; enopthalmos is less than 2mm; and the entrapment of intraocular muscles or other soft tissues has been avoided. The extent of the injury should be judged using CBCT rather than standard spiral CT because of a significant reduction in radiation dose (Brisco et al., 2014). They recommended evaluation after a period of two weeks which, combined with the need to allow swelling to subside, explains why AM or CAM implants are suitable in this trauma scenario when compared to many other surgeries. That said, orbital reconstruction has also been demonstrated for patients following tumour ablation (Markiewicz et al., 2012), and for aesthetic reasons in anopthalmic patients (Rana et al., 2012).

2.1.2.5. Key Pathology Focus – Zygomatic Osteotomy

Incorrect primary reconstruction is the underlying problem behind virtually every post-trauma facial deformity (Hammer and Prein, 1995). The forward projection of the zygoma increases the risk of fractures – which can often be comminuted (Liu et al., 2013). Zygomatic osteotomy is challenging – it involves the cutting and repositioning of bone in an area critical to the aesthetics of the face. Indeed, a good aesthetic result is just as important as a good functional result (Becelli et

al., 2002). Further complications arise when this is undertaken as a secondary procedure following trauma; due to the ossification of bones in displaced positions. In this scenario, the bones are osteotomised along the fracture lines, mobilised, and repositioned (ibid).

2.1.2.6. Key Pathology Focus – Meningioma and Fibrous Dysplasia

Fibrous dysplasia is a benign disorder involving abnormal bone growth - whose slower progression after adolescence usually limits excision and reconstructive surgery to only those patients experiencing severe aesthetic or functional problems (Yetiser et al., 2006). Functional impacts include hearing loss, headaches, diplopia, vision loss, and sinusitis – with cosmetic concerns stemming from abnormal swelling of craniofacial bones (Lustig et al., 2001). Meningiomas (tumours of the brain membrane and surrounding tissues) are also usually benign and slow-growing; though some cases can be malignant - dictating a greater degree of urgency and full-excision where possible (Marosi et al., 2008). In benign cases on the other hand, the speed of pre-operative planning and device design is not generally a concern; with Gerbino et al. (Gerbino et al., 2013) reporting 20-35 days to produce patient-specific PEEK implants via an external supplier.

2.1.2.7. Key Pathology Focus – Hemimandibulectomy and Fibula Free-Flap Reconstruction

Partial mandible excision and reconstruction is indicated following malignancies, benign lesions, osteoradionecrosis, and more rarely, hyperplasia (Lethaus et al., 2012a, Hatamleh et al., 2017). The fibula flap (replacement bone graft) was introduced by Hidalgo (1989) and has since become the standard graft for bridging all broad defects in the maxillofacial area (Leiggener et al., 2009). It is popular for mandible reconstruction because of an ability to provide adequate bone stock length, and it will accept dental implants (Logan et al., 2013). On the

other hand, it offers a maximum bone height of 15mm – which is less than half that of the typical original mandible (ibid).

2.1.3. Maxillofacial Laboratories

Combined or standalone maxillofacial and dental technology laboratories are in-house NHS facilities with a wide range of functions. They support oral and maxillofacial units' outpatient and inpatient care, by producing and delivering patient specific devices and services using (for the most part) conventional tools and techniques. These can, depending on the size and location of the laboratory, include: obturators; jaw repositioning wafers for orthognathic surgery; soft tissue prostheses; partial denture frameworks; dentures; retainers; surgical guides; patient specific surgical implants like orbital floors or cranioplasty plates; surgical plans; and some rehabilitative devices like burns splints or protective sports masks. Cranioplasty implants are somewhat of an outlier from that list – being neurosurgery devices, but are included in some laboratory remits nonetheless – and were therefore included in the maxillofacial remit of this research.

Maxillofacial prosthetics has recently been reclassified as a clinical science role under the NHS' Scientist Training Program (STP). Entry onto this program for 'Reconstructive Science' demands a background in dental technology (Health Education England, 2017). Most significantly for this research, the STP candidate's background, and the work placement emphasis of their training, does not guarantee a consistent exposure to digital surgical planning, and device design training. In fact, the institute itself has begun to deliver introductory training to the concepts behind AM and CAD surgical planning, to dental technology degree students – such is the demand.

Another important theme for the research is raised by this fact – that of evolving skillsets and laboratory staff makeup. Opposing these are themes of protectionism and entrenched beliefs. Protectionism was an issue which was experienced by the institute over six years of advocating for fully-digital plans, guides, and implants to customers who previously relied only on conventional or semi-digital fabrication methods. There were concerns expressed by some about ceding design and

fabrication work to computers and machines; and the potential for seeing all or part of their manual skillsets made redundant. This trend has eased noticeably however, and has in some ways reversed. More customers have obtained funds for software and low to mid-range polymer AM machines for their units – to ensure they are, in fact, undertaking the conventional and semi-digital work for themselves. In the experience of institute staff, this has had mixed results, especially in situations where a designer or design engineer has not been involved. Staff with design skillsets have been employed by a small number of former customers – with more robust results.

2.1.3.1. Laboratory Environment & Infrastructure

Figure 12 - Manual Presses

There are no standard models for laboratory setup – either in terms of accommodation and machines, or in terms of staff. However, experience from visiting institute customers and CARTIS collaborators provided a general overview of typical resources. Normally, these resources included manual presses (Figure 12); polishing wheels; vacuum forming machines; grinding wheels; boiling-out machines; ovens; burners; drills (Figure 14); spot welders; and laser engraving machines – all spread across plaster rooms (Figure 13), workbenches, workshops, and offices.

Figure 13 - Plaster Room Setup

Such conventional facilities were, in some select units, complimented by polymer AM machines, computers, surgical planning and design software, and other digital technologies such as handheld scanners or desktop scanners for capturing 3D information.

Figure 14 - Reaming Tool

2.2. Commercial and Industrial Research Context

2.2.1. Commercial Design Tools and Implant Production Services

In the UK, several medical companies compete for maxillofacial patient specific implant business. The subject of that competition depends on the service model of the individual hospital unit, or otherwise, on the relationship between company and prescribing surgeon. In the rare instances where a hospital laboratory has design tools, and design engineering expertise in-house, surgeons can liaise with laboratory staff to arrive at a verified device design before paying an external sub-contractor to fabricate the component or components. This is a scenario witnessed by the institute, of its CARTIS research collaborators. More conventionally, individual surgeons procure holistic design and fabrication services from external commercial companies when the complexities or otherwise unusual aspects of a clinical problem cannot be resolved using conventional (off-the-shelf) devices. This sub-Chapter briefly presents an indicative overview of major products and services in the field.

2.2.1.1. External Services and Service Models

Service touchpoints refer to moments of interaction when customer and service provider meet, literally, or via artefacts and interfaces, on the customer's journey to obtaining a product (Zomerdijk and Voss, 2009). Holistic, end-to-end implant design and fabrication services differ in their touchpoints, customer journeys, capabilities, pricing, degree of customer involvement, terminology, branding, and speed. For example: Synthes (Oberdorf, Switzerland) TRUMATCH service (Synthes GmbH, 2017b) is facilitated in the first instance by their existing numerous local sales representatives, before engaging the client in-detail through proprietary surgical planning software developed by Materialise (Leuven, Belgium); Stryker's (Freiburg, Germany) iD Patient Specific Implants service (Stryker, 2014) is delivered in a similar fashion, with detailed online planning delivered by 3D Systems Medical Modelling (Colorado, USA); Medical

Modelling also deliver their own services in addition to their work for Stryker (3D Systems Medical Modeling, 2017).

Other service providers appear to deliver their own online planning and fabrication solutions – but are less specific about the precise nature of their interfaces and tools: KLS Martin (Freiburg, Germany) (KLS Martin Group, 2017); Anatomics (Melbourne, Australia) (Anatomics Pty Ltd, 2017); Cavendish Implants (London, UK) (Cavendish Implants, 2016); and Xilloc (Sittard-Geleen, The Netherlands) (Xilloc Medical B.V., 2017); to name but those most known to the institute and its CARTIS colleagues. Though their specific planning and design interactions with customers are described vaguely or withheld entirely (understandably, given the increasingly competitive market (Wohlers, 2018)), they share online screen-share meetings in common. The planning and design work is directed by the customer either verbally or in-writing. Generally, the customer does not operate the CAD software programs themselves, when procuring implants from these services. Instead, they provide product and user requirements, and verify iterations of plans and designs (to a greater or lesser degree, depending on the service). The institute has received anecdotal feedback from customers, praising its frequent-contact and high-engagement approach; which is contrasted against more sporadic, verification-only approaches of at least one other service provider. Of course, the downside to the institute's approach is a limit on the number of cases it can undertake at any one time.

Aside from the lack of consistency in touchpoints, the services vary across stated durations: Synthes takes two days to set-up a new account, fifteen days to deliver a completed implant (assuming no re-work or customer approval delays), and offers a premium service for more urgent devices (Synthes GmbH, 2017b, Synthes GmbH, 2017a); Stryker claims fourteen working days for their custom titanium mandible implants (Stryker, 2014); 3D Systems Medical Modelling order form suggests nine-to-eleven days as a best-case scenario (3D Systems Medical Modeling, 2016); KLS Martin state five-to-fifteen days for fabrication, after a maximum of one week for delivering a design proposal (KLS Martin Group, 2017); with other suppliers metrics being difficult to discern from their publicly available materials. What's more, AM is far from reaching (at least explicit) exclusivity for those services which deliver titanium implants. Stryker

use subtractive milling for at least some of their titanium parts (Stryker, 2014); Cavendish Implants provide press forming as a manufacturing option (Cavendish Implants, 2016); and KLS Martin offer titanium mesh which is heated and deep-drawn, alongside solid titanium sheet, and AM (KLS Martin Group, 2017). PEEK is delivered by the major suppliers through subtractive machining, though significant work has been undertaken into sintering PEEK to produce parts (Berretta et al., 2015). This offers promise – but is not yet at the point of being routinely available.

It is reasonable to draw themes from even these brief overviews of commercial services – such is the clarity with which key factors have arisen. They include fragmented services and inconsistencies in approach; a lack of commonly accepted standard design considerations or processes; and a high degree of protection relating to design process specifics – presumably favouring commercial sensitivity over academic dissemination.

2.2.1.2. Software Products for In-house Work – Scan-Data Processing

For hospital laboratories or external suppliers undertaking model-fabrication or patient-specific device design, the first stage of any product-realisation workflow is to process the scan data from greyscale 2D images into 3D virtual models. As this research focused on devices for replacing, fixing, or cutting bony anatomy, only products which permitted the segmentation of CT scans (including CBCT) were relevant to the work. The institute uses Mimics (Materialise, Leuven, Belgium) because it meets stringent European regulations and is CE marked (Materialise, 2017) for medical use. It also has a long history of use at the institute. It has five main functions to segment data – features which are (in one way or another) common across competitor products and open-source alternatives. It permits the user to extract all of the pixels with a given Hounsfield value to a new layer mask (or masks), which overlay but are independent of the scan data below (Figure 15); it allows all adjoining pixels to be copied to a new layer (region grow); it permits manual fine-tuning of the layered masks with local thresholding (adjustment of captured Hounsfield unit range), local drawing, and local eraser tools; and it is able to convert a mask's worth of data from 2D pixels

into 3D voxels for display, and export these as STL files for fabrication or further processing. Mimics' use is reported most frequently in the literature included in this thesis: Mazzoli et al. (2009), Mustafa et al. (2010), Lethaus et al. (2012a), Huang et al. (2015), and Podolsky et al. (2016) provide five examples. It is a well-established tool, and can interface with Materialise's other Innovation Suite tools such as 3-Matic, for device design (Philippe, 2013).

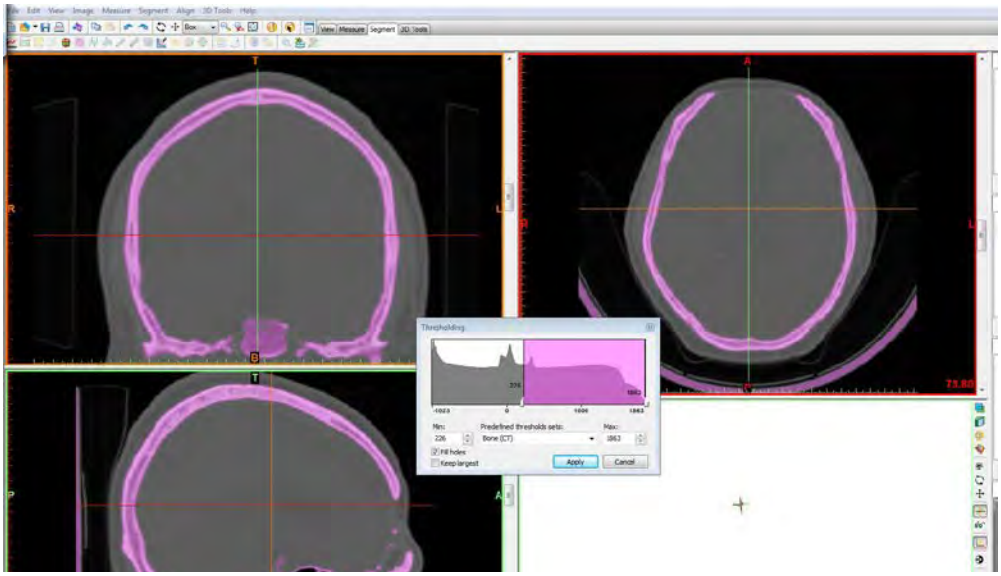


Figure 15 - Thresholding at the Default Hounsfield Units for Bone in Mimics

Other occasionally-reported tools for scan-data processing form a relatively short list: Simpleware Scan IP (Synopsis, USA) – used by Ma et al. (2016) for example; Osirix (Pixmeo, Switzerland) – used by Liu et al. (2009) for example; and iPlan CMF (Brainlab, Germany) – used by Essig et al. (2011). Osirix was originally an exclusively open-source software, but has offered a paid-for version since 2010 to enable CE-marking and FDA approval (Pixmeo, 2017). Brainlab's product shares these approvals, whereas there are no such claims from Simpleware. As was addressed in sub-Chapter 1.6, regulatory compliance and quality management were major themes in this research, both for the finished patient-specific devices and for the tools and procedures used to create them.

Automation of scan-data processing is made possible by some tools – most notably Brainlab's iPlan CMF software (Essig et al., 2011). However, Brainlab is most notable for its navigation software and hardware. Surgical navigation is a

technique involving the spatial registration of a patient scan or digital surgical plan, with the real patient's anatomy in-theatre by way of sensors and intra-operative imaging. It can improve the accuracy of implant placement (Rana et al., 2015b), tumour resection (Nijmeh et al., 2005), and has achieved numerous good clinical outcomes for high-risk procedures. However, navigation systems (including those from other companies) are often prohibitively expensive for maxillofacial units in the UK NHS, and can actually lengthen the duration of surgical procedures due to prolonged in-theatre setup (Wong et al., 2015a). On this basis, and on the basis of CARTIS collaborator infrastructure, navigation was not a central theme of this research. It was though, an important factor in the literature about surgical positioning, cutting, and drilling guides. As will be explored fully in Chapter 3, there were a surprising number of instances where physical AM guides were preferred over navigation for reasons beyond cost alone (Kaneyama et al., 2015).

2.2.1.3. Software Products for In-house Work – Surgical Planning and Device Design

Both context-specific surgical design software (Adolphs et al., 2013) and more general product design software (Ciocca et al., 2012a) have been successfully adopted for surgical planning and for device design. As stated, the institute has used a specialist medical software for scan-data processing, and a more adaptable, general modelling software for device design; albeit one with a significant track record of use in this field (Bibb et al., 2002, Scolozzi, 2012). CARTIS collaborators with the capacity for in-house planning and design have mirrored the setup and techniques developed by the institute.

In more usual scenarios – where existing models, tools, and best-practice support did not exist, specialist surgical software tools are often more appropriate than general design or engineering packages. This is the case particularly given their use of jargon and workflows which are closer to the surgical field of knowledge compared to more generic counterparts. Context specific tools which are frequently reported as being used successfully by hospitals themselves include: 3-Matic (Materialise, Belgium) (Hatamleh et al., 2017); SimPlant (Dentsply,

Sweden) (Tarsitano et al., 2016); and ProPlan CMF (Materialise, Belgium) (Weitz et al., 2016). Though tools of this nature may have a shorter and flatter learning-curve for the average surgeon (with no special interest or background in digital technologies), there are notable drawbacks. Some products lock users into one proprietary fabrication service; with many being expensive to purchase in the first instance and to maintain over subsequent years.

General design, modelling, and engineering tools used in-house with success include: FreeForm (3D Systems, USA) (Kittur et al., 2012); Solidworks (Dassault Systèmes S.A., France) (Jaffry et al., 2014); and Rhinoceros (Robert McNeel & Associates, USA) (Tarsitano et al., 2016). FreeForm and Solidworks share problems of high up-front costs and ongoing maintenance costs, which has led some technologically savvy, enthusiastic authors to resort to freeware (Ganry et al., 2017) when designing and fabricating models and devices. Rhinoceros has a lower cost, but is still not freeware. The regulatory implications of using free (and, or open-source) software remain unclear – such is the lag between innovative applications and specific regulatory standards.

Beyond the question of whether it results in the ability of a software to achieve a given modelling function, underlying technical or mathematical modelling characteristics lack practical significance to this research. For example, software in the solid modelling category is synonymous with primitives, user-defined parametric features, and Boolean operations (Paterson, 2013). The 3D surface modelling category encompasses polygon faceted surface modelling, and mathematical curve-based surface modelling (Bibb et al., 2015). The latter (such as Rhinoceros) is designed for modelling smooth but accurate mathematical curve-based surfaces, and is therefore relatively unsuited to the high complexity of the human anatomy (ibid). Nevertheless, surface modelling capabilities are occasionally co-opted by the institute; such as when there is no anatomy available to mirror. This approach is facilitated by FreeForm Modelling Plus, which is an example of a hybrid modelling tool. Hybrid tools combine solid modelling and surface modelling features for improved efficiency (Paterson, 2013). In this instance, FreeForm's solid modelling is realised through voxels (3D pixels); to create solid, unconstrained, complex shapes (Bibb et al., 2015). These issues

though, are less important than what the software tools can achieve, with how much training or background knowledge, and at what cost.

These factors have been mostly unaddressed in the published literature; with the exception of the use of FreeForm (3D Systems, USA) (Mazzoli et al., 2009, Mustafa et al., 2017, Bibb et al., 2002). The associated haptic pen PHANTOM hardware (3D Systems, USA) is relatively unusual and usually prompts explanation. The benefits have been described variously as being an intuitive mode of interaction , and enabling an improved ease and speed of modelling for complex organic forms (Bibb et al., 2009, Mustafa et al., 2011b). However, the reports of software tools which rely solely on the more standard keyboard and mouse hardware interfaces made no mentions of difficulties, or of specifically prohibitive input barriers. The ability to use a haptic device is desirable, but by no means essential.

2.2.2. PDR – International Centre for Design & Research

The host organisation for this research was PDR – International Centre of Design and Research; a research institute and design consultancy at Cardiff Metropolitan University. It was established in 1994, and at the time of writing comprised of eight research and practice groups: User Centred Design; New Product Development; Service Design; Prototyping and Manufacture; Ecodesign; Design Management; Design and Innovation Policy; and Surgical and Prosthetic Design. Each group undertakes a mix of three core activities to varying degrees – enterprise service delivery, academic research, and knowledge exchange (e.g. facilitating workshops, running training courses, or delivering university teaching in select instances).

PDR is funded by winning research grants, partnering closely with industry and the third sector, and on delivering commercial services. As such, it is fundamentally interested in, and dependent on the relevance and applicability of research to generate tangible benefits for clients, for itself, and for stakeholders. By definition then, PDR is concerned with application, rather than fundamental or abstract research in isolation. To deliver on these necessary aims, PDR employed twenty-eight staff members at the time of writing, spanning experienced mechanical engineers, to early

career researchers, marketing professionals, academics, and fabrication technicians. Its combined semi-commercial, and semi-academic nature created a unique and privileged research context for this work; merging academic ideals with real-world pragmatism.

2.2.3. Surgical & Prosthetic Design (SPD)

Of PDR's eight research and practice groups, Surgical and Prosthetic Design (SPD) was the specific setting for this research. This group, comprising five staff and one doctoral student at the time of writing, was founded in 1998 – towards the beginning of CAD and AM's upward trajectory for medical applications in the UK. Driven by the enthusiasm of the specialty in those early years, and by the significant size of the respective units at local hospitals, SPD focused mainly on maxillofacial applications for those emerging technologies. That enthusiasm was driven in turn by the intricacy of the anatomy in the head and neck region – amplifying the benefits from better visualisation and surgical planning as a result of using accurate, patient-specific anatomical medical models. This maxillofacial plurality was, and continues to be reflected across the discipline (Martelli et al., 2016). This focus endures in the main, to the present day. That is, in addition to an expansion of SPD's activities to surgical, prosthetic, and rehabilitation specialties well beyond maxillofacial surgery. Furthermore, SPD's commercial design consultancy work has steadily evolved in complexity. Demand and capability has moved from segmenting Computed Tomography (CT) scan-data for producing AM file outputs; to designing patient-specific, custom devices.

In terms of research and knowledge exchange funding, SPD has delivered an array of high-value projects - alone, and in collaboration with larger partners. Most notably, SPD was the academic partner in an Innovate UK and EPSRC funded project in collaboration with a major NHS trust, a global engineering and AM machine manufacturing company, and an AM materials company. It sought to develop new design software tools for the patient-specific device design process. This partnership, and those from other funded projects (such as delivering patient-specific design expertise to small and medium size enterprises on behalf of the national government) further enhanced the research context by developing new

relationships and cementing existing ones. Benefits were manifest most tangibly as robust background knowledge about pragmatic and technical drivers and barriers to CAD and AM deployment in healthcare.

The researcher's full-time role at SPD, within PDR, has developed over the duration of this research. Initially focused on producing medical models, it now encompasses device design, marketing, quality management, business development, academic research outputs, commercial research outputs, and bid-writing assistance. This, combined with previous consumer product design experience created a solid grounding for this work.

Figure 16 - Render of PDR Patient-Specific Surgical Device Designs

Commercially, SPD undertakes collaborative maxillofacial surgical planning, device design (Figure 16), and some model fabrication (Figure 17) for prosthetists, laboratory technicians, surgeons, or as a subcontractor to a fabrication partner. Every project is for an individual, named patient and the resulting models, plans, and device designs are custom solutions tailored to the unique requirements of the single case (as defined by the clinician). Typical current commercial interactions with clinicians follow a general pattern of: enquiry; data receipt; online surgical planning meeting; design activity; quotation and verification; dispatch of the designed digital file; and finally, post-market surveillance. Methods of communication, collaboration and

sign-off vary between in-person discussions, online meetings with shared screen views, telephone calls, and emails.

Surgical plans and their associated device designs are typically delivered (as STereoLithography files – STL's) within two days of a planning meeting. They are delivered to either the clinician-customer directly, or to the fabrication partner for production and finishing. Said partner typically produces end-use titanium parts within approximately ten days, and places them on the market. PDR-SPD does not, in any circumstances, place medical devices on the market. There are five main categories of design consultancy services offered by the institute. The following sub-Chapters 2.2.3.1 – 2.2.3.8 characterise those services. They also list typical applications for devices which are manufactured from the digital files provided by PDR-SPD. This is to define and develop an understanding of the terminology used throughout the remainder of this thesis. All of the services are relevant to this research, and are often used in fluid combinations, as needed.

2.2.3.1. Scan Data to Medical Model Build Files Service

This is mainly a service provided as a subcontractor to the fabrication partner – but it is delivered directly to clinicians, for cases which fall outside of the service agreement between the organisations. Medical Models are custom physical reproductions of anatomy from Computed Tomography (CT), Cone Beam Computed Tomography (CBCT), Magnetic Resonance Imaging (MRI), photogrammetry, or surface scan data. They are used to rehearse surgeries, to communicate procedures to patients, as in-theatre visual references, or as jigs to assist the shaping of off-the-shelf implants. The work is undertaken using CE-marked scan-data processing software for model preparation. PDR-SPD can receive Digital Imaging Communication in Medicine (DICOM) format scan data by posted CD-ROM, or digitally via the secure Image Exchange Portal (IEP) online upload service. The latter is favoured because of the increased security and speed, however the registration process for the customer is a significant barrier. Best fabrication turnaround time is one day from receipt of data to model dispatch (with the model being fabricated overnight).

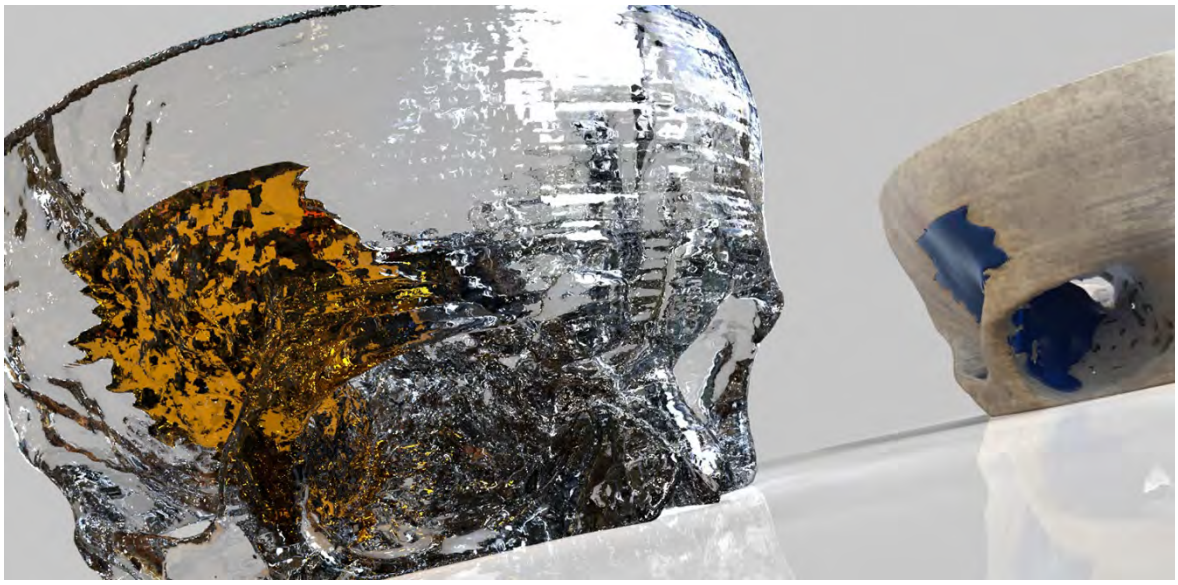


Figure 17 – Rendering of SLA Medical Model with Selective Colouring

The finished model designs are fabricated by the institute, by the fabrication partner, or by the hospital themselves, using AM technologies. At the institute, vat polymerisation (SLA) is typically used – which has the capacity to produce transparent models with highlighted anatomical features (such as the highlighted bone tumour in Figure 17).

2.2.3.2. Typical Medical Model Applications

- Midface model: extending from the upper teeth to the supra-orbital rims, and from the nasal bone to the auditory meatus.
- Mandible model: the lower jaw and teeth.
- Orbits model: the entirety of the eye socket(s) and orbital rims (including the optic foramen).
- Cranioplasty model: extending to include the craniectomy defect plus a customer-defined margin.
- Fibula model: the entire fibula – usually intended for planning free-flap reconstruction of a facial defect.

2.2.3.3. Reconstruction Aid Design Service

Like the scan data to medical model build file service, this is provided as a subcontractor to the fabrication partner; but also delivered directly to clinicians for cases falling outside of service agreements. Reconstruction Aids are Medical Models of scan data-derived anatomy, which has been modified in the CAD environment prior to fabrication. For example, this includes mirroring healthy anatomy across the midline to restore missing or displaced bone. They are used in a number of important ways: to physically represent a digital surgical plan outcome and permit test-fitting of implants; to save time in hospital laboratories by eliminating time-consuming manual carving; to reduce model costs by decreasing the need for bilateral models - as references for that manual carving; to improve the accuracy of custom laboratory-bent stock implants by acting as a jig; and to improve predictability during planning discussions.

All modifications to processed scan data are explicitly agreed with the customer. PDR-SPD utilises FreeForm Plus voxel modelling design software through a PHANTOM Desktop haptic interface (3D Systems, USA) which allows the institute to cater to any specific, unique request (interface and software shown in Figure 20).

2.2.3.4. Typical Reconstruction Aid Variants

- Defect-filled cranioplasty: a model of a digitally-repaired craniectomy defect. Only the defect plus an approximate margin of 20mm is fabricated. A groove on the model delineates between the unmodified area (outside of the defect margin) and the modified area (inside the defect margin). The reconstruction is usually based on mirroring the contralateral healthy side (where available). Figure 18 illustrates an example where mirroring was not possible, so manual modelling was employed instead. The physical models are used directly as press tools, or indirectly with impressions taken first, for laboratory fabrication of cranioplasty implants, using sheets of commercially pure titanium. Model size is reduced, relative to full cranium models, and the hand-carving reconstruction time is eliminated.

Figure 18 - Rendering of Cranioplasty Reconstruction Aid

- Orbital floor jigsaw (Figure 19): a model of a defective orbit with a separate on-lay jigsaw piece to repair the defect. Only the affected orbit is printed and the jigsaw reconstructive piece eliminates the need for full original and repaired models. Hand carving time is saved and digital measurements ensure good accuracy. The models are used as visual references, as direct or indirect press tools, and as verification models to check those laboratory-pressed implants.

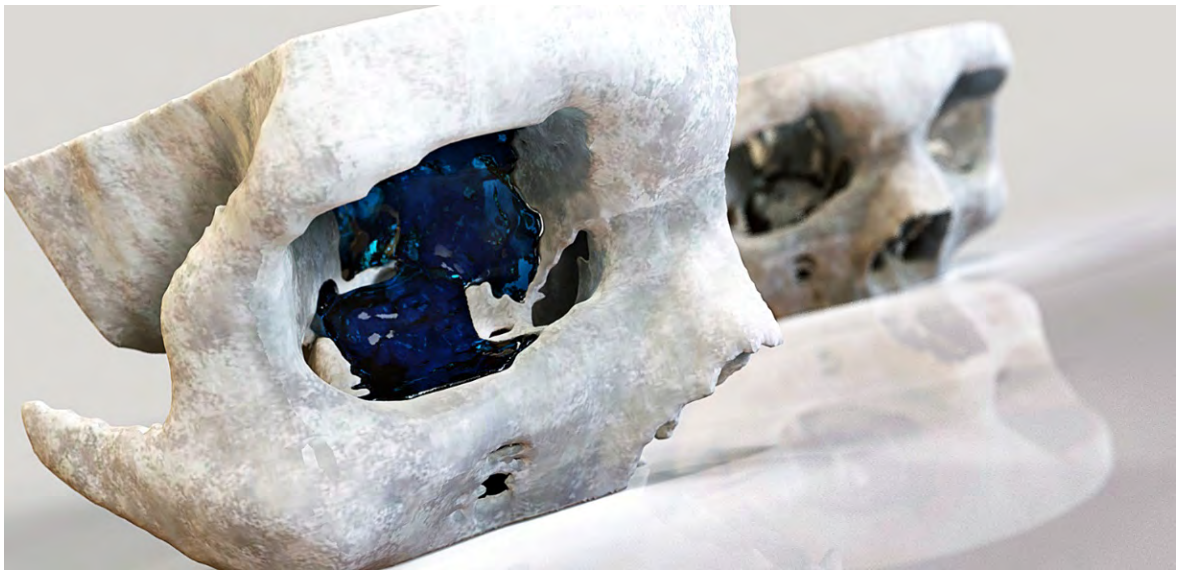


Figure 19 - Rendering of Orbital Floor and Medial Wall Reconstruction Aid

2.2.3.5. Digital Surgical Planning Service

This again, is mainly delivered as a subcontractor to the fabrication partner. Digital Surgical Plans are computer based visualisations, concepts, rehearsals, and final designs for the cutting and / or moving of bones. They are undertaken prior to surgery. Plan collaboration happens in-person (for local surgeons), or via online meetings with a shared screen-view (Figure 20) and conference voice calls. The service aims to improve the predictability and accuracy of surgery and its outcomes, reduce theatre time, and create a foundation for custom surgical guides and implant design services.

2.2.3.6. Custom Surgical Guide Design Service

This service results in designed geometries for custom surgical guides. They are designed to sit securely onto consistent anatomical landmarks and to guide saw cutting vectors, drilling angles, drilling locations, or bone translations. Manufacturing is undertaken by the fabrication partner using powder bed fusion (SLM) for titanium.

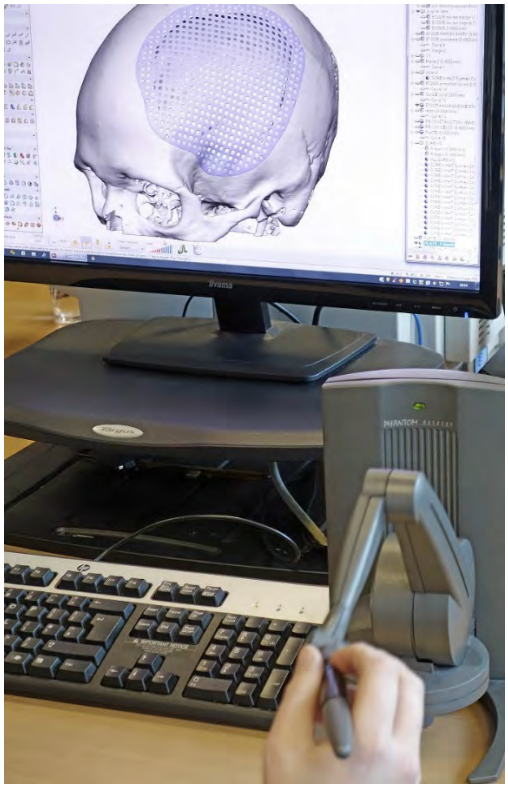


Figure 20 - Designer's View of Digital Surgical Planning

2.2.3.7. Custom Implant Design Service

Custom implants are AM or CNC fabricated devices in titanium or PEEK respectively. They are matched exactly to an individual patient's anatomy to restore mechanical or aesthetic functions. They can be designed independently, following a customer's precise specifications, or as an extension of the digital surgical planning process. Typically, they are used to replace missing bone, or to fix existing bones into new or corrected positions.

2.2.3.8. Typical Digital Surgical Plan / Custom Surgical Guide / Implant Variants

- Tumour excision and fibula-flap reconstruction (Figure 21): digital surgical plan for removing a tumour from the mandible or maxilla; design and fabrication of custom cutting guides to translate the planned margins to theatre; design and fabrication of guides to harvest the correct length and angles of bone from the fibula to reconstruct the missing area; and a custom implant to fix the harvested fibula in the planned positions.

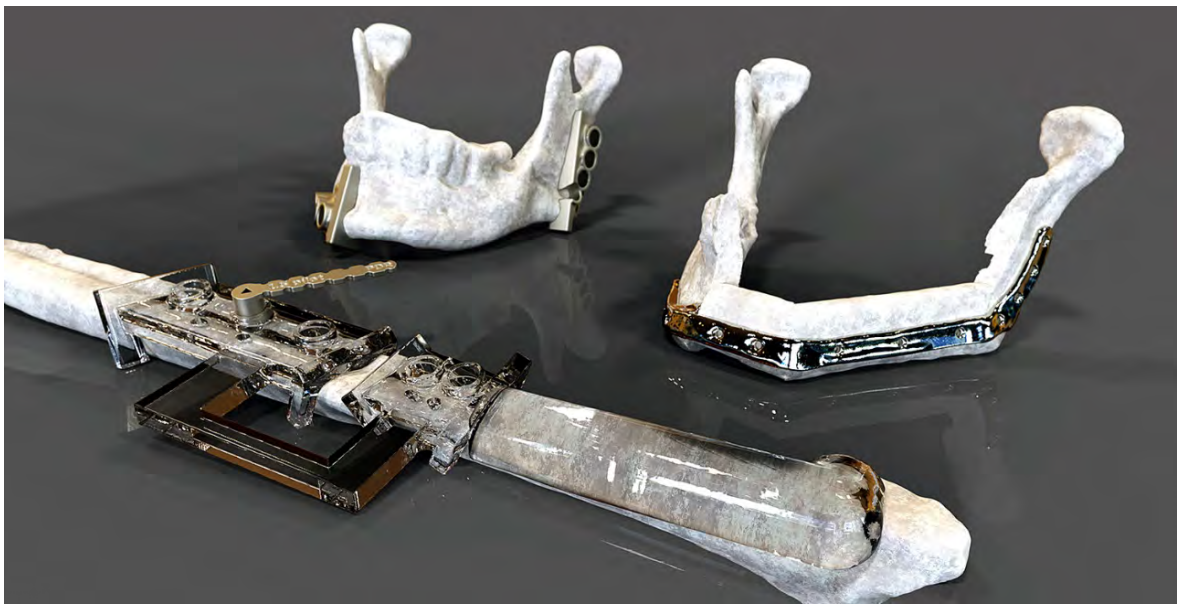


Figure 21 – Rendering of Custom Guides and Implant for Hemimandibulectomy and Fibula Free Flap Reconstruction

- Orbital / temporal lesion excision and reconstruction (***Figure 22***): digital surgical plan for removing a tumour from the orbit / temporal region; design and fabrication of custom cutting guides to translate the planned margins to theatre; and a custom implant(s) to repair the morphology of the excised region.

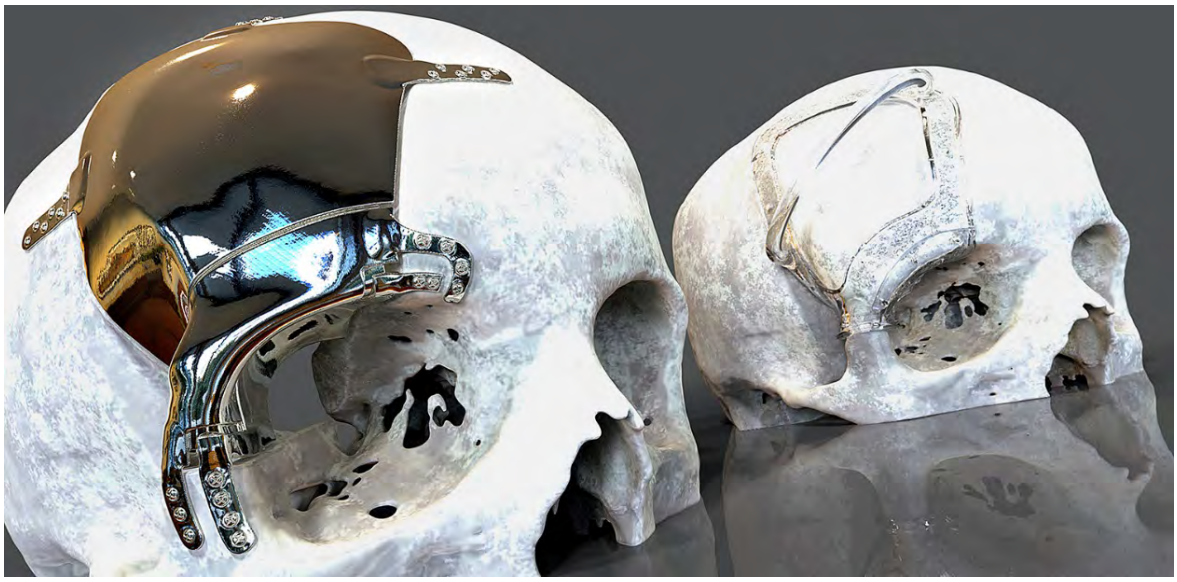


Figure 22 – Rendering of Custom Guides and Implants for Meningioma Excision and Reconstruction

- Zygo-maxillary-complex osteotomies and fracture reduction (Figure 23): digital surgical plan for cutting bones affected by trauma (having healed in a sub-optimal position); surgical cutting and positioning guides to mobilise and reduce the bones to their new planned positions; and custom implants to fix those bones in their pre-planned new positions.

Figure 23 - Render of Custom Guides and Implants for Zygomatic Osteotomy

- Cranioplasty implant (Figure 24): custom implant to repair a craniectomy defect.

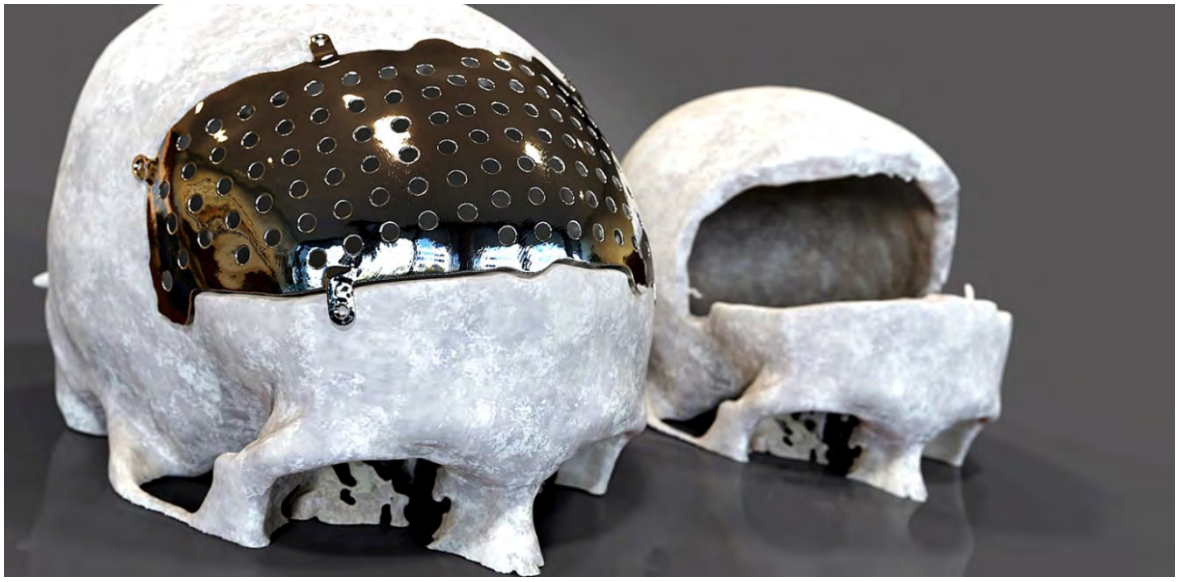


Figure 24 - Render of Custom Implant for Cranioplasty

- Orbital floor implant (the superior-most component in Figure 25): custom implant to repair an orbital floor and / or medial wall defect.

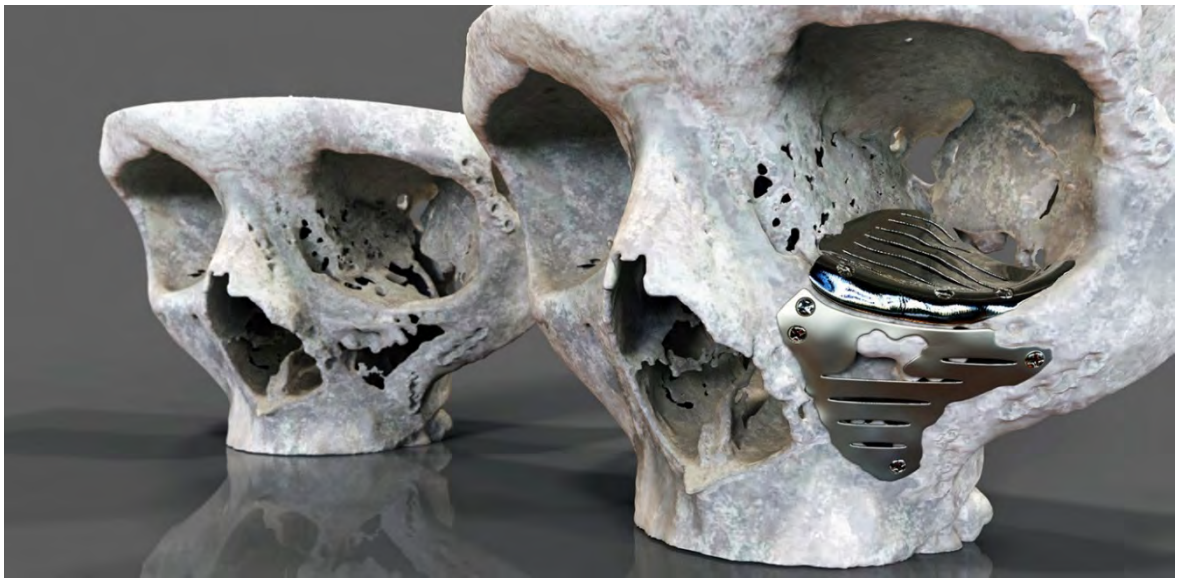


Figure 25 - Render of Custom Titanium Orbital Floor and Re-Contouring Implants

- Onlay re-contouring implants: custom implant(s) to repair or enhance deficient bony contours (Figure 25). Sometimes, gap-filling is a further aim as with the multi material PEEK and titanium implants in Figure 26.

Figure 26 - Render of Custom Titanium Orbital Floor and PEEK Re-Contouring / Gap-Filling Implants

2.3. Chapter 2 Summary

In summary, Chapter 2 has:

- identified the over-arching political (Chapter 2.1.1.2), commercial (2.2), and clinical (2.1.2) themes influencing this research (directly, and indirectly);

- highlighted specific sub-themes for the NHS, including marketization, privatisation, outsourcing, demographics (2.1.1.2 - 2.1.1.3), protectionism, audits and statistics, training and specialised knowledge, funding, and infrastructure;

- identified sub-themes emerging from current implant services, ranging from service model fragmentation, touchpoint inconsistencies, commercial secrecy, and its relationship to academic dissemination (2.2.1.1);

- outlined sub-themes from surveying the digital design tools for in-hospital or in-company work, including costs, training, flexibility, interoperability, specialist knowledge, and collaboration (2.2.1.2 – 2.2.1.3);

- made pre-existing institute and researcher knowledge and experience explicit (2.2.2 – 2.2.3);

- collectively justified serious consideration of these themes in both the literature review (Chapter 3), and in the proposed design process intervention;

- contributed to meeting objective 1 from Chapter 1.9.

3. Literature Review – Patient-Specific CAD and AM (or CNC Machining) for Surgery

This Chapter (Figure 27) establishes the scope, nature, and success of previous work on topics which are similar to, or otherwise valuable to, the research context documented in Chapter 2. It contributes to meeting objectives 1 and 2 from Chapter 1.9. It is a pragmatic narrative literature review which identifies, frames, and evaluates key publications, in order to characterise variations in research quality, perspectives, and relevance in this somewhat ambiguous field. Generally, the coherence of the highlighted work grows-and-shrinks in parallel with either the relative isolation, or relative collaboration, between those individual perspectives which contribute to surgical AM research. Roughly, those perspectives may be grouped as: surgeons reporting mainly on clinical results, for an audience of other surgeons; engineers reporting on technical AM minutiae, with little appreciation of immediate real-world translation; or more rounded multi-disciplinary reports from combined university hospital-and-engineering faculty setups, which are rarer but have a higher practical relevance for application of CAD, AM, and CNC to surgery. On the whole, this field is becoming increasingly difficult to define; with the boundaries between medics, designers, engineers, technicians, and fundamental scientists becoming progressively blurred. As is demonstrated below, this blurring of roles is reflected in the literature, and is a useful lens through which to view omissions in reports. Subsequently, it may be used to identify specific gaps in *published* knowledge.

Structurally, for the research presented in this thesis, the literature review contributed to isolating the most appropriate research questions (for the context, and for the project resources). Those questions are presented and refined in Chapter 4.2. Initially, a general overview of themes and trends was sought, which gave way to more in-depth consideration of specific types of implant for certain chosen procedures. In particular, it addressed the application of digital design and AM to cranioplasty, and to orbital floor or medial wall implants. They represented simpler, routine devices which the institute was most-frequently involved with delivering. Relative to those, the bodies of work relating to more complex, more unusual surgeries were considered: of post-traumatic zygomatic osteotomy; single-stage craniofacial lesion resection and reconstruction; and the more routine but still complex hemimandibulectomy and fibula free-flap reconstruction. Full methodological justifications are provided in Chapter 4, but essentially, these particular sub-categories of maxillofacial

surgery were selected on the basis of availability to the institute from CARTIS-affiliated surgeons.

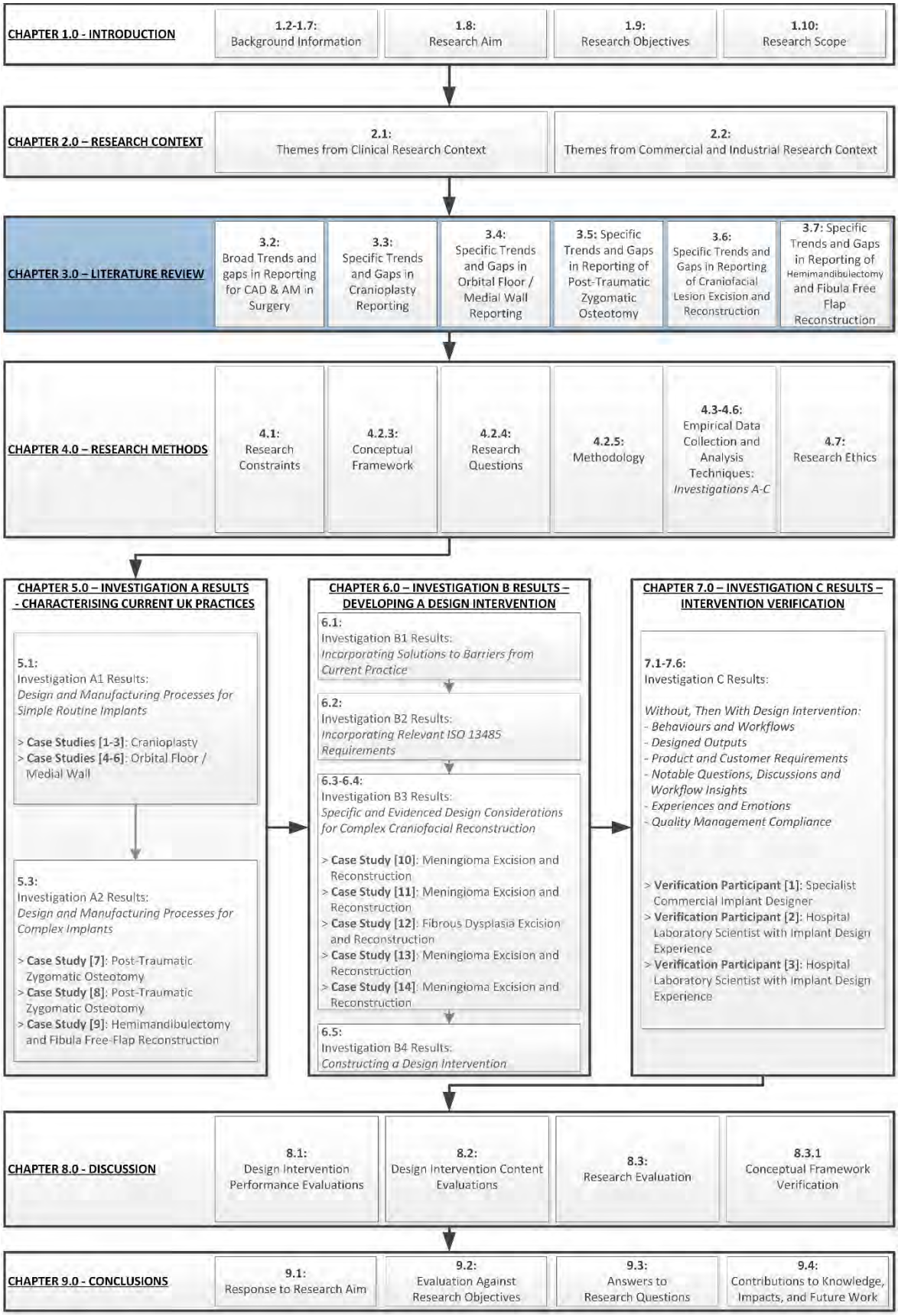


Figure 27 - Thesis Overview, With Current Location Highlighted (Chapter 3)

3.1. Overview - Themes

Published evidence has established clinical and technical efficacy for CAD, AM, and CNC in planning and producing patient-specific surgical devices. These tools have been successfully exploited to produce: patient-specific anatomical models (Mankovich et al., 1990, Petzold et al., 1999, Sanghera et al., 2001); pre-operative and intra-operative shaping jigs (Murray et al., 2008, Stoodley et al., 1996, Bartlett et al., 2009); digital surgical plans (Olszewski et al., 2010, Mertens et al., 2013, Essig et al., 2011); custom drilling guides (Vrielinck et al., 2003, Bibb et al., 2009, W. Joerd Van der Meer, 2012); custom cutting guides (Levine et al., 2013, Schepers et al., 2012, Gerbino et al., 2013); custom bone re-positioning guides (Herlin et al., 2011, Li et al., 2013a, Ciocca et al., 2012b); and custom implants in titanium (Lethaus et al., 2014, Jardini et al., 2014, Salmi et al., 2012) or polyether ether ketone (PEEK) (Alonso-Rodriguez et al., 2015, O'Reilly et al., 2015, Guevara-Rojas et al., 2014). However, due to: the relatively small number of published cases; the short follow-up periods; inconsistencies between a broad range of software tools and procurement approaches; and a general trend in the literature to skip detailed device design analysis; commonly agreed design considerations do not yet exist for use by design engineers or surgeons.

There are numerous potential reasons why AM is still not fully integrated into everyday practice. Multiple studies have demonstrated positive technical applications of a CAD and AM / CNC, but very little evidence has been published relating to the economic viability of the techniques and how they may best fit the constraints of healthcare systems and existing workflows (per Chapter 2.1.3). This could be a cause for scepticism and concern within a profession and health service that must be critical of new techniques; where improved patient outcomes and economic viability are of utmost importance.

Best practice in planning for complex maxillofacial surgery involves close collaboration between surgeons and technicians (Sugar et al., 2004). This collaborative approach across hospital laboratory and surgery departments, originally led to well-established and widely-accepted conventional and hybrid techniques to design and fabricate patient-specific implants, and supporting devices such as cutting guides (Thomas et al., 2013). In the last decade, improvements in dedicated software to assist 3D surgical planning have increased the capacity to undertake complex procedures with greater degrees of

accuracy (Adolphs et al., 2013). Even with specialised 3D planning software, proven AM technologies, and well-established laboratory-based fabrication techniques, the design and production of patient-specific implants remains a relatively time consuming, labour-intensive, multi-disciplinary and highly skilled process, that is inherently expensive – regardless of the nature of the techniques used.

3.2. Broad Trends

3.2.1. Reporting of Polymer AM in Medicine

In the UK, the AM equipment, build materials, and operational expertise have traditionally been too specialised and expensive for the majority of hospital units to own and operate in-house (Bibb, 2006). As a result, the AM equipment and expertise was still generally located in, and services provided by universities, research institutes and private enterprises – with all of the associated profit margin imperatives, data transfer security implications, and delivery intervals which that entailed. However, some mid-range professional machines have (in the last decade) come within reach of larger units with technologically driven staff, as demonstrated by Aleid et al. (2010). As equipment prices continue to fall (Wohlers, 2018), it is reasonable to expect this trend to accelerate – particularly in light of the hype highlighted in Chapter 1.0.

Desires to undertake polymer printing in-house may have been driven in-part by frustrations with the time taken for prints to arrive by courier. Kozakiewicz et al. (2009) reported that this was the most time-consuming in the entire requisition process. These understandable frustrations do not however, justify the increase in reports of low-cost consumer-grade desktop printers being inappropriately deployed to build transient surgical devices. For example, Huang et al. (2015) describe their innovative and pragmatic use of a Makerbot Replicator 2x (Stratasys, USA) to fabricate surgical drilling guides; but do not directly or indirectly address any process validation, material safety, or regulatory compliance issues to justify the choice of tool. This is especially significant in light of the large degree of variation between

potential cleanliness levels, from even mid-range (professional-grade) printing processes (O'Malley et al., 2016).

3.2.2. Reporting on Anatomical Models

With the clinical validity of anatomical models long established, more contemporary studies have focused on making narrower measurements: of differences in the accuracy of models produced by modern AM processes (Salmi et al., 2013); of the effects of input scan-data type on model accuracy (Primo et al., 2012); and of Hounsfield unit values for various AM samples when scanned using CT (Bibb et al., 2011). As the oldest validated application for AM in medicine, it is not surprising that the scope for new *novel* research into medical models has been drastically reduced. The most recent studies, such as those by Chae et al. (2015), Friedman et al. (2015), Mendez et al. (2015), and Legocki et al. (2017), demonstrated a shift in focus – towards navigating radiologists and other hospital staff through the AM equipment marketplace, and through the technical pitfalls of low-end, consumer-grade printing. These included the technical difficulties associated with warping, and support structure removal; particularly for complex geometries (Pei et al., 2011). This expansion of active stakeholders reflects the increased move of design and AM capabilities to hospital settings. Other authors make wider assessments of this trend, by exploring centralisation of printing services in hospitals and regions (Eley, 2017), and by highlighting the discrepancies in the regulatory burden between industrial printing, and point-of-care printing (Christensen and Rybicki, 2017).

It can be reasonably concluded that modelling literature has evolved from proving technical and clinical efficacy, to addressing structural and service delivery barriers which block routine AM adoption. This is an important development – because it probably foreshadows the journey which is also required for surgical guide and custom implant literature. Said journey appears to have begun, as will be highlighted in the following sub-Chapters. However, the more sensitive nature of transient use devices and permanent implants, in combination with their more recent introduction and shorter follow-up timelines, mean that they lag behind the maturity of anatomical modelling studies.

3.2.3. Reporting of Virtual Surgical Planning and Patient-Specific Guides

A wide range of software tools were demonstrated to be functionally suitable for planning: from mainstream engineering CAD software (Stojkovic et al., 2010); to voxel modelling software with a haptic interface (Bibb et al., 2009); two-dimensional graphical software programs (Shapií et al., 2012); and specialist medical planning packages (Adolphs et al., 2013) which channel users downstream towards proprietary device design services. There was no consensus as to which approach is most effective in terms of economics or training requirements. This factor is closely related to service delivery and the design context – addressed in Chapters 3.2.9 and 3.2.10.

Guided surgery has been demonstrated to translate digital plans accurately while reducing operation durations (Tarsitano et al., 2016, Honigmann et al., 2016); even when comparted to cutting edge robotic approaches (Jaffry et al., 2014). In a slight variation, Mazzoni et al. (2015) successfully used custom drilling guides for pre-planned orthographic surgery. The resulting holes were used to fix custom implants which doubled as positioning guides to pull the bones into position. The authors described design details to a moderate degree – noting for example, deliberate avoidance of teeth roots, and the inclusion of backup screw holes.

Like with digital planning in isolation, relatively few authors have explored the rich verification possibilities offered by making comparisons between guided surgical intent and post-operative CT scans (O'Malley, 2016), or with post-operative radiographs (Weitz et al., 2016, Shehab et al., 2013). Reports with these levels of quantified objective verifications (as opposed to more subjective and descriptive clinical verification) were the exception, not the rule. Consensus was lacking on prescribing post-operative CT follow-up scans as a matter of routine; thanks to the clinician's obligation to balance increased radiation doses (Weitz et al., 2016) with the myriad visual and statistical outcome measures made possible by CT, such as those measured by Lin et al. (2015).

Justifications for the use of surgical guides for specific procedures ranged widely in scope and fidelity. Typically, Wong et al. (2015b) justified their use of SLS cutting

guides in pelvic tumour resection on the grounds of procedure complexity (by relating restrictions in tumour site access to restrictions on resection trajectories). Similarly, the even greater-than-normal importance of accuracy, justified guided revision fracture reduction surgery in the arm (Honigmann et al., 2016). Mitigation of particularly elevated risk was the primary driver for Chen et al. (2016b), in exploring pedicle screw drilling guides for spinal surgery. Free-hand error rates can be as high as 30-40% and interference with the nerve bundle can have devastating functional impacts for the patient (ibid). Similarly, the mitigation of known risks from unsatisfactory existing approaches played into work by Soleman et al. (2015). They emphasised a relapse rate of up to 65% for paediatric cranial synotosis patients who had their affected bones re-shaped conventionally, without guides. This very high rate justified the extra pre-operative time invested by the authors for iterating and optimising their plan.

A key trend for justification emerged with a report by Li et al. (2016), who addressed tumours affecting the mandibular condyle. They registered CT data with scans of dental casts for high imaging accuracy around the occlusion; and said occlusion was adjusted in-theatre using custom AM positioning wafer guides, following osteotomy. Their emphasis was on improving the performance of novice surgeons in a procedure which was highly dependent on surgeon skill and experience. However, they also noted that their approach may have been cumbersome for experienced surgeons, and lacked accurate pre-operative soft-tissue simulation – leaving some patients disappointed with their outcome. Other justified innovations included drilling and positioning guides for total shoulder arthroplasty; devices which assumed increased significance in the absence of definite or reliable anatomical landmarks (Gauci et al., 2016). Once again, surgeon experience was raised as a significant justification – with 80% of procedures being undertaken by surgeons who performed fewer than 10 cases each year (ibid). The shoulder guides served to position guide wires; the subsequent manipulation of which achieved the desired downstream outcome. Several instances of this guided-guidewire technique recurred in orthopaedics literature about: revision foot surgery (Hirao et al., 2014); revision radius fracture reduction surgery (Honigmann et al., 2016); and complex tibial fracture surgery (Huang et al., 2015). But only Hirao et al. (2014) described the value of the K-wire approach – which facilitated easy visual alignment for the surgeon.

Many reports exhibited either continued low fidelity in their discussions and justifications of methods; or demonstrated ignorance of previous work. This led to some unjustified decision-making which went wholly unexplained, such as that by Liang et al. (2017). They used digital design and AM, but only as far as producing modular implants in discrete sizes; and entirely without comment on the cutting guide literature. Nkenke et al. (2016) used anatomical models and digital surgical planning, but failed to explore (or to explicitly discount) the use of patient specific surgical devices. This was despite having all of the workflow pre-requisites in place. Huang et al. (2015) described a technically complex, but relatively inefficient method for reducing complex fractures by using custom guides and reverse-engineered off-the-shelf implants. One can speculate as to the cost or inventory-based justifications for adopting this approach, but it was not openly addressed. Under-reporting posed (and continues to pose) a persistent obstruction to cross-disciplinary research across engineering and clinical perspectives. After all, the examples above were published in established, peer-reviewed journals, within three years prior to writing. The first AM surgical guide reports emerged towards the end of the last decade (Bibb et al., 2009).

The most significant barriers to the use of guides which were identified in those reports *with* justifications for the extent of digitisation, was that of tumour margin-uncertainty. Reiser et al. (2015) affirmed that tumour margins could only be finalised during surgery; and thus ruled-out the use of custom guides and custom implants in mandibular reconstruction. They proposed a partial-plan, and a polymer-printed tray-like guide which cradled the bottom of the residual mandible and subsequently, the manually harvested fibula graft segments. Whilst being a novel and, on its own terms, successful technique, this was at odds with the majority of the rest of the surgical guide literature; which did demonstrate the successful pre-planning of safe margins. Indeed, in a review by Kirke et al. (2016), the improved anticipation afforded by planning was a specific driver over and above margin certainty. More simply, Mazzoni et al. (2013) defined a two-week limit between scan and surgery to mitigate margin problems. Aranda et al. (2015) shared similar margin concerns as Reiser, but described a different philosophy to overcoming them in chest-wall tumour resection and reconstruction. Again, they asserted that tumour resection margins could only be definitively determined intra-operatively; which this time permitted the use of both planning *and* a cutting guide, but ruled out the use of a

precisely sized patient specific implant. Their highly refined sternum and articulating rib implant included clamps for gripping the residual rib bones. Those clasps were adjustable (laterally away from, and medially towards, the fixed sternum component) to adapt to potentially modified margins, relative to those which were planned and translated by the guide. However, the relevance of such a sophisticated implant to other less complicated, non-articulating applications was not addressed.

Surgical navigation references were the major 'competitor' to surgical guides, in terms of accurately translating a surgical plan into the realities of the operating theatre. Surprisingly, in light of the prevalence of, sophistication of, and relatively long history of navigation publications (Watzinger et al., 1997, Gellrich et al., 2002, Lübbers et al., 2011, He et al., 2013), physical guides were mostly preferred when directly compared. Navigational drawbacks included: process complexity and hardware cost (Shuang et al., 2016, Ma et al., 2016, Collyer, 2010, Mazzoni et al., 2015, Kaneyama et al., 2015); and longer surgeries (Chen et al., 2016b, Wong et al., 2015b). Most promisingly in terms of encouraging the routine use of CAD and AM, guides were able to succeed in plan-translation even when the anatomy of interest moved (Kaneyama et al., 2015). Furthermore, guides were stable enough to permit one-handed use (Chen et al., 2016a).

Finally, for planning and guides literature trends, there were surprising gaps relating to material choice justifications and the implications of these choices. Bibb et al. (2009) stated that metallic guides can be thinner, which can result in smaller excisions. Generally though, the guide material and printing process choices were noted in a strictly procedural, matter-of-fact manner. Dong et al. (2017) produced an extremely valuable study about the accuracy of three different cutting surface designs. However, even here there was no mention of wear debris, the mechanical performance of the guide, or the precise nature of the friction interface between bone and guide.

3.2.4. Reporting of Metal AM in Medicine

For metal-based AM, the even higher costs relative to polymer AM (Wohlers, 2018) for expertise, equipment, materials, standards compliance, insurance, and post-

processing facilities, mean fabrication outsourcing is usually unavoidable; just like in the early years of polymer AM in surgical applications. The literature evidenced metal printing (and often design) services being delivered by commercial companies which are external to the hospital, including: Mobelife (Belgium) (Wong and Pfahnl, 2016); Anatomics and CSIRO (Australia) (Phan et al., 2016); Renishaw (UK) (Goodson et al., 2017); and KLS Martin (Germany) (Toso et al., 2015). In-house metal printing for medical institutions themselves appeared to be limited to specialist military institutions (Aita-Holmes et al., 2015, Green et al., 2016, Turna et al., 2014) and possibly to those co-located within universities with collaborating engineering departments. The setup, workflows, and financial implications were often difficult to infer, because service structure was another under-reported dataset in journal articles.

As a result of the physical location of metal AM machines, there were none of the 'democratising the process' articles about how best to operate and situate lower end machines. Instead, technical articles were focused on parameters for laser power, scanning strategies, or powder makeup (Kruth et al., 2005, Mercelis and Kruth, 2006, Ljungblad, 2010). This was to be expected, with industrial experts and engineering researchers primarily talking to each other when they publish. Robust design procedures and expertise are yet to make any widespread move in-house to UK hospitals; let alone optimised metal AM fabrication which is fully-compliant with regulations. It is reasonable to expect the specialist metal AM literature to continue to reflect this technical focus for some time.

3.2.5. Reporting of Metal Implants - CAD and AM (or CNC)

Those major categories of AM / CNC implant factors highlighted above, were not addressed universally across papers; rendering comparisons difficult. Unfortunately, reporting consistency remained a problem for both research and clinical purposes in other ways too; with no standardised approach to quantifying outcomes. Usually, post-operative subjective judgements were used (Rotaru et al., 2015, Cabraja et al., 2009, Watson et al., 2014, Kirke et al., 2016) which, may be entirely appropriate. It could even indicate an over-emphasis by authors on achieving high technical accuracy; but this reasoning, if true, was not elucidated. Important details, such as

statements about specific printer models, or specific software programs, were frequently left unaddressed. Even when they *were* acknowledged, they were presented in vague ways which were unsatisfactory for allowing study reproduction, or for allowing proper criticism of methods (Hsu and Ellington, 2015, Aranda et al., 2015). In the future, greater clarity from regulators about what they deem to be acceptable validation procedures may offer an indirect route to improving AM implant reporting. Patient-specific implants lack standardised and commonly accepted validation routes or definitive acceptance criteria (Phan et al., 2016, Morrison et al., 2015). As such, authors often simply compared aspects of their implant performance against the most-similar stock devices (Mroz et al., 2015). Some authors verified the mechanical performance of their implant designs using FEA (Nasr et al., 2017, Sutradhar et al., 2014, Li et al., 2014, Harrysson et al., 2007) but again, this was done using varied methods and arbitrary criteria.

Many authors have experienced one or a combination of the highlighted CAD/AM implant benefits, in scenarios ranging across: cranioplasty plates (Poukens et al., 2008); orbital floor reconstruction implants (Salmi et al., 2012), total mandible replacements (Xilloc, 2012); mandible plates (Bibb et al., 2015); prosthesis retention devices (Toso et al., 2015); orbital rim reconstructions (Eolchiyan, 2014); zygomatic contouring implants (Rotaru et al., 2015); spinal implants (Phan et al., 2016); pelvis implants (Chen et al., 2016b); ankle implants (Hsu and Ellington, 2015); knee implants (Bibb et al., 2015); humeral plates (Shuang et al., 2016); and acetabular cups (Wong et al., 2015b). Despite this breadth of reported applications, publications almost always focused on an individual case study or small case series. Subsequently, studies often identified their own weaknesses as being characterised by limited follow-up periods and limited case numbers (Phan et al., 2016, Ganry et al., 2017, Mao et al., 2015) but this was difficult to reconcile with the unavoidable nature of those temporal constraints; which were after-all contingent on the relatively recent introduction of CAD and AM implants.

On an individual paper-by-paper basis, the sample size weaknesses were possibly over-stated relative to the reporting fidelity weaknesses, but they were important to acknowledge nonetheless. Routine use is difficult to achieve without more evidence, and more evidence is difficult to achieve without large samples resulting from routine use. However, these criticisms are valid in light of a rightly risk-averse sector which

takes a long time to accept new developments (Pucci et al., 2017). The burden of proof remains on CAD and AM advocates. More multi-centre studies, large case series (such as (Lethaus et al., 2014)) and randomised control trials or prospective studies (in the vein of (Shuang et al., 2016)) will be required in the future; and the results should be reported in a standardised format (Martelli et al., 2016, Mitsouras et al., 2015). The latter point can be addressed fairly quickly, in that there is a clear scope for *better* reporting of small case series or individual case studies in the short term, even while unavoidable case quantity and follow-up limitations inevitably take longer to fix.

Most obviously, echoing the commercially-driven and systemic publication bias in pharmaceutical literature (Goldacre, 2013), *no* examples of published AM implant failures or, perhaps even more importantly, *aborted* CAD/AM implant projects were found. These could have provided highly valuable design process lessons – possibly permitting better anticipation of mistakes in processes, and in design-detail decision-making. In their review, Martelli et al. (2016) noted that twice as many benefits as drawbacks were published across device literature; further emphasising the massive scope for publishing negative results in the future. Of those drawbacks to digital implants which *were* occasionally cited, the most frequently stated were: higher up-front costs (Wyatt, 2015, Lethaus et al., 2014, Ciocca et al., 2012a, Ciocca et al., 2012b, Mobbs et al., 2017); relatively long planning and production times compared to stock parts (Wong et al., 2015b, Kirke et al., 2016, Mazzoni et al., 2015); and reduced intra-operative adaptability (Tarsitano et al., 2016, Duttenhoefer et al., 2017, Kim et al., 2017).

3.2.6. Reporting of PEEK Implants

In the custom implant literature, published case numbers (or case series) demonstrated a slight bias towards the use of PEEK. This is likely attributable to its longer history in commercial custom device services, thanks to relying on more conventional subtractive machining. PEEK devices were reported to exhibit greater similarity than titanium to bone strength, stiffness, and elasticity; which can reduce stress shielding and bone resorption (Lethaus et al., 2014). Moreover, PEEK devices promoted better patient comfort compared to titanium – by exhibiting lower thermal

conductivity, lower density, and a lighter weight (Shah et al., 2014). PEEK's radiolucency was often cited as a major benefit – for improved post-operative imaging (Rudman et al., 2011, Eolchiyan, 2014, Manrique et al., 2015, Camarini et al., 2011) which was particularly valuable in oncological patient cases. Authors highlighted PEEK's suitability for intra-operative shape adjustments using burrs; which was necessary on an infrequent to moderate basis (Alonso-Rodriguez et al., 2015, O'Reilly et al., 2015, Jalbert et al., 2014, Pritz and Burgett, 2009, Adetayo et al., 2015, Manrique et al., 2015). Details about the precise reasons behind the need for these adjustments were not covered in depth. This was especially true in terms of causes related to poor design process decision-making.

Patient-specific PEEK implants were planned and designed using a similar array of tools and workflows as was evident for titanium implants. Such are the increased prices of PEEK material relative to AM powder, previous work cited external commercial service providers as the primary sources of design and fabrication. Indeed, very high up-front costs proved to be the overwhelming barrier to the routine use of PEEK (Shah et al., 2014, O'Reilly et al., 2015, Thien et al., 2015); in addition to its inherent bio-inertness (Kurtz and Devine, 2007), and consequent need for coatings where bone on-growth is desired (Walsh et al., 2015). Subsequently, there were no examples of in-hospital PEEK implant fabrication. PEEK has been successfully applied to: orbital and zygomatic reconstruction (Goodson et al., 2012); assorted bone deficiencies of the midface (Scolozzi, 2012); cranioplasty (Hanasono et al., 2009); and complex craniofacial reconstructions (Alonso-Rodriguez et al., 2015).

3.2.7. Reporting of Functionalisation - Microporosity

Evidence for particular surface treatments and coatings on AM titanium or PEEK implants was common; but was often presented from a predominantly technical-mechanical (Ruppert et al., 2017) or biochemical perspective (Zhao et al., 2013b); without proper design consideration of when *particular* manipulations were most appropriate. Given the prevalence of fundamental science papers, one can attribute this deficiency to the relative immaturity of work on this topic. There was a gap between principles and application. This was especially true in the absence of

explicit design rules or considerations for coatings on *specific areas* or features of given implant types. Though relevant far beyond microporosity, the emphasis Salmi et al. (2012) placed on using clear documentation as a vehicle for improved clarity across competences, was perhaps most evidently needed here. Many papers specified particular finishes (such as Turna et al. (2014) and Jardini et al. (2014)), without properly (or even partially) justifying their choices. On the whole, microporosity was a tangential issue in this research – and is just another design requirement or product specification point. But its treatment by authors was indicative of wider trends.

Deliberate manipulation of implant surface microporosity has been used to improve osseointegration; to kill bacteria (Necula et al., 2013); and to deliver drugs (Perez and Mestres, 2016). Although PEEK was mainly bio-activated via titanium coatings (Han et al., 2010) or ceramic coatings (Mao et al., 2015); Zhao et al. (2013b) uniquely created a nano-structured surface network via sulfonation. However their work lacked in-vivo human results. Titanium implants too, were coated to improve osseointegration: by plasma spraying (Walsh et al., 2015); AM itself (Ruppert et al., 2017); or otherwise roughened by sandblasting, chemical modification, or acid etching (Tan et al., 2017). One potential drawback was highlighted by Necula et al. (2013) in noting the brittleness of plasma-sprayed coatings; which may negatively impact the mechanical properties of the underlying implant.

3.2.8. Reporting of Functionalisation - Macroporosity

Titanium has been demonstrated to more closely match the stiffness of bone when porosities are introduced into their structure (Schouman et al., 2016). However, no comprehensive or universal criteria existed for lattice cell designs relative to their intended effects (Tan et al., 2017). One of those desirable effects was bone in-growth. By aiming for a pore size of between 300 and 600 microns, an interconnected porosity of no less than 40%, and a graded pore size moving from smaller deeper pores to larger superficial pores, a starting-range of promising cellular design specifications could be extracted from publications which aimed to improve osseointegration (Tan et al., 2017, Arabnejad et al., 2016, Perez and Mestres, 2016). Cellular lattice designs within those parameters sought to optimise the balance

between nutrient flow, waste flow, vascularisation, cell anchorage, surface area, and mechanical strength.

Evidence for the manipulation of macroporosity to optimise mechanical properties and encourage implant-bone integration (Liang et al., 2017) generally suffered similar weaknesses to those for microporosities. Correlation was observed, without being able to consistently prove causation. Often, the mere absence of implant loosening was enough to claim validation for a lattice design (ibid). Other authors quantified bone integration (Arabnejad et al., 2016, Wieding et al., 2015) but through in-vitro studies, or in animal models. Kim et al. (2017) represented a potential maturation of the literature on this topic, towards application, as they combined both clinical assessment and imaging verification to provide robust claims about implant stability. As with so much of the surgical AM literature though, evaluations of the effects of a design decision (e.g. porosity) were impossible to compare to a control. Overall, macroporosity manipulation was of most concern to load-bearing orthopaedics publications and as such, did not play a major role in the maxillofacial-specific literature, beyond establishing itself as another potential field in the design specification or requirements list.

3.2.9. Reporting of Design and Collaboration

Generally, design workflows were outlined in functional stages (Chahine et al. (2008); Singare et al. (2009); Cevidanes et al. (2010); Derand et al. (2012); Khan and Dalgarno (2009)); with little consideration given to optimising user interactions or interfaces (either between collaborators or with software tools). Truscott et al. (2007) underscored the need for better software and more effective communication to minimise design iterations in collaborative working. Cronskar et al. (2012) highlighted the need for process refinement and greater user-friendliness for surgical co-operators, particularly in enabling them to undertake planning aspects of the design process themselves. The relative merits of outsourcing, versus upskilling healthcare practitioners has not been investigated thoroughly for patient-specific implants and guides. As a result, outcomes in maxillofacial laboratories remain dependent on the contextual factors highlighted in Chapter 2.1. Paterson et al. (2014) supported the retention of practitioner input, skills, and expertise when designing a

different kind of patient-specific device - AM wrist splints. Aside from potential job redundancies, they noted that CAD automation approaches, as opposed to creating new sympathetic software tools, would likely result in mistranslation, errors, and so increased costs, and frustration. However, this work cannot be overlaid directly on the maxillofacial context, due to the increased complexity and resource requirements created by regulatory requirements, quality management standards, and the additional consultant surgeon stakeholders. No work was found addressing the relative merits of surgeon design versus laboratory technician design.

Reports noted an inherent difficulty in designer-clinician teamwork because of divergent technical languages and terminology (Mazzoli et al., 2009), with clear documentation becoming more important as a result (Salmi et al., 2012). Face-to-face relationships could improve the process (using the available design tools) by facilitating interpretation as well as communication (ibid); though this reduced efficiency. No work was found on the economic efficacy of (or specifications to enable) the transfer of implant modelling responsibility from specialist design-engineers towards in-house, non-CAD-specialist clinical staff. Even with mid to low-end AM machines becoming increasingly affordable to individual hospital units (Chae et al., 2015, Friedman et al., 2015) effective patient-specific device design still remained contingent on close multidisciplinary collaboration for some authors; across engineering and clinical specialties (Huotilainen et al., 2013); because the successful operation of design software usually required specialised skills which most surgeons did not have (Martelli et al., 2016).

These context-specific examples corroborated some analyses from, and were lacking in other aspects of, research into other examples of interdisciplinary design collaboration. Pei et al. (2010) identified key collaboration problem areas between industrial and engineering designers, and proposed a solution - by way of ensuring consistent shared understanding of intra-team visual design representations, their purposes, and their limitations. Disharmony during product development occurred when team members approached a project with different training, communication methods, and principles (ibid). While this is certainly the case for designer and surgeon approaches, it has not been investigated in the surgical device context. The effective communication of design concepts, by deploying both functional and non-functional representations, are pre-requisites for avoiding rework and delays

(Alisantoso et al., 2006) but were not examined in this most time-sensitive of fields. Likewise, the implications for reaching the correct people with design information across organisations (Chiu, 2002), such as between implant supplier and surgical department for example, remain unaddressed except by regulatory implication. Furthermore, the social dynamic between design collaborators, including factors associated with trust, power, control, transparency, and understanding have been explored in management research (Jassawalla and Sashittal, 1998) but not, almost by necessity, in the emerging context of intra-hospital design collaboration.

Clinical papers about individual cases (or case series) often overlooked detailed reporting of device design specifications, device modelling operations, or device detailing decisions. This could have been because the production processes which were undertaken by some external commercial companies were relatively detached from the surgeon; with limited collaboration beyond an initial device request (Marbacher et al., 2011, Camarini et al., 2011). Alternatively, this may simply have been because the importance of including such details for a wider audience (including design engineers) was overlooked - in favour of detailed descriptions of the pathology and the surgical procedure. Published cases generally described and justified material choices and the application of a conventional or digital approach, at least at a broad level. Similarly, there was often little detail on implant shape; beyond the near-universal recommendation to mirror contralateral healthy anatomy wherever possible (D'Urso et al., 2000, Pritz and Burgett, 2009, Scolozzi, 2012, Mertens et al., 2013, Stoor et al., 2014, Watson et al., 2014, Rotaru et al., 2015, Eolchiyan, 2014, Jalbert et al., 2014). Where design details were described, no effort was made to investigate how far one could generalise and synthesise a given consideration across surgical scenarios.

Linking well with the quality management issues raised in Chapter 1.6, and with the issues of inconsistent design approaches and reporting, Hollister et al. (2015) stressed the need for rigorous characterisation, documentation, and standardisation of design operating procedures. Crucially, they recommended a modular approach. This essentially equated to defining dynamic conditional parameter ranges for specific interdependent design characteristics. Although their work was related to tissue-engineering scaffolds, their assessment (that design control was dramatically underexplored as a valid research topic) corroborates closely with, and provides a

good label for, the weaknesses in previous work as a whole. Kinsel (2012) described an overview of design control requirements in a batch-production, USA context, with an emphasis on the design file. Morrison et al. (2015) published a similar review in a similar context; serving to further illustrate the obstacles to successful regulatory compliance. However, no work was found relating design control regulatory requirements, to patient specific device design performance characteristics. This is a highly significant gap, and one which will only grow in importance as the field continues to mature.

3.2.10. Reporting on Services

Articles alluding to the tools, contexts, and touch points of implant design and fabrication services were addressed throughout Chapter 2.2.1.1. Some further criticisms are made possible by connecting author perspectives to their conclusions and recommendations. Ma et al. (2016) claimed in-house designed and printed guides were highly cost-effective; but only accounted for the material costs of the small guides themselves. They overlooked costs relating to design time, training, software purchases, printer purchases, maintenance, and raw materials. The sensitivity of this field to cost implications has been made clear in every aspect of the literature review. Therefore, it is reasonable to question such incomplete assessments. Similar deficiencies were present in reporting by Mendez et al. (2015); which had the express aim of demonstrating in-house viability of model printing. Claiming unrealistically high commercial model costs (compared to other reports and institute experience) and wholly unrepresentative 2-3 week fabrication times, they again presented material costs alone, as the comparative in-house metric. Eley (2017) on the other hand, compounded their own vague claims of commercial-supplier drawbacks, by also explicitly referencing a financial crisis occurring within their own institution. With that major difficulty acknowledged, they proceeded to stress the necessity for expensive new in-hospital staff to operate their in-house service, and then noted their intention to purchase yet more high-end multi-material printing capability even in the face of lower-than-expected demand.

Collectively, studies with perspectives and weaknesses like these did little to quell an impression of politically-driven advocacy for certain service models. Surely, just

as the burden of proof is on CAD and AM advocates to prove their worth over stock parts; the burden of proof should be firmly on in-hospital staff to prove that planning, designing, and production should be performed by themselves. This is especially important in light of the potential for a downgrade in quality and safety compliance, compared to commercial providers, if capabilities are brought in-house without proper risk management and design control (Christensen and Rybicki, 2017). Finally, aside from safety and quality impacts, it was left to Roser et al. (2010) to uniquely describe *mutual* benefits for clinicians when working in collaboration with professional biomedical engineers. Their teamwork prompted trainee surgeons to learn more about techniques, anatomy, and healthcare resource allocation. It also allowed surgeons of all levels to dedicate more of their focus to their particular, more exclusive areas of expertise.

3.3. Key Surgery Focus – Simple Routine Implant – Reporting on Cranioplastys

Generally, implant geometry was reported to be based on mirroring contralateral healthy anatomy – unless the defect crossed the midline, in which cases contours were assessed for aesthetic continuity with surrounding tissues (Bibb et al., 2002). Edwards (2007) highlighted the importance of keeping cranioplasty implant extents as small as possible – to reduce the size of the raised skin flap. Raising the skin flap is the most time-consuming stage of the surgical procedure (Koppel et al., 1999). After inserting the implant, suturing without tension of the skin is essential to prevent implant exposure (Carloni et al., 2015). This can be achieved by using skin expanders (ibid) or by depressing the otherwise optimal cosmetic contours of an implant design before fabrication (Kung et al., 2013).

Previous studies have assessed the quantified geometric accuracy of: automated die design for hydroforming (Gelaude et al., 2006); differences between cast and machined polymethyl methacrylate (PMMA) (da Costa and Lajarin, 2012); an algorithm for implant design based on combining low-resolution diagnostic CT scans with high-resolution surgical-planning scans (Liao et al., 2011); an algorithm for cranial defect reconstruction with depressed contours to ease wound closure (Kung et al., 2013); and the degree of compliance of a conventionally-pressed titanium plate with the edge of defective anatomy. In many studies however, the evaluation of cosmetic outcomes was again based

on subjective judgements by patients and / or clinicians - in person or via imaging (Cabraja et al. (2009); Stoodley et al. (1996); Morrison et al. (2011); D'Urso et al. (2000); and Kim et al. (2012)).

If implant accuracy is taken as the degree to which the final implant form matches a pre-defined ideal result, no published literature was found with quantified accuracy comparisons between conventional and CAD/AM production techniques. Such evidence may contribute to capturing any differences between the high-skill, artisanal results of current laboratory or digital methods (D'Urso et al. (2000), Gelaude et al. (2006)) and the comparatively de-skilled, potentially more accessible, digital methods.

3.3.1. Autologous Reconstruction

Reconstructing with the patient's own bone flap (after storing it cryogenically, or in the patient's abdomen post-craniectomy) is still, strangely, considered the 'gold standard' (Klammert et al. (2010); Lethaus et al. (2012b); Alonso-Rodriguez et al. (2015)). This was surprising – given the frequency of major bone resorption which required revision surgery (Stieglitz et al., 2015). Patients with PEEK or Titanium cranioplasty implants experienced lower complication rates and shorter hospital stays than patients with re-implanted bone flaps (Lethaus et al., 2014), but prices were higher. This was potentially a further indication of the enormous influence of cost on accepted best-practice. Lethaus et al. (2014) also noted the relatively short follow-up history for alloplastic materials – which may have indicated the reason for an enduring 'gold standard' label resting with bone flaps.

However, when successful, the autologous approach can result in complete biological integration (Alonso-Rodriguez et al., 2015). Furthermore, Lauerman and Stein (2015) recommended recreating the original cranial vault volume to avoid potential complications – if the swelling is low enough. Logically, replacing the full-thickness of original cranium – by using the original portion of cranium itself – is one method of achieving this.

3.3.2. Alloplastic Reconstruction

Cranioplasty crosses neurosurgery, maxillofacial surgery, and (for alloplastic solutions) maxillofacial prosthetics. This probably explains the large volume of studies about the procedure, relative to the other key surgery focuses in this Chapter. It is also clearly still a major topic of disagreement, or at least, different preferences. The use of acrylic (PMMA) has been commonly described – thanks to its low cost, and ability to be easily shaped (D'Urso et al., 2000). Implants can be fabricated intraoperatively – mixing a liquid polymer and powdered monomer before forming the flowing material manually as it polymerises – and can be adjusted using burrs after hardening (Eppley, 2003). Alternatively, the implants can be pre-formed via a moulding technique (D'Urso et al., 2000) – saving time in-theatre. However, Vahtsevanos et al. (2007) list several major disadvantages including: incomplete biological inertia, tendency to fracture, high local temperatures (during intraoperative polymerisation), and inflammatory scarring. Other intraoperatively shaped materials included titanium mesh and hydroxyapatite - the latter can exhibit bioactive behaviour and avoids many of the listed problems with PMMA – but does require a dry anatomical defect site and takes longer to set (Eppley, 2003).

Assessing the nature of a craniectomy defect during pre-operative alloplastic implant planning used to involve taking an impression manually – through the patient's skin-flap (Koppel et al., 1999). In the 1990's, techniques were developed for representing defects using stacked cross-sections derived from individual scan-data slices (Stoodley et al., 1996) and milled polyurethane foam models (Joffe et al., 1999). Now, the conventional approach in the NHS can be characterised as utilising AM medical models (Edwards (2007), Bartlett et al. (2009)).

It is these models on which the hospital-laboratory design and fabrication processes for common pressed titanium implants are based. This process results in implants which: can achieve aesthetically pleasing results in a material which is strong and dimensionally stable (Bartlett et al., 2009); are inexpensive; which can be adjusted in-theatre by trimming or bending, and which have excellent biocompatibility (Eppley, 2003). However, the specific methods employed by UK practitioners vary widely in terms of post-processing stages, post-processing tools, contamination of the underlying commercially pure titanium; and do not follow international standards

for manufacture (Davey, 2017). In the published literature, the highly-skilled, combined design-and-fabrication process is undertaken by maxillofacial prosthetists or laboratory technologists – and not by the operating surgeon as referenced in autologous reconstruction and acrylic examples. However, surgeon-consultation was recommended by Edwards (2007). Similar implants were produced by pre-shaping titanium mesh (Thien et al., 2015) or in a non-NHS laboratory setting, by hydroforming titanium sheet (Gelaude et al., 2006).

3.3.3. CAD and AM / CNC Implants

Digitally designed cranioplasty implants have been fabricated from: titanium using AM (Poukens et al. (2008); Lethaus et al. (2012b); Jardini et al. (2014)), titanium using CAM (Eufinger et al. (1998); Eolchiyan (2014); Cabraja et al. (2009)), and from PolyEther Ether Ketone (PEEK) using CAM (Lethaus et al. (2014); Ko et al. (2014); O'Reilly et al. (2015); Thien et al. (2015)). Lethaus et al. (2014) emphasised the relevant benefits of PEEK in relation to AM titanium. PEEK, with an elastic modulus of 3.7 GPa, is closer in stiffness to the surrounding bone (0.5-20 GPa) compared to titanium alloy (114 GPa) (Parthasarathy et al., 2010, Toth et al., 2006). Properly loading the bone by using PEEK, or porous titanium can prevent bone resorption and implant loosening caused by stress shielding (Parthasarathy et al., 2010). It has a lower thermal conductivity, lower density, and lighter weight than titanium – contributing to improved patient comfort (Shah et al., 2014) which is of a greater importance for large implants. PEEK cranioplasty implants can be modified in-theatre using burrs to accommodate deviations from a plan (Alonso-Rodriguez et al., 2015) and are radiolucent for post-operative imaging (Costello et al., 2010). Although AM Ti64AlV ELI cranioplasty implants are difficult to modify intra-operatively, the possibility of mitigating this issue through robust design processes, which build-in flexibility, and collect high-fidelity specifications, has been under-explored. Unsurprisingly, where often large cranioplasty implants were concerned, high upfront expense was frequently raised as a significant drawback (Shah et al. (2014); O'Reilly et al. (2015); Thien et al. (2015)).

3.4. Key Surgery Focus – Simple Routine Implant – Reporting on Orbital Floors and Medial Walls

3.4.1. Autologous Reconstruction

As alloplastic materials gained acceptance over twenty years ago, bone graft reconstruction was recommended only for larger orbital defects - because bigger sheets of titanium mesh were difficult to remove thanks to connective tissue growth (Sugar et al., 1992). Mesh could address more complex defects (ibid). Since then though, autologous orbital reconstruction has appeared rarely in the literature. When it has, calvarial split bone grafts (from the superior aspect of the cranium) have been used in Germany, with excellent accuracy via navigation equipment, but no justification for the autologous material choices (Gellrich et al., 2002, Schmelzeisen et al., 2004).

3.4.2. Alloplastic Reconstruction

Conventional alloplastic orbital implants were divided between: custom manually swaged and pressed titanium sheet (Hughes et al., 2003); stock titanium plates which were manually pre-shaped - usually before surgery (Rana et al., 2012); stock titanium plates which were manufactured into population-averaged shapes (Lee et al., 2014); pre or intra-operatively shaped porous polyethylene (Podolsky et al., 2016); and pre or intra-operatively shaped titanium mesh (Kozakiewicz et al., 2009).

In the UK context, the first category was most prevalent. The semi-digital approach where a reconstruction is manually carved on an AM model of the defect, then using this as the basis for a press tool design, was first published by (Hughes et al., 2003). They reported good accuracy, correct placement, low costs, and a relatively simple production process. However, the design and fabrication process received only brief coverage – especially in relation to post processing specifics. This approach offered the best contour restoration accuracy compared to manually bent stock mesh, or manufactured average-shape stock mesh in a study by Strong et al. (2013). The

longevity and efficacy of this technique was further emphasised by Mustafa et al. (2011b) via their case series; and specific publications about CAD process refinements (Mustafa et al., 2010) and fabrication technique evolutions (Mustafa et al., 2011a).

Titanium mesh was employed both before medical models were in widespread use (Sugar et al., 1992), and long after their introduction (Kozakiewicz et al., 2009). Interestingly, even between these two groups, opinion was divided between those frustrated by cross-disciplinary and cross-location collaboration (ibid); and those embracing it (Sugar et al., 2004). Although pre-bending titanium mesh saves time in theatre compared to intra-operative bending, it shifts that time commitment to the planning stages, and still does not guarantee correct placement (Kozakiewicz et al., 2009). Titanium mesh can exhibit sharp edges after trimming, and exhibits poor contour accuracy when shaped intra-operatively (Strong et al., 2013). Crucially though, it can be stored on-hand, in-theatre to be used in emergency surgery – which is not possible for pre-bent mesh or custom titanium sheet implants (ibid). Alternatives to titanium for either pre or intra-operative shaping predominantly involve porous polyethylene. Indications for material choices were vague. van Leeuwen et al. (2012) specified minimum thicknesses for the given materials; which was of particular importance for porous polyethylene which is susceptible to peri-operative and post-operative sagging; so undoing any aesthetic correction.

Stock plates manufactured into average orbit shapes were shown to be useful in bilateral orbital fractures – where copying the contours of contralateral healthy anatomy was not an option (Lee et al., 2014). Trimming results in smoother edges, compared to mesh (Strong et al., 2013) and they are also readily available in the operating theatre. However, their utility and availability comes at an increased cost (ibid). Their long history and simplicity meant that further technique developments were limited to tangential issues such as soft tissue outcome simulations. Rana et al. (2012) used FEA calculations to predict the effect of alloplastic reconstruction on the globe and associated muscles. Their successful work focused on anopthalmic patients (with the absence of a globe); but the potential application to other patients was limited.

Given the low fidelity of these studies, especially in covering and justifying design details, even small improvements (such as authors justifying why unreported factors were deemed unimportant) could have enhanced the understanding of the author's purpose. An example of confused purpose was found in the article by Podolsky et al. (2016). They surprisingly claimed *novelty* for a technique where custom implant material was shaped against anatomical models; an approach reported many years prior in a basic form by Hughes et al. (2003), then developed by Mustafa et al. (2010) and expanded the following year (Mustafa et al., 2011b). Indeed, novelty in orbital floor implants has been mostly related to the use of AM since then (Salmi et al., 2012, Rana et al., 2012, Gander et al., 2015, Rana et al., 2015a); further compounding the difficulty in determining a reason for the study, or for its acceptance into a leading journal.

3.4.3. CAD and AM / CNC Implants

CAD and AM orbital floor implants have been fabricated using EBM (Stoor et al., 2014) and SLM (Rana et al., 2015c). They have also been fabricated from PEEK, in two parts which interlocked upon insertion (Goodson et al., 2012). CAD and AM implants have been judged more accurate than conventionally produced devices (Gander et al., 2015, Rana et al., 2015b), though suffer the now familiar drawbacks associated with cost – especially when used in conjunction with navigation equipment for placement verification (ibid). They have been based around both solid surfaces with venting holes (Gander et al., 2015); and mesh or lattice surfaces (Salmi et al., 2012) to target lower temperature sensitivity and so improved patient comfort, through mass reduction. Unfortunately, these studies manifest similar weaknesses as have been highlighted previously - such as missing key details about the success of e.g. temperature conductivity as was referenced above. Design aims were identified, but their success not evaluated. Gander et al. (2015) claimed that the planning process can be undertaken by "any" surgeon and that it requires no specialist knowledge. This directly contradicts many other reports from this Chapter – without evidence to support the claim. Lack of awareness regarding previous work also played a role in the conclusions drawn by Stoor et al. (2014); who did not anticipate intraoperative bending would result in a longer surgery compared to pre-operative bending.

3.5. Key Surgery Focus – Complex Unusual Implant – Reporting of Post-Traumatic Zygomatic Osteotomy

3.5.1. Alloplastic Reconstruction

Previous published applications of digital planning encompassed navigation assisted surgery and surgical guides. He et al. (2013) used navigation to pre-plan and then verify the correct repositioning of the mobilised bone fragments. The zygoma lacks obvious landmarks and is irregularly shaped; so navigation was indicated to achieve good symmetry.

A polymer surgical guide replaced navigation in work by Herlin et al. (2011) to relocate a single mobilised bone piece (Herlin et al., 2011). More complex, comminuted injuries were reconstructed by Liu et al. (2013) using polymer AM positioning templates and titanium stock microplates. They recommended bracing the templates against uninjured, reliable landmarks like the residual zygoma; and minimising the thickness of the guide to reduce the size of the required incision. However, they did not acknowledge the possibilities of using metal AM guides or custom metal AM implants to optimise the incision size. Finally, they advocated for design by surgeons on account of their intimacy with the surgical procedure. Unsurprisingly, given the omissions from many other articles, the implications of this were not explored; on quality control, regulatory compliance, and explicit documentation.

3.5.2. CAD and AM / CAM Implants

There was no evidence found regarding prior application of digital planning, CAD, and AM or CAM custom implants to zygomatic osteotomy.

3.6. Key Surgery Focus – Complex Unusual Implant – Reporting on Single-Stage Craniofacial Lesion Excision and Reconstruction

3.6.1. Alloplastic Reconstruction

Complex craniofacial reconstruction generally occupies and overlaps the borders between simple cranioplasty implants, orbital reconstructions, and occasionally zygomatic reconstructions. The issues around material choice disagreement; methodology weaknesses; and reporting omissions were already evaluated in the preceding Chapters. Noteworthy reconstructions not already addressed included AM mould tools to pre-shape: titanium mesh (Sunderland et al., 2015) and bio-resorbable mesh (Murray et al., 2008). Finally, the use of a hard tissue replacement (Biomet, USA) implant made from PMMA spherical macrobeads that were coated and fused together with polyhydroxyethylmethacrylate (PHEMA) proved successful for (Rosen et al., 2008) and Pritz and Burgett (2009). The latter reports were especially unhelpful in their explanations of the material, its manufacturing process, its limitations, and its history. However, Rosen et al. (2008) highlighted a now common issue relating to margin uncertainty. They deliberately under-sized the implant and filled the resulting gap with bone cement – in order to increase flexibility and permit margin widening in-theatre. By using an implant material which could be adjusted using burrs, they also accommodated the unlikely need to use a smaller margin. The prevalence of this concern makes flexibility (relative to the plan) a key outcome from previous work.

3.6.2. CAD and AM / CNC Implants

Perhaps the greatest value from digital approaches is when implants are used to replace missing or excised bone with highly complex shapes - which would be difficult to accurately reconstruct using conventional techniques. Complex AM and CNC implants have been produced to successfully replace the temporal bone, orbital rim, sphenoid, frontal bone, and zygoma (Eolchiyan, 2014, Jalbert et al., 2014, Gerbino et al., 2013, Goodson et al., 2012, Rudman et al., 2011, Marbacher et al.,

2011). As suggested though, detailed evaluations of these reports have been presented in preceding sub-Chapters.

3.7. Key Surgery Focus – Complex Routine Procedure – Reporting on Hemimandibulectomy and Fibula Free-Flap Reconstruction

3.7.1. Alloplastic Reconstruction

Conventional surgery based around freehand mandibular excision, fibula harvesting, and fixation, was relatively imprecise and frequently resulted in facial asymmetry (Ganry et al., 2017). The most frequently reported reconstruction methods involved some degree of surgical planning and mandibular medical models or templates; to pre-bend flap-supporting stock implants, or to pre-trim average-shaped stock plates (Duttenhoefer et al., 2017, Roser et al., 2010, Liu et al., 2009). By pre-bending stock plates, the number of bending adjustments were reduced, along with the stress on the plates, and their chances of subsequent fracture (Lethaus et al., 2012a). The use of digital surgical planning permits the surgeon to select the portion of harvested fibula to optimise function, aesthetics, and flap blood supply at the mandible site (Leiggener et al., 2009). Their major limitations stemmed from being unable to perfectly contour the stock plates manually.

Excellent studies by Modabber et al. (2012), Logan et al. (2013), Gil et al. (2015), and Weitz et al. (2016) directly compared conventional and guided approaches to mandibular reconstruction in both clinical and non-clinical scenarios. They found specifically that the digital approaches with planning and guides: significantly reduced procedure duration; potentially improved flap survival; reduced the size of the fibula donor site defect; improved outcome consistency; reduced incidences of dental malocclusion; reduced instances of titanium plate exposure; and improved bony consolidation. Additionally, although Roser et al. (2010) did not compare approaches directly, they did report that planning, guides, and models resulted in a reduction of the procedure's sensitivity to surgeon experience.

Whereas methods which only use planning and models (Wang et al., 2013) are becoming less common, the translation of the surgical plan into the operating theatre with guides has increased in prevalence. Guides have been successfully used in lesion excision (Ganry et al., 2017); in bracing the residual mandible bones (Reiser et al., 2015); in harvesting the donor fibula (Roser et al., 2010); and in placing immediate dental implants (Levine et al., 2013). They have usually been fabricated from a range of polymers (Leiggener et al., 2009, Goodson et al., 2017) and occasionally from titanium (O'Malley, 2016, Bibb et al., 2015) – both using AM. Whereas the choice of titanium was generally justified robustly (surgeon preference for strength, lower chance of debris) the far more popular use of polymer was not. A reasonably inferred motivation would be that of lower cost, but again, this represents an area of low fidelity reporting which lacks clarity and prevents proper critical comparisons.

3.7.2. CAD and AM / CAM Implants

Increasingly, the full-digitisation of the reconstruction process has been shown, through the use of custom AM mandibular implants to fix the bone graft in place at the mandible site. Some designs have mimicked the stock plates which were explored above (Bibb et al., 2015) while some have expanded their functions relative to the conventional plates. Goodson et al. (2017) improved the height of the fibula graft for dental rehabilitation, whilst maintaining aesthetic accuracy in the contour of the lower mandible border. This represented a genuine design innovation, but as was common, detail was lacking as to the purpose of illustrated but unmentioned design features. Ciocca et al. (2012a) designed an implant which extended to the superior aspect of the mandibular condyle to replace the excised portion of the temporomandibular joint (TMJ). Their work was especially thorough in its reporting of design details; including descriptions of visual alignment features, part thicknesses, fixation in the context of the surgical plan, weight-saving considerations, and fabrication specifics. Other work described apparently innovative designs which included features to assist dental rehab planning, but failed to justify mimicking mini-plates instead of the more widely used mandible bar implants (Schouman et al., 2015). Finally, Al-Ahmari et al. (2015) reported on a unique, FEA-led approach to mandible implant design to optimise stress

distributions. Its optimised sinusoidal (wave) form demonstrates the scope for device innovation, when custom plates aren't simply based on existing stock equivalents.

3.8. Chapter 3 Summary

In summary, Chapter 3 has:

- identified key overall trends in the surgical device literature: from proving technical and clinical efficacy, to evaluating outcomes and promoting routine use (throughout);

- identified the blurred but also sometimes conflicting author perspectives: from engineers to maxillofacial prosthetists, radiologists, technicians, and surgeons (throughout);

- examined previous work on five surgical procedures which are key to this research (Chapters 3.3 - 3.7);

- evaluated the literature to identify methodological weaknesses including: small sample sizes, minimal follow-up periods, occasional ignorance of previous work, outdated interpretations of gold-standard treatments, lack of standardised reporting fields, and a frequent ambiguity of purpose (throughout);

- evaluated the literature to identify reporting omissions including: design details and justifications, high fidelity technical details, key clinical assumptions, acknowledgement of study weaknesses, and suggestions of generalisable findings or design rules (throughout);

- identified publication biases including: unwillingness to publish negative results, and publication with unacknowledged advocacy - stemming from protectionism or politics (3.2.5);

- identified gaps in the published surgical device literature including: healthcare economics, health technology assessment (throughout), design control, and service design (3.2.9 – 3.2.10);

- and contributed to meeting objectives 1 and 2 from Chapter 1.9.

4. Research Methods

This Chapter (Figure 28) describes and justifies the methods employed to achieve the research aim from Chapter 1.8 and meet the research objectives from Chapter 1.9. Sub-Chapter 4.2 deals with pre-empirical, structural issues. Sub-Chapter 4.3 justifies the selected research tools. Sub-Chapters 4.4-4.6 describe the mechanics of the empirical data collection phases in detail. Finally, sub-Chapter 4.7 details the steps that were taken to ensure ethical compliance.

In this research (Figure 28), there were three phases of data collection and synthesis: Investigation A (Characterising Current UK Practice), Investigation B (Developing a Design Process Intervention), and Investigation C (Verifying the Intervention). Fourteen real-world surgical design case studies were split across Investigations A and B. The number of, limitations with, and justifications for the design case studies will be addressed throughout this chapter – particularly in light of the research constraints highlighted in Chapter 4.1. Existing design practice was either observed, or tracked and recorded (in those instances where the author was leading or supporting the design and fabrication work first-hand). Standard institutional or clinical practices were not manipulated in any way. Only Investigation C involved modifying participant behaviour and design outcomes; but this happened in isolation - on patient geometry with *simulated* disease. Those designed outcomes from Investigation C were segregated and not manufactured, or used on patients. This was essential – to prevent compromised treatment for patients as a result of this research.

There was a sustained effort towards developing an evidence-based intervention to the patient-specific device design process that addressed particular problems highlighted by the analysis of current practice. Investigation A responded to the conclusions from Chapters 1 – 3 to better characterise current practice with primary, real-world data. Investigations B and C responded to the issues highlighted in the conclusions from those data, taken together as a whole. As the research focus narrowed, across these research activities, the significance of the regulatory and quality management requirements (as highlighted in Chapter 1.6) increased. As did the significance of evidence gaps highlighted througout Chapter 3 – particularly about patient-specific device design details. Investigation A informed the list of requirements for a design intervention from a hospital laboratory and design consultancy perspective. Investigation B informed the list of intervention requirements based on a higher

quantity and quality of evidence specific to a particular surgical procedure. It also included a systematic prototyping process to arrive at the content and nature of that design process intervention – ultimately, a paper based pro-forma. Investigation C verified the impact of the prototyped intervention and suggested developments for future investigations.

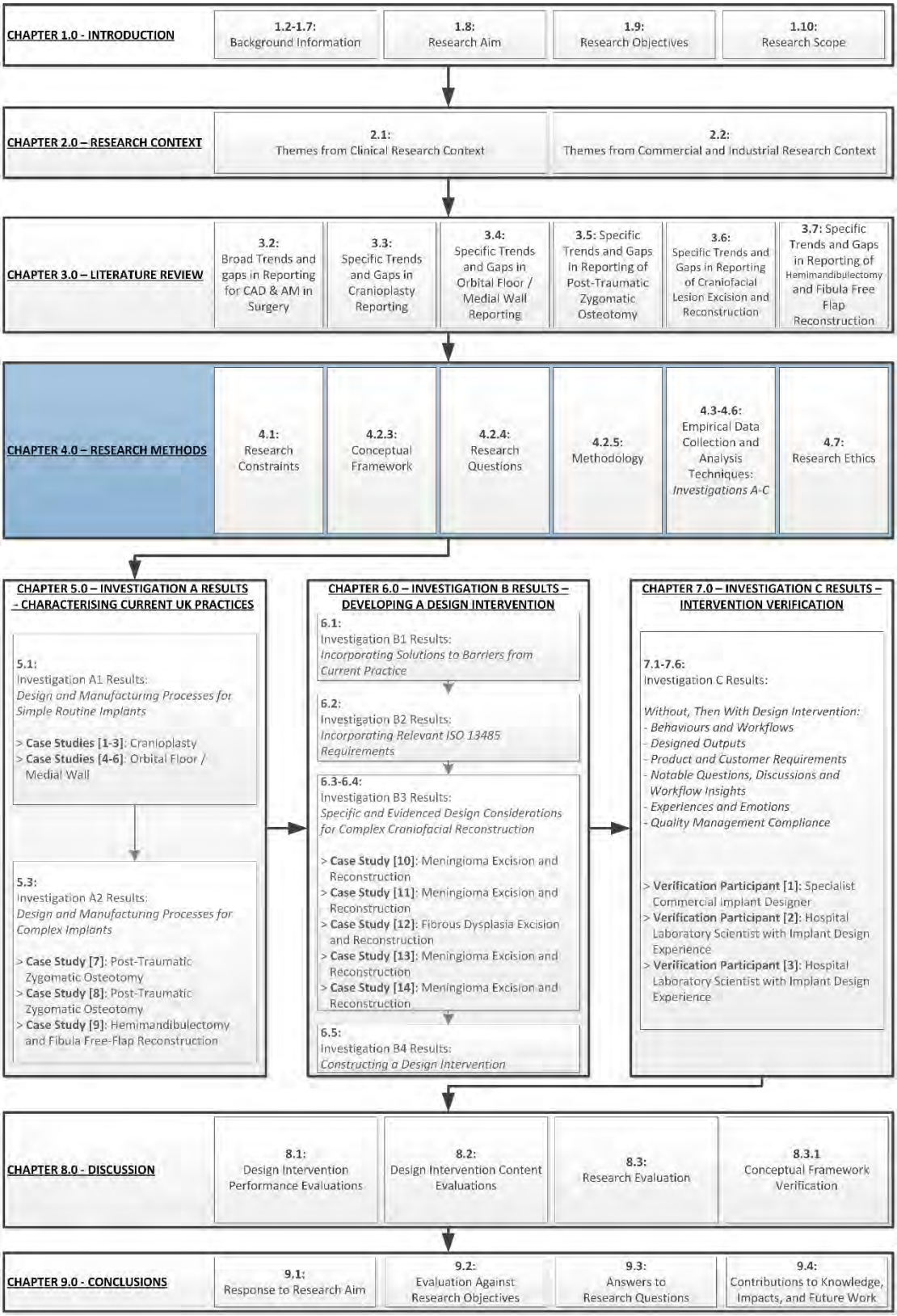


Figure 28 - Thesis Overview, With Current Location Highlighted (Chapter 4)

4.1. Research Constraints

As highlighted in Chapter 1, this research project was set in the applied, semi-commercial context of a university research institute and design consultancy. As such, it aimed to generate contributions to both academic knowledge and to design practice. Academic contributions were defined as new knowledge that began to address gaps in the scientific literature. Contributions to design practice were defined as improvements to internal procedures that could be generalised beyond the host organisation – into other UK contexts that undertake patient-specific device design. These contributions aimed to make it easier for more people (designers, engineers, and clinicians) to design more functionally and economically effective products (custom implants and guides) more often (by overcoming barriers related to the design process). The primary research context was the UK, because of the institute's location and experience; the institute's health service customers and collaborators (all from the UK NHS); the practical limitations on clinic access and travel for this research; and the commercial utility of addressing regulatory factors for the institute's home region. Within those contextual and geographic constraints, such as working with CARTIS members because of existing agreements, research methods were selected according to the resources available to the researcher, and the nature of the issues under investigation, as recommended by Blaxter (2010).

Everyday practical constraints mainly centred on the availability of appropriate case studies, on finding patterns of injury or disease manifest in those case studies, on the design tools and skills available at the institute, on the fabrication methods available, and on the clinics and clinicians who had close relationships with the institute. The latter was of particular importance due to the sometimes-significant commitment asked of participants during data collection. For most of the case studies the CARTIS collaboration, as described in Chapter 1.3, facilitated access to and co-operation from technical and clinical staff.

Investigation B3 (Incorporating Clinical Design Considerations) focused on meningioma and fibrous dysplasia of the craniofacial skeleton, simply because of having five analogous complex cases to draw upon. A focus on that specific disease was impossible to plan before the research began – it relied on flexibility and agility to react to the

opportunities for analysis as a viable case series developed. However, the research focus was already refined towards complex implants and guides by that stage (following the conclusions from the literature review and from Investigation A), so the five case studies of that type were very well suited. Through purposive sampling, many interesting case studies were deliberately overlooked in favour of those most appropriate for answering the research questions in sub-Chapter 4.2.4. This pre-emptive focusing and deliberate filtering, ensured that the approach was systematic rather than wholly reactive, and that there was a good questions-methods fit; both of which are important markers of research validity (Punch, 2005, Blaxter, 2010). Purposive sampling is one form of non-probability sampling; a family of techniques which is used when the researcher lacks either a frame, or a need for probabilistic sampling (e.g. random or cluster sampling) of an entire population (Blaxter, 2010). Given the lack of previous published work on characterising and comparing implant and guide workflows, and given the resource-heavy nature of the data collection involved, probability sampling was not appropriate for this research. Within the non-probability sampling class, other techniques like convenience sampling (assessing the easiest cases), voluntary sampling (assessed cases are self-selected), or quota sampling (convenience sampling within a group), would not have guaranteed the same deliberate questions-methods fit as described above. Undoubtedly, probabilistic sampling of a much larger population to generate statistically relevant data would be desirable in theory, but was certainly beyond the scope and resources of this work.

Although researcher time constraints are clearly not unique to this particular piece of research, its part-time nature, and its requirement to compliment the institute's unpredictable commercial consultancy caseload are worth noting. Complications which arose from this, like a lengthened overall research duration, should be balanced against the positives associated with part-time research work. Here, that meant the cases studied in this thesis were real-world examples of patient-specific devices, which were deployed to reconstruct bony defects after real injuries and disease, by real clinicians. This aimed to lend a high degree of validity and legitimacy to the work.

4.2. Pre-Empirical Stage

As suggested by Punch (2005), the pre-empirical stage of this research analysed the issues raised by the original research aim, and developed appropriate research questions to partially or fully address them. The identification of relationships between these specific research questions and universal, established research philosophies (detailed in sub-Chapter 4.2.5) was undertaken to further support the validity of this research. However, this thesis does not claim to specialise in, or contribute to paradigmatic debates.

4.2.1. Research Structure

This research developed and addressed research questions. Research questions should be specific enough to provide an indication of the type of data required to answer them, and the analyses which need to be undertaken on those data (Punch, 2005, Blaxter, 2010). Their content should be defined before the particulars of research methods and data collection; to minimise the restrictive influence of methodological paradigms on research questions – or 'methodolatry' (Punch, 2005). In this research, it was not reasonable to formulate *specific* pre-defined questions due to the lack of published evidence describing current UK patient-specific device design practice; so some initial empirical work aimed to construct and refine a conceptual framework to map the key design factors and their presumed relationships. This framework (presented in sub-Chapter 4.2.3) assisted with the refinement of *general* research questions (sub-Chapter 4.2.2) into more specific research questions (sub-Chapter 4.2.4) by way of empirical data from Investigation A (described in Chapters 4.4 and 5.0).

This iterative approach to research question development is supported in the methodology literature both generally (Blaxter, 2010, McNiff, 2013) and more specifically – through being driven by an empirically-informed conceptual framework (Punch, 2005, Blessing and Chakrabarti, 2009). Aside from helping to refine research questions, developing a conceptual framework provided a process for making the researcher's existing vocational knowledge and assumptions explicit. This is an acknowledged benefit of the question-development process, in addition to

it promoting clarity, and encouraging early selective focusing towards the most promising and realistic factors and relationships for investigation (Punch, 2005).

Further to the above, it follows that this research initially aimed to generate theories rather than verify those that existed already. The possibility of deploying a fully defined research structure was only realised after gathering context-specific data through Investigation A. As the notion of testing hypotheses actually represents testing the underlying theories behind them (Punch, 2005), this research did not rely on hypotheses to drive its design. Investigation C, with its verification role, presented a more classical opportunity to deploy a hypothesis-driven deductive approach. However, Investigation C was designed to permit data collection in both pre-defined (structured) and unfolding (semi-structured) fields which, when combined with an inability to predict results with confidence, meant that driving the research structure by using hypotheses was not appropriate (ibid).

4.2.2. Initial Research Themes & Questions

The initial research questions formulated for this research were derived from: the aim and objectives in Chapters 1.8 – 1.9, from the institute's aims, prior vocational knowledge, and the research context presented throughout Chapter 2.

4.2.2.1. Initial Research Question 1

What is the nature of current patient-specific device production techniques?

4.2.2.2. Initial Research Question 2

What are the drivers and barriers experienced by medical professionals when adopting digital surgical planning, digital device design, and AM fabrication techniques?

4.2.2.3. Initial Research Question 3

Is it possible to formulate a practical and effective design intervention that satisfies contextual *and* design requirements for the routine production of patient-specific devices?

4.2.3. Conceptual Framework

As indicated previously, the research focus and these general research questions were refined by way of a conceptual framework which attempted to link the evidence presented and analysed through Chapters 1-3, and then incorporating the primary data from Chapter 5 (Investigation A Results). This framework helped to plan the data collection for Investigations B and C in Chapters 6 and 7. The final version of the framework, validated in full or in part by the new data gleaned from Chapters 6 and 7 is presented and analysed in Chapter 8 (Discussion).

The Design Research Methodology (DRM) outlined by Blessing and Chakrabarti (2009) is a cyclical, mixed methods, iterative approach which seeks to address the lack of common research methodology in the field of design. In addition to assisting in the selection of research tools, it is intended to focus new research projects through building a thorough, evidenced understanding about the real needs of a given situation; to generate design practice improvements and result in design outputs that are more successful than the existing situation (ibid). This was of particular value for helping to structure the investigations in this research about describing, and then improving the design process for patient-specific surgical devices. This research adopted key relevant recommendations from the DRM; to influence the creation and refinement of conceptual models; and to exploit its design-centric and pragmatic approach to description and then intervention.

The DRM describes the value of identifying influencing design factors from literature, specific experiments, and participatory experience; and using these to formulate and validate models of their relationships for both current and intended

future practice – as a means of focusing research activities and refining the conceptual framework (ibid). As recommended by Blessing and Chakrabarti (2009), each influencing design factor in the model created for this research (Figure 29) was formulated as (an attribute) of (an element). For example, in "degree of NHS adoption", "degree" is the attribute and "NHS adoption" is the element. This formulation allowed links to be drawn (with arrows) between each factor – then values added (positive or negative) to those relationships.

The initial conceptual framework (Appendix 2) drew upon existing researcher and institutional knowledge and findings from the literature. Several key themes, assumptions, and connections are worth highlighting here before moving onto the refined conceptual framework in Figure 29. The initial framework was very large and encompassed political, structural, economic, and educational factors with a view towards not discounting any potentially important links in the first instance. Even in the early stages, such factors were obviously outside of the scope of this research in terms of direct impacts, but their inclusion was worthwhile to permit assessment of whether they would be tangentially impacted. AM fabrication factors were also included at this stage – including issues of AM cost, build times, post-processing or finishing tasks, device sizes, and geometrical complexity. This catch-all approach was high on relevance, but also highly specific to the researcher's workload, most frequently used fabrication methods, and the host organisation's standard operating procedures.

Even in those early stages, the emergence of the "initial fidelity of the product design specification" as the key factor for this research was clear. It was at the centre of the links relating to design and modelling development factors specifically (as opposed to for example fabrication, management, and customer co-operation factors). The framework indicated important links between the key factor and issues of time-in-motion (and therefore labour costs), issues of collaboration between surgical, technical, and design specialists, and issues of surgical outcomes success. Generally, the themes from these links to (and from) the key factor were maintained as the conceptual framework was refined and updated.

The refined conceptual framework (Figure 29) reflects the inputs from the first empirical investigations (A1 and A2) as well as from new inputs from an evolving

literature review. The effects of those new inputs are manifest in the model as: the consolidation of some factors; the elimination of other factors (due to evidence source or relevance limitations); and as the addition of two new branches of factors which had emerged as crucial (about evidence quality, and regulatory compliance).

With the aim of improving potential generalisability, factors like "number of AM device prototypes" and "amount of time from design proposal to sign-off" were eliminated from the initial conceptual framework for being driven by the institute's service model. Here, and throughout this research, "generalisability" and "transferability" refer to the potential for the conceptual framework and design intervention to be developed in future research (with new ethics approvals) for other surgical procedures or specialties. It should be noted that the issues of quality compliance and generalisability also prompted the switch from "fidelity of initial device design specification" to "fidelity of captured user and product requirements list" for the phrasing of the key factor. An ISO13485 compliant QMS demands a full list of product and user requirements prior to manufacture. Achieving 'perfect' fidelity in an efficient way is more representative of the spirit of that factor, than achieving good fidelity from the very outset of a new design project.

Less explicit from looking at the refined framework alone, is the specific nature of the narrowed research focus. Existing publications, and results from Investigation A (presented in Chapter 5) demonstrated that the largest benefits from a digital design and fabrication approach were to be found in complex surgeries. The wide variety of service models (from commercial, to research, to in-hospital), the associated wide variety of design tools, and the variety of people acting as designers and using those tools, also supported the narrowed research focus - onto the specification-building and design verification stages of the complex device production process. Consequently, the focus was independent of tools, environment, and personnel. The narrowed focus is reflected in the specific research questions in sub-Chapter 4.2.4.

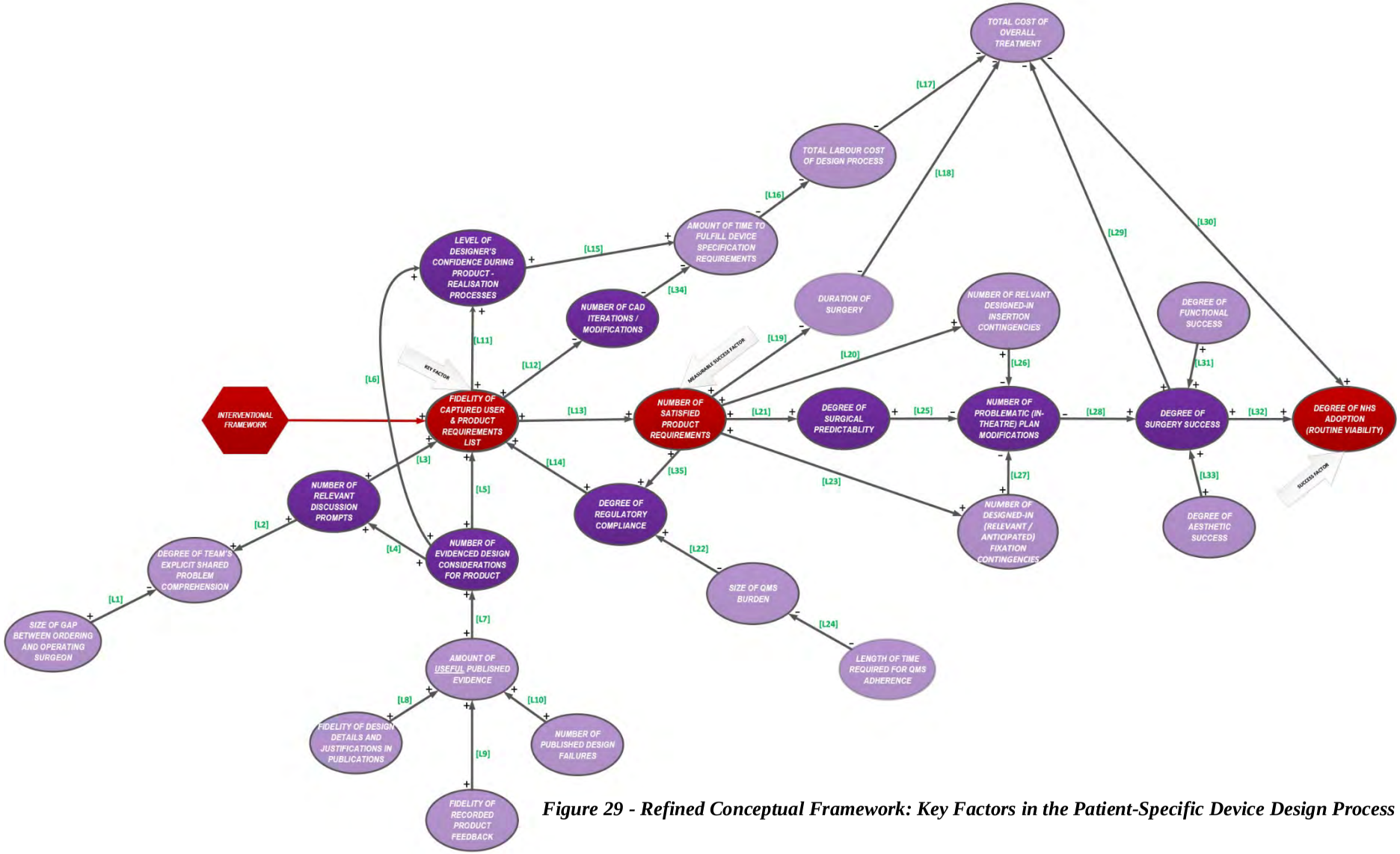


Figure 29 - Refined Conceptual Framework: Key Factors in the Patient-Specific Device Design Process

To this end, and as directed by Blessing and Chakrabarti (2009), an overall success factor was identified, and an indication provided of where the design process intervention was targeted. This method diverges slightly from the DRM at the point of identifying a *measurable* success factor (that which realistically suits the research project timeframe and resources). Figure 29 clearly indicates a selected measurable success factor, however it should be noted that the plan developed for Investigation C culminated in measuring several factors, whose veracity required support beyond that in the academic literature, and that which was documented in Chapter two's contextual insights. This was suited to the narrow, but deep data from the participants who were involved in the testing.

Although the refined framework contained only factors and links which have been documented in Chapters 2 and 3, or which had been indicated by the first sets of empirical evidence in Chapter 5 (Investigation A Results), the quality and volume of evidence was irregular. As such, the data collection stages in Investigations B and C were targeted towards verifying the weaker groups of links. For example, Investigations B1, B2, and B4 targeted links related to quality control and regulatory compliance.

Table 2 provides a summary of the primary and secondary evidence sources for the links in the conceptual framework. It also indicates where the weaker themes were targeted for the collection of new data. The conceptual framework presented in this research is new – and it contains many *new* links between design process factors; relative to those in existing published work. Hence, Investigations B and C had reasonably broad scopes compared to the slightly more granular approach of the DRM – due to the relative importance of each link being difficult to discern. This method reflects the mostly inductive approach of this research as a whole – with the final version of the conceptual framework (presented in Chapter 8.3.1), driving the recommendations for future work – with a view to improving the underlying evidence further.

Table 2 - Evidence Sources for Key Factor Links in Refined Conceptual Study

Individual Links from Refined Conceptual Framework	Evidence Source(s)
[L1]	Investigation A1. / (Peel and Eggbeer, 2016)
[L2]	Chapter 2 – Research Context. *Targeted by Investigation C.*
[L3]	Investigation A1. / (Peel and Eggbeer, 2016) *Targeted by Investigations B and C.*
[L5]	Investigation A1, Investigation A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016). *Targeted by Investigations B3 and C.*
[L7]	Chapter 3 – Literature Review. Investigations A1 and A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016) *Targeted by Investigation B3.*
[L8]	Chapter 3 – Literature Review. *Targeted by Investigation B3.*
[L9]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. Chapter 3 – Literature Review. *Targeted by Investigation B3.*
[L10]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)
[L6]	Chapter 2 – Research Context. *Targeted by Investigations B3 and C.*
[L11]	Chapter 2 – Research Context. *Targeted by Investigations B3 and C.*
[L12]	Investigation A2. / (Peel et al., 2016) *Targeted by Investigations B3 and C.*
[L34]	Chapter 2 – Research Context. Investigation A2. / (Peel et al., 2016),
[L15]	*Targeted by Investigation C.*
[L16]	Investigation A1. / (Peel and Eggbeer, 2016), (Peel et al., 2016)
[L17]	Investigation A1. / (Peel and Eggbeer, 2016)
[L13]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. Investigation A1. / (Peel and Eggbeer, 2016)
[L14]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. *Targeted by Investigations B4 and C.*
[L35]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards.

[L22]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. *Targeted by Investigations B4 and C.*
[L24]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. *Targeted by Investigations B4 and C.*
[L21]	Chapter 3 – Literature Review. Investigation A2.
[L25]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)
[L20]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)
[L26]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)
[L23]	Chapter 3 – Literature Review. Investigations A1 and A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016)
[L27]	Chapter 3 – Literature Review. Investigations A1 and A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016)
[L28]	Chapter 3 – Literature Review. Investigations A1 and A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016)
[L29]	Chapter 3 – Literature Review.
[L31]	Chapter 3 – Literature Review.
[L33]	Chapter 3 – Literature Review.
[L32]	Chapter 3 – Literature Review.
[L30]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)

4.2.4. Refined Research Questions and Specific Empirical Tools

Quite aside from the focus provided by a refined conceptual framework, the research questions from sub-Chapter 4.2.2 were developed in line with technical best practice. Effective research questions are clear, specific, answerable, interconnected, relevant, and worthwhile (Punch, 2005). They should provide clear indications of *how* they will be answered, suggest what evidence will be required to answer them, omit value judgements, and avoid inferring causation (ibid). The refined questions for this research adhere to those recommendations and are presented below. Question 3 was split into three individual sub-questions to improve specificity, manageability, and better reflect the sharpened research focus. Ambiguity was reduced in questions 1 and 2 without the need to sub-divide the questions further.

4.2.4.1. Refined Research Question 1

What are the tasks, processes, materials, resources, expertise, tools, and costs involved in current patient-specific device production techniques?

In order to answer this question, several types of data were indicated to characterise current processes in hospital units - which met the scope and resource constraints of this work. Data required were both primary and secondary, and were mostly quantitative, with some qualitative input: process tasks, task order, task personnel, process timeframes, task timeframes, process costs, process materials, process tools, standard operating procedures, design intent, key design decisions and any deviations from standard practice.

4.2.4.2. Refined Research Question 2

What are the clinical, technical, and structural drivers and barriers experienced by medical professionals when adopting digital surgical planning and digital design techniques?

To answer this question, the data indicated were both primary and secondary, and were mixed between quantitative and qualitative approaches: device procurement methods, device service provision and availability, delivery methods, personnel requirements, expertise distribution, clinical pulls, management drivers, and consensus about clinical best-practice.

4.2.4.3. Refined Research Question 3.1

To what extent can quality management system and regulatory compliance functions be incorporated into, and satisfied by, a prototype design process intervention for complex patient-specific devices?

To answer this question, the data indicated were both primary and secondary, mainly from the quantitative family, and based largely on deskwork: to synthesise quality standard requirements, statutory requirements, and contextual requirements with the findings from Investigation A.

4.2.4.4. Refined Research Question 3.2

What level of fidelity is required in a device specification or requirements list for successful design outcomes in complex craniofacial reconstruction?

To answer this question, the data indicated were both primary and secondary, mainly quantitative, and were split fairly evenly between fieldwork and deskwork: to ascertain the fidelity of design details in previously published work, and to generate new evidence to fill some of those evidence gaps to the degree permitted by this work's resources.

4.2.4.5. Refined Research Question 3.3

Can a practical and effective design intervention be formulated, that contributes to meeting regulatory, clinical, technical, and user requirements for the routine design of complex patient-specific devices?

To answer this question, the both primary and secondary quantitative and qualitative data were gathered and analysed. Collection was split fairly evenly between deskwork (to formulate) and fieldwork (to validate). This included synthesis of requirements highlighted by Investigations A and B, prototyping, validation through observation, and interviewing.

4.2.5. Methodology

This research is rooted in the post-positivist social research paradigm. That is, it maintains the same basic tenets of positivism on one hand (mirroring quantitative natural science procedures where possible, as a detached and objective researcher, using controlled experiments to capture reality) while acknowledging that social reality can only be known semi-objectively; that methods for capturing it are flawed; and that qualitative techniques should be used to validate findings (Blaxter, 2010, Denzin and Lincoln, 2005). Relevance to this research is clear, as demonstrated by the mixing of empirical quantitative data (about barriers to routine patient-specific implant applications in current practice), with qualitative data about designer's real behaviour and emotions when a targeted intervention to overcome these barriers was introduced.

Indeed, even within the verification exercise of Investigation C, robust experimental measurements about CAD modelling behaviours were combined with rich subjective insights into the participating designer's feelings towards the new approach. This combination painted a more rounded picture about framework performance than could have been achieved with a more classical approach. This was particularly useful in being able to suggest future improvements towards promoting long-term compliance with the design process intervention – by assessing more than simply whether the framework had "worked"; but focusing additionally on complementing this information with data about user engagement and enthusiasm.

Quantitative and qualitative approaches were mixed by this research – not just to provide validation of results as mentioned above; but to reflect both the project constraints, and the broad gaps in the research literature. For example, large-scale statistically-relevant studies of the depth undertaken in Investigation C would not have been realistically feasible within the timeframe and resources. Furthermore, the weaknesses and scarcity of previously published work (as described throughout Chapter 3) served to increase the value of the new data, even despite their statistical limitations. Finally, as noted in the previous sub-Chapter, the refined research questions each suggested types of data and modes of data analysis which would be most suited to answering them; and those data types were mixed.

The already minimal relevance of defining and adhering to a separation of the two research approaches was muted further by the mixing of techniques within investigations themselves, and within analyses. Quite apart from the justification provided by the affinity between research questions, and from mixing research families, the researcher's industrial and product design background (encompassing ergonomics, designing for usability, and emotions) also lent itself to this mixed families approach. For example, these design skills were deployed to survey the gulf between strict technical requirements of quality control and the sometimes intangible, ill-defined human needs of users.

Unquestionably, this work appropriated many of the fundamental arguments and ideals most closely associated with Action Research advocates. Action research deploys cyclical problem solving through systematic critical reflection and action (Costello, 2003, McNiff, 2013); with a view towards the co-generation of new information to transform practice in a democratic direction for the people involved (Greenwood and Levin, 1998); all of which is particularly well suited to research in one's own workplace (Blaxter, 2010). This work aligns with all of these descriptors. Most obviously, Investigation B3 presents iterative (surgeon-derived) treatment plans for patients with similar conditions; with those iterations being driven by reflection on the preceding patient's outcomes. The characterisation of current practice in Investigation A, and the modification of standard operating procedures in Investigation B2 (to meet quality standards) both embodied critical (sometimes self) reflection; followed by the development and validation of new practices in Investigations B4 and C. Said refinement of standard operating procedures involved other staff at the host research institute and design consultancy – aiming to deliver consistent design outcomes to a defined gold-standard, based on the shared knowledge and preferences of all staff. By aiming to create an evidenced design intervention which was independent of software tools or context, the research presented in this thesis intended to encourage wider implementation of best practice by establishing a standard structure and design process where it previously did not exist.

Briefly, constraints with this research revolve around restricted sample sizes, tools, and contexts. This work is mostly reliant on rich data about a low number of selected cases, rather than being in a position to feasibly deduct statistically relevant

conclusions from quasi or true experiments - as they are defined by Punch (2005) and by Blessing and Chakrabarti (2009). However, just as quantitative research is not any more scientific than qualitative research (with all of the ideological social support and prestige which that brings); it can be confidently argued that Action Research as a whole is closer to the practices of those physical sciences than mainstream social research (Greenwood and Levin, 1998). This claim argues that Action Research is more likely to produce reliable and useful information about social phenomena – the validity of which can be tested in action (ibid), just as in Investigation C.

In this regard, Action Research as a concept, and the research presented in this thesis as tangible reality is fundamentally local; with internal credibility amongst the researcher and the institute. Nevertheless, by rejecting a design process intervention tailored to specific design tools, the potential for external credibility amongst clinical participants was enhanced. This was important, to ensure alignment with the values of this research. Explicitly, those values were about supporting the NHS and its patients in accessing the best care routinely - through using digital design and AM for maxillofacial device production. The design intervention had to be at least targeting external credibility – to have potential future success beyond the one institute and two hospitals involved. Action Research holds that a researcher's values and their socio-political intent are intertwined with, and mutually reciprocal towards the methodology (McNiff, 2013). As such, it was prudent to acknowledge them from the outset, to maintain a clear path towards validity and credibility.

Within the stated research paradigms, this project mixed four research tools – case studies, observations, simultaneous verbalisation, and interviews, along with elements of experimental reasoning. Case studies are most common in previously published work in this field. Experimental research and observation are not as common in the clinical literature, as surgical events are usually self-reported by a member of the operating team. Experiments and observational approaches are seen more regularly in design research, and in *pre-clinical* quasi-experiments (Logan et al., 2013); this research project required a bridging of the clinical-research to design-research gap.

4.3. Empirical Stage

Table 3 (below) presents an overview of each investigation, in relation to what they achieved, what data were collected, which tools were used to collect those data, who was involved, and which research questions they contributed to answering. Relevant commentary on the data collection tools will follow.

Table 3 - Empirical Studies Overview

Inv.	Description:	Research Families & Data Collected:	Data Collection Tools:	Data Collection Contexts & Summary of Participants:	Research Q's :
A1	Characterised existing production processes for simple patient-specific devices.	Quantitative data: tasks; task lengths; task orders; materials; material quantities, material costs, tools, human resources, time-in-motion human resource costs. Qualitative data: task aims, design decisions, degree of planning, design justifications.	Observations; simultaneous verbalisation.	2x maxillofacial laboratories; 1x research institute and design consultancy. 2x prosthetists; 1x dental laboratory technician; 1x consultant maxillofacial surgeon; 1x consultant neurosurgeon; 1x device designer / AM technician (researcher).	1; 2.
A2	Characterised existing production processes for complex patient-specific devices.		Observations; case studies.	2x maxillofacial clinics; 2x maxillofacial theatres; 1x maxillofacial laboratory; 1x research institute and design consultancy. 2x prosthetists; 3x consultant maxillofacial surgeons; 2x device designers / AM technician (including researcher).	

B1	Critically reflected on current processes, and specified improvements.	Quantitative data: identification of institute workflow tasks; categorised tasks; grouped paperwork; re-ordered design protocols; re-ordered project management protocols.	Deskwork.	1x research institute and design consultancy. 3x device designers / AM technicians (including researcher).	1; 3.2; 3.3
B2	Identified and analysed ISO 13485 requirements relevant to the research / design process intervention.	Quantitative data: QMS compliance requirements list; procedures, forms, and records lists for institute context; QMS structure. Qualitative data: evaluations of QMS components for generalisability.	Deskwork.	1x research institute and design consultancy. 1x device designer / AM technician (researcher); 1x external auditor.	3.1; 2
B3	Identified, evaluated, and extracted design rules / considerations from a 5x case series of complex devices.	Quantitative data: designed devices technical characteristics; device costs; pre-surgical patient conditions; surgical outcomes; existing design rules / considerations from literature. Qualitative data: designed devices performance; validity of new design considerations.	Case studies; observations; simultaneous verbalisation; systematic literature review.	1x maxillofacial clinic; 1x maxillofacial theatres; 1x research institute and design consultancy. 1x consultant maxillofacial surgeon; 1x consultant neuro surgeon; 1x consultant ophthalmologist; 2x device designers / AM technicians (including researcher).	3.2; 3.3
B4	Synthesised findings of B1-3 to prototype a paper-based design process intervention.	(N/A)	Deskwork: design, formatting, digital prototyping.	1x research institute and design consultancy. 1x device designer / AM technician (researcher); 1x external auditor.	3.3

C1 C2	Design process intervention – validation pilot test. Design process intervention – validation tests.	Quantitative data: number of design iterations; fidelity of the requirements lists; participant behaviours and durations; participant behaviour orders or patterns; number, nature, and relevance of questions asked by participants; degree of process compliance with ISO 13485 requirements; degree of design completeness, in the allotted time. Qualitative data: reasons for design iterations, participant emotional responses; appropriateness of designed solution(s).	Observations; simultaneous verbalisation; interviews; deskwork (design review).	1x maxillofacial laboratory; 1x research institute and design consultancy. 1x prosthetist; 1x biomedical 3D technician; 1x device designer / AM technician.	3.3

4.3.1. Data Collection Tool – Observation

Observations were carried out repeatedly throughout this research and were, along with case studies, the major foundation on which this work was built. It is therefore worthwhile to review their benefits, limitations, and limitation-mitigation strategies (as used) in some detail. Observations are well-suited to identifying and accurately describing meaningful interactions (Blessing and Chakrabarti, 2009), via the production of authentic data without the need to rely on second-hand accounts, and also act as effective reality checks on what people actually do relative to what they claim to do (Cohen et al., 2013). They permit the formation of holistic perspectives (including context), are discovery-oriented, and allow identification of routine actions which can otherwise be overlooked in interview answers (Patton, 2002). In these fundamental ways, observational research was appropriate for this work;

particularly in light of the findings from the literature review in Chapter 3; which emphasised the dearth of formal, explicit, unambiguous publications devoted in full (or even in part) to describing the current device production processes. With so little published evidence, data with a high degree of authenticity was deemed to be important – to characterise those design and production processes where parochial variations exist across the specialty; in a vacuum caused by that lack of commonly-accepted best-practice. Aside from the methods-questions fit described above, observational research offered the best pragmatic fit (and importantly, ethical fit) to the research context. Given the wholly inappropriate expectation to ever undertake fully experimental interventions into a surgeon's everyday practice, the ability to observe that practice in rich detail, in real time, and in its own settings was determined to be both technically proper and philosophically worthwhile.

Patton (2002) defines six dimensions of observational fieldwork: role of the observer; insider vs. outsider perspective; degree of collaboration between researchers and participants; overt vs. covert observation; duration of observations; and focus of observations. The observational research presented in this work (summarised above in Table 3) can be measured against these dimensions in order to justify the choice of tool (and acknowledging limitations with that choice).

Firstly, the researcher's role trended towards the onlooker-spectator end of the spectrum (as opposed to being a full-participant in the setting) except in cases when this was not practical; such as instances where the researcher was delivering a commercial service in parallel with observing the same scenario, or when playing a role in the simulated environment of Investigation C. Spectator status was pursued to enable complete focus on data collection and note-taking. Complimentary data (photographs, recordings, artefacts) were collected to mitigate distractions from participation, or from information overload.

Secondly, an insider perspective was the only option; given the research context and the fairly rare selection of specialised services offered by the host institute – and by the researcher. Particular care has been taken to describe the settings for outsiders in this thesis.

Thirdly, the degree of collaboration with participants was mixed between zero (when characterising processes) to effectively having surgeons as periodic co-designers when recording steps taken to design and deliver devices on a commercial basis (such as with Investigation B3).

Fourthly, only overt observations were used. While this has some concerns relating to authenticity, with participants changing behaviour *because* of being observed (Patton, 2002); only partial explanations of the planned analyses were provided to participants, which is an acknowledged mitigation strategy to minimise influence on the processes which are being measured (Blessing and Chakrabarti, 2009).

With regard to Patton's penultimate dimension, the duration of each observation was relatively short, and in single sessions. This reflected the nature of the observed phenomena themselves (surgeries, fabrication procedures, surgical planning sessions etc.). Occasionally, multiple observations were used to capture details which spanned days, but this was restricted to unavoidable instances in Investigation A. Deliberately using multiple observations over a long period to assess the *same* factor is acknowledged as being useful for studying design support effectiveness (Blessing and Chakrabarti, 2009) despite, as in this case, being frequently overlooked because of resource, time, and participant commitment constraints.

Finally, the focus of the observations was broad – seeking a holistic view of multiple factors whilst being discovery-oriented. Again, this reflects the relative lack of existing evidence for answering the research questions, and the broader aims of Investigation C particularly – to enhance *multiple* weaker links in the conceptual framework.

Naturally, it follows that the observations in this research were fundamentally semi-structured, with some small variations to either side of this point on the unstructured to highly-structured scale. Semi-structured observations have an agenda of issues on which to gather data, but resist tightly defined observation categories in favour of being hypothesis-generating and responsive to what they find (Cohen et al., 2013). A semi-structured approach was clearly synchronised then, to the discovery-driven, theory-generative research structure described in Chapter 4.2.1. Illustrated tangibly, this approach was a good fit, for example in Investigation A; when the observation

agenda included some specific factors highlighted by the initial conceptual framework as being (probably) important, whilst still allowing unexpected aspects of the observed situation to develop and ultimately feature prominently in the data analysis (e.g. the "degree of design intent" on the part of the participants).

Cohen et al. (2013) note the drawbacks to semi-structured observations (relative to those which are highly structured), where they require longer periods of time for data analysis; although the preparation time for fieldwork can be shorter. This aligns with Blessing and Chakrabarti (2009) and their warning about audio and video recordings of observed scenarios; large amounts of rich data can be enormously time-consuming to analyse, not least because of the burden of transcription. To mitigate this risk, comprehensive notes were taken during observations – to highlight key points during recordings, or key photographs in a set, to focus transcriptions and data extraction to those key moments only. On the one hand, this increases the risk of observer bias, given the inevitably selective nature of this technique and the dependency on the skill of the observer (Cohen et al., 2013, Blessing and Chakrabarti, 2009). On the other hand, it provided a means of collecting a larger quantity of rich data within the resource limitations of the research, for a topic which is lacking existing evidence. Extra care was taken during analyses to differentiate between the different kinds of notes as defined by Blessing and Chakrabarti (2009) when adapting the work of Ten Have (1977): pure observational notes; pure interview notes; methodological notes; reflective notes; theoretical notes; and organisational notes. Strict separation of inferences and their on-the-fly interpretations from separate factual annotations can reduce analysis biases (Blessing and Chakrabarti, 2009).

4.3.2. Data Collection Tool – Simultaneous Verbalisation

Throughout Investigation C's observational research sessions (which were not situated in operating theatres), participants were asked to speak aloud while working - and verbalise their thoughts. This simultaneous verbalisation can provide insights into their cognitive behaviour, in real time, which would otherwise remain hidden during normal conversation (Blessing and Chakrabarti, 2009). Eckersley (1988) goes further; citing the remarkable accuracy of the approach, for providing a picture of a participant's cognitive processes whilst engaged in problem solving. At its heart,

design as a discipline represents systematic problem solving – and at a finer level, those problem solving scenarios present themselves each time a design decision is taken. Those design decisions about small details, as noted in Chapter 3, were mostly glossed-over in published reports of previous work – or indeed completely overlooked altogether and taken for granted. The use of simultaneous verbalisation with a view towards unearthing the thinking (or absence thereof) behind such routine decisions, was then an obvious choice. The logical decision was taken to refrain from *asking* for this kind of commentary in operating theatres on account of the much more critical risks involved with potentially distracting a surgeon. However, in the majority of instances, explanations and justifications were offered unprompted to help more junior members of the surgical team understand and progress as part of their training. Important comments were recorded in notes as described in 4.3.1.

As recommended by Blessing and Chakrabarti (2009), the wording of the requests to participants to verbalise their thoughts was carefully considered before delivering the request; to avoid suggestion or leading their focus towards a particular factor (or factors). Wording aside, simultaneous verbalisation shares the same limitation relating to analysis as the recordings of observations – that of significant time costs. This burden was eased in the same ways as for the recordings of observed scenarios; by including important participant quotations in the comprehensive field notes, in order to be selective about which parts to transcribe.

4.3.3. Data Collection Tool – Case Study Research

As shown by Chapter 3, in the clinical literature about patient-specific device design and use, case study or case series approaches have been used very regularly and can be considered the norm. There is a clear precedent for their use. This is because of ethical barriers to randomising treatment across a patient cohort, and limiting potentially better treatment for a theoretical control group (Logan et al., 2013). It is also of course, impossible to undertake the same procedure in a conventional and then again in a digitised way on the same patient. Case studies are strategies, rather than an outright method (Punch, 2005), but are included in this sub-Chapter nonetheless, because they represent a key overarching approach to structuring and

discussing discrete instances of collated data on a per-patient basis (from observations, reviewing design records, participation, and interviews).

The cases in Investigation A were instrumental case studies – as categorised by Stake (1995). Instrumental case studies are undertaken to understand a wider issue, as opposed to intrinsic studies which are interested only in the single case itself. Those case studies in Investigation B3, and C were collective case studies; they were instrumental in learning about themes and theories larger than themselves, but also featured important co-ordination across their number (ibid). This co-ordination was manifest in the complex craniofacial reconstruction cases of B3 (in which iterative lessons were learned from treating meningioma and fibrous dysplasia patients sequentially); and in the comparative case studies in C.

Both Punch (2005) and Stake (1995) stress caution against generalising findings from case studies; an aim which the former notes can only be achieved through conceptualisation and propositions. This occurs when the in depth study of individual cases permits the development of new concepts, or new causal propositions to link factors within a case (ibid). The applicability of said new propositions may then be assessed for relevance to other situations. Just as described in Chapter 4.2.1, and its discussion of research structure; this represents a discovery-oriented approach to research. This meant that key valuable insights and contributions to knowledge are in fact new hypotheses for further investigation in future work. This offers a route to validation, for a niche subject lacking readily citable frameworks, theories, and so hypotheses.

Finally, whereas case study research is not sampling research (Stake, 1995), the selection of suitable cases for inclusion deserves comment. This Chapter has already addressed the filtering of available cases from the institute to identify an emerging case series for Investigation B3, so it will not be repeated here. The remaining cases were selected on the basis of what Blaxter (2010) defines (using sampling terminology) as purposive sampling – hand-picked as representative or interesting cases. For example, a complex zygomatic osteotomy case was included in Investigation A2 for being representative of highly complex design problems. These selection strategies are supported by Stake (1995) with his simple recommendation to maximise what can be learned from an individual case or collective studies.

4.3.4. Data Collection Tool - Experimental research

Experimental reasoning was used in the analysis of data generated by Investigation C. That investigation, with its primarily comparative purpose, was most suited to an experimental approach. However, no experiments were used in this research because the context did not provide the possibility of performing true experiments; a scenario which is common in design research (Blessing and Chakrabarti, 2009). To qualify as classical experiments, tests must involve random assignment of participants into control and treatment groups, pre and post-tests, the ability to repeat the experiment under controlled conditions, manipulation of an independent variable, measurement of a dependent variable, and statistical analyses to detect significance in the findings (Blessing and Chakrabarti, 2009, Punch, 2005). This was unachievable across each aspect of the definition – because of time, resources, access, and participant availability restrictions. Although experiments provide the most rigorous methods available for determining causality, research performed in other ways simply reflects the current lack of understanding in design (i.e. few hypotheses to test), and is not a comment on the ease or worth of this type of research (Blessing and Chakrabarti, 2009).

Quasi experiments and non-experiments relax aspects of the definition above, but still require pre-tests and post-tests in the absence of random assignment; or at least a post-test across groups with natural variation, respectively (Blessing and Chakrabarti, 2009, Punch, 2005). As such, the tools deployed in Investigation C for a very small number of participants, qualified only as comparative observations. Consequently, causation could not be inferred with confidence, or with significant validity. Instead, it produced rich data across a range of multiple measurable factors, containing some indications of correlation. These provided clear direction for recommending future work to improve the external validity of the conceptual framework further, whilst improving the performance of the design process intervention - for other complex surgical plans and device designs.

4.3.5. Data collection Tool - Interviews

Interviews were deployed during Investigation C – after each comparative observation. Their strengths lie in the collection of data which cannot be captured through observation or simultaneous verbalisation – such as beliefs, opinions, and reasons for behaviours (Blessing and Chakrabarti, 2009). They capture human interpretations of the world and are well suited for use in conjunction with other methods to validate their findings, through probing for deeper responses about participant motivations (Cohen et al., 2013). The relevance of the strengths of this approach to this research was clear. In light of the acknowledged limitations from the other observational, simultaneous verbalisation, and case-study approaches, a capacity to validate the correlations and rich suggestions of causation, which were provided by the other tools, was deemed an important benefit. Interviews also offered the only way to address some of the weaker links in the refined conceptual model which were focused on factors of personal opinion and emotion – like "level of designer's confidence during product realisation process".

Patton (2002) defines four types of interview, ranging from more tightly structured to less: 'closed quantitative' (participant chooses from pre-defined answers); 'standardised open-ended' (precisely worded questions asked in the same way and same order to each participant, with limited flexibility); 'guide' (pre-defined issues, less precision in the wording and free to explore new avenues before ensuring all topics were covered); and 'informal conversational' interviews (no questions at all – more relaxed and without structure). Cohen et al. (2013) had a similar interview categorisation scale – albeit with only three labels: formal, informal, and non-directive. Generally, those interviews at the more structured end of the spectrum are easier and quicker to analyse and compare, whereas those which are less structured are better for exploratory means (Blessing and Chakrabarti, 2009). Using the nomenclature from above, the interviews in this research were guide, informal, (or more commonly) semi-structured interviews. This was in order to facilitate relatively efficient comparisons between participant responses on given themes, whilst being free to follow interesting avenues of conversation as they emerged spontaneously. Being unfamiliar with the particular nature of the participants daily working contexts, (at least in an emotional sense), meant that perfectly precise

questions could not be formulated in advance to cover all possible influences on their design activities.

Limitations with the interview approach follow similar themes as the limitations associated with simultaneous verbalisation. They rely on a participant's ability to describe their thoughts, to do-so without reciting what they may think the researcher (and creator of the intervention) wants to hear, and they rely on a researcher's ability to interpret what was said correctly (Blessing and Chakrabarti, 2009). Furthermore, they are expensive in time for analysis, are open to interviewer bias in analysis, and can be adversely affected by interviewee fatigue (Cohen et al., 2013). Risks to validity stemming from these limitations were mitigated through adopting interview best practice. As recommended by Blessing and Chakrabarti (2009) and by Cohen et al. (2013), the questions were formulated to be unambiguous and interesting, did not suggest an answer, were suited to the participant's expertise, were supported by audio recordings to allow the researcher to focus on the conversation, relied on some key notes by the researcher to record direction changes for later analysis, started with uncontroversial questions to warm-up, and limited the number of background questions.

4.3.6. Triangulation

With the aim of improving the clarity and support of the research findings, tentative analyses or ambiguous conclusions from each of the discrete datasets were triangulated between each other: categorised field-notes from observations; selected transcriptions from observations and interviews; photographs or video frames from observations; and design output artefacts (like finished implants from Investigation A, or CAD models and associated forms in Investigation C). Furthermore, these findings were compared against the conclusions drawn from the literature and contextual reviews – particularly, in the latter case, through discussion of the findings (to come in Chapter 8). Triangulation is recommended by Blaxter (2010) as a way of increasing the validity of collected data. But when the findings from two or more data collection methods are consistent, not only is their validity is increased, but the deficiencies of personal bias (from having one researcher use a single method) are minimised (Frankfort-Nachmias and Nachmias, 1996). In this research, as described

in Chapter 4.1, the single-researcher approach and the size of the achievable dataset samples, were significant and fixed constraints. As such, triangulating between the disparate datasets was a reasonable approach to improve the validity of the data without achieving statistical significance.

4.4. Investigation A Procedure – Characterising Current UK Practice

This sub-Chapter describes the mechanics of data collection and analysis for Investigation A. It is worth highlighting the absence here of any explanations of detailed implant-production processes. Simply, the rich descriptions and documented chronologies of those processes were key data contribution *results* from this work. Indeed, as described in Chapter 3, such data had never been published in this comparative fashion before – until the publications of Peel and Eggbeer (2016), and to a lesser extent, Peel et al. (2016). The documented processes are the major focus, along with analyses of said processes, not the implants themselves (beyond a brief discussion of their success). Implant design and fabrication processes are presented as results of this research – in Chapter 5.

Investigation A1 characterised three different design and fabrication workflows for two types of simple, patient-specific, craniomaxillofacial implant. It recorded actions, aims, tools, materials, human resources, success measures, design decisions, process durations, and overall costs to the NHS of each process type. It was conducted across two different maxillofacial unit laboratories with links to the research institute, and one other maxillofacial unit which was a long-standing customer. It established what each process was typically capable of, in their given contexts, at the time the data was recorded. Every typical stage of the highlighted processes was chronicled - by following whichever (comparable) patient implants were at the relevant production stages during the data collection visits. Comparison between processes was an important factor in the data analyses; especially as more 'conventional' processes were recorded in the first instance.

Investigation A2 described three single digital design and AM fabrication workflows for complex patient-specific surgical guides and implants. Two case studies represented interesting, notable, and unusually difficult patient treatments – relative to those which had been experienced by the institute and the surgeons previously; and in one case,

relative to anything in the published literature. One case represented a highly complex, but slightly more frequent surgery – for which established institute processes had been refined and established. The devices were designed by institute staff (including the researcher) and fabricated by the institute and its commercial partners. Commercial costs for each of the case studies in Investigation A2 were difficult to calibrate for reliable comparisons. Crucially, they were undertaken in collaboration between institute and hospital units to be mutually beneficial, and in two instances, had design time and fabrication partially funded by an innovation project. That scheme (Advanced Surgical Technologies Network – ASTN) was funded by the Welsh Government Health Technology and Telehealth fund, was delivered by PDR with Abertawe Bro Morgannwg University Health Board and Photometrix Ltd., and was entirely separate to this research. This research observed those cases in Investigation A2 which coincidentally benefitted from financial support. This was reflected by artificially (and sometimes arbitrarily) lowered costs. As such, it was reasonable in the results from this research to provide indicative guide prices in these cases – as if the projects were commercially costed at the time of writing.

Comparisons were more difficult for A2 than for A1; not least because conventional, non-digitally-designed equivalent devices did not (and do not) exist in any reasonably similar forms. Rich detail and new insights into innovative case studies therefore substituted for precise timings and costings. Comparisons were possible however, between the processes employed for highly complex patient-specific device designs with no standard operating procedures, those with procedures in-development, and those with fully-developed and refined procedures.

4.4.1. Investigation A1 – Simple Routine Implants

This investigation was built around the collection of six new datasets (thesis case studies 1-6) which benchmarked, sometimes using composite datasets, clinical implant case studies. Cranioplasty implant production techniques were selected as the basis for the initial batch of benchmarked case study data, since this procedure represented the most frequently delivered commercial service by the institute. Orbital floor implants (sometimes including reconstructions of the medial or lateral

orbital walls) were selected next – as the second most numerous product delivered by the institute.

Observing and participating in each process (from simply providing medical models at one extreme, to managing and designing AM implant projects at the other) assisted with detailed logging of the practices, contexts, and their influencing factors. Best-case process timings were recorded; with idiosyncratic variables omitted (such as processes being interrupted by patient consultations or lunch breaks). This decision was important to the aim of identifying what each process was capable of; and for removing chance factors (like interruptions) from the analyses – potentially causing unfair comparisons. Each process has its advocates – so removing these variables offered a reasonable means of seeking to improve external validity of the results.

The three workflows differed in the degree of their digitisation and in the extent of manual work carried out in hospital laboratories. 'Conventional' production was the term used in place of 'traditional' production on the basis of relatively modern AM medical models being integral to its use. 'Semi-digital' was the label devised for an intermediate approach; using medical models which had been manipulated in CAD software prior to fabrication, to lower the manual crafting burden. "Fully digital" referred to the digital design and AM of end-use implants. Through consultation with the participants, who were members of the Institute of Maxillofacial Prosthetists and Technologists (IMPT), these three approaches were confirmed as generally representing techniques used across the UK, give-or-take small differences stemming from individual prosthetist preference or capability. Each process was followed to the point of the implant being sterilisation-ready. The only exception was the fully-digital orbital floor implant case study – which was characterised to the point of being verified and approved by the surgeon, before a change in patient condition led to treatment being abandoned. Fabrication timings and costs were derived from a later, analogous institute project.

Observation of the conventional cranioplasty implant production process took place over the course of one visit to the maxillofacial laboratory at Morriston Hospital (Swansea, UK). A medical model of the craniotomy defect had been requested by the lab – which was designed and fabricated at the institute using proprietary processes to ensure quality. This case was not a composite case – a single implant

was followed from beginning to end. Observation findings were recorded (with informed consent – see Chapter 4.7 for ethics measures) using: extensive field notes, a dictaphone, and extensive digital photography. The field notes included pure observational notes, reflective notes, and organisational notes, which were collected in a semi-structured fashion to ensure key details were captured (e.g. value of titanium sheet used). Audio recording acted as a backup – for retrospective clarification of details missed during the session. The process was undertaken by a maxillofacial laboratory manager (beginning) and a principal maxillofacial prosthetist (end). Calculations for staff time costs were based on the relevant NHS salary band guidance at the time of the observation. The two participants were not asked to provide their salaries directly – to avoid a potentially sensitive conversation, potentially affecting their openness and comfort.

Semi-digital cranioplasty implant data collection took place using the same approaches and tools. As requested in this process, the medical model provided to the laboratory staff by the institute had seen the defective anatomy reconstructed (via a mirroring function) prior to fabrication. In this case, three visits were required to the dental laboratory at the University Hospital of Wales (Cardiff, UK). This was because of the part-time working arrangements of the participating technician. Again, this was a single implant, not a composite case. The process was undertaken by a dental technologist – with final approval provided by a consultant maxillofacial surgeon.

Fully-digital cranioplasty implant data collection took place at the institute, and consisted of the researcher designing an implant on a commercial basis for the University Hospital of Wales. Extensive notes were recorded about the precise steps taken to design the device, with standard institute costings used to establish the cost of this activity to the NHS. Institute costings naturally incorporated staff costs. Aside from the researcher, a consultant maxillofacial surgeon was involved (implant specification and procurement), along with a dental technologist (reaming screw holes in the implant at the dental laboratory as a finishing process). Screen-captures were taken intermittently to provide explanatory illustrations of key actions. This was a single case – composite data was, once again, not required here. In this instance, owing to this method being new to the unit in question, the researcher and other institute staff were invited to observe the surgical procedure. This involved

one primary stakeholder – the senior consultant neurosurgeon – alongside a typical array of junior doctors and nursing staff. Extensive notes were captured during this surgical procedure. Secondary reports were relied upon for assessing the relative performance of the conventional and semi-digital process outputs.

Data collection for characterising the conventional, semi-digital, and fully-digital orbital floor implant process followed the same patterns, and the same general approaches as for the equivalent cranioplasty processes as described above. Conventional orbital floor implant production required one visit to Morriston Hospital's maxillofacial laboratory on one day. Actions and staff time were recorded for one maxillofacial laboratory manager (in a supervisory role), one principal maxillofacial prosthetist, and one consultant maxillofacial surgeon. This was a composite case study – where two different (but analogous) implants were followed at different stages of their development in the interests of efficiency and ensuring participant availability. Semi-digital process observation happened in one day, on one visit to Morriston Hospital's maxillofacial laboratory. Staff involvement (aside from the reconstructed model design on the part of the researcher) was limited to a principal maxillofacial prosthetist and a consultant maxillofacial surgeon. A single implant was followed through the process to sterilisation readiness. Finally, the fully digital orbital implant process was recorded via notes and screen-captures of the researcher's own actions, like for the cranioplasty. A consultant maxillofacial surgeon at Frenchay Hospital (Bristol, UK) was the customer in this instance – with no in-person contact required. Telephone and email correspondence were used – for specification and design verification. Two different (but analogous) implants were followed to make a composite case study here; as highlighted previously.

Data collection was geared towards eight analyses for each process – to permit comparisons between them, having generated new insights into them individually. Those analyses (presented with the results in Chapter 5) were designed to extract information about: the processes used and design decisions taken within them; materials used; material costs; staff time involved; staff costs; tools used; total (best case) process durations; and outcome artefact features. Photographic flow diagrams (Chapter 5.1.1-5.1.6) were deemed most appropriate, alongside written description, for presenting the tasks and decisions. This approach was efficient and effective for communicating niche techniques from unusual design contexts. Easy-to-

comprehend overviews were created by grouping each process' actions into categories and relating them to one another through longitudinal Gantt-derivative charts (Chapter 5.1.7). The remainder of the analysed data was best presented in concise tables. The accompanying cost calculations were made explicit for interrogation and to target external validity, even in the presence of some assumptions and generalisations; such as acknowledging that conventional laboratory tools were not priced in to the results, nor was the acquisition of skills for those smaller units which lack them at present. Such measures would have required much larger scale economics and business research – which were not the focus here.

Finally, the data analysis was directed towards constructing an intermediate conceptual framework – as a developmental step towards the final framework presented in Chapter 4.2.4 above. Its factors are presented later in the results Chapter for this study, because it was an important iterative step between the initial model and the refined model.

4.4.2. Investigation A2 – Complex Implants

This investigation was built around the accumulation of three new datasets which captured individual, complex, mostly novel case studies in rich detail. The range of cases spanned a post-traumatic zygomatic osteotomy with orbital floor reconstruction, post traumatic zygomatic osteotomy with orbital floor reconstruction and maxilla contouring, and a hemimandibulectomy with fibula free flap reconstruction. The initial osteotomy case study was the seventh overall case study in this thesis and will be referred as such (Case Study 7) for clarity. The following osteotomy was Case Study 8. The hemimandibulectomy and fibula flap reconstruction was Case Study 9. For this investigation, both the documented processes and the finished devices themselves were valuable outputs for recording and analysis.

Case study 7 was a non-urgent elective procedure carried out clinically at Morriston Hospital's maxillofacial unit and designed at the institute – primarily by the researcher. From initial receipt of the patient's scan data, through several design iterations, detailed development work, prototyping stages, and surgeon feedback, the

total project duration was eight months. This unusually lengthy timeframe was dictated entirely by the clinical context – where other urgent cases took precedence, and clinician availability for ad-hoc design input and evaluations was severely limited. Because this was the first known instance of such a procedure being carried out entirely 'digitally' – with digital surgical planning, AM cutting guide, AM repositioning guide, medical models, and AM implants, neither the institute nor the hospital had standard, proven device-specific procedures to follow from the start. Naturally, each collaborating institute had validated procedures for the production of similar devices and treatments, but the specifics of, and solutions to the particular design problem could only be concluded at the end of the project. Extensive field notes, screen-captures, CAD project files, quality management system records, prototyped artefacts, and surgical photographs were collected, logged, and analysed throughout the case. The process, key design decisions, experiences, design outputs, surgical procedure, functional outcomes, and aesthetic outcomes are presented in Chapter 5.3.1.

Case study 8 was a similarly non-urgent elective procedure – designed by a member of institute staff (not the researcher) for a Consultant maxillofacial surgeon from Prince Charles Hospital (Merthyr Tydfill, UK). Unlike case study 7, the project duration here was closer to the norm for the institute – 10 working days. Whilst there was still a developmental and exploratory approach to the case, and an absence of a fully-realised standard-operating procedure for zygomatic osteotomies (on account of their rarity), the key design rules (or at least, design considerations) were copied and adapted from case study 7. The process and its outcomes were recorded in the same way as for case study 7 with some key exceptions. Briefly, the dataset did not include residual prototypes from older iterations or from testing (as they were not required in this case), and surgical performance was reported by the consultant surgeon as the researcher was not present. The same fields and analyses are reported as for the previous case study; in results Chapter 5.3.4.

Case study 9 reflected the culmination of a logical progression: from the complex and unstructured process for case study 7; through the complex and semi-structured process for case study 8; to its own complex but highly-structured process as applied to a hemimandibulectomy and fibula free flap reconstruction. Custom cutting guides and a custom implant were designed by the researcher according to specifications

agreed with a consultant maxillofacial surgeon from the University Hospital of Wales (Cardiff, UK). As was highlighted in the literature review in Chapter 3, this treatment is not only generally common for patients suffering from oral cancers, but is also one of the more common procedures to be undertaken with the assistance of CAD and AM devices (guides and implants). As such, the institute had experienced nine previous analogous commercial cases. Because the fibula flap device design and CAD modelling process was disproportionally dependent on, and sensitive to the precision and order of software functions, the researcher compiled a high-fidelity standard operating procedure for use across all institute staff (see Appendix 3 for an extract). This document had two main purposes: standardise the customer experience and design outputs regardless of the designer; and increase the speed of the modelling process by eliminating as many trial-and-error steps as possible. The latter aim was of particular importance because of the intensity of cases such as this – being both clinically urgent and requiring major modelling effort. The procedure was reviewed with other institute staff, recorded in a step-by-step list of instructions and reminders, and illustrated with example screen-captures. Work instructions aside, the case was delivered inside a ten working day timeframe, and was recorded and analysed across the same fields as case studies 7 and 8.

4.5. Investigation B Procedure – Development of a Design Process Intervention

This sub-Chapter describes the mechanics of data collection and analysis for Investigation B. As a whole, this investigation was about developing a design process intervention to address the barriers in current practices, as extracted from the literature and from the results of investigation A. It was designed to achieve this improvement in the context of compliance with the BS EN ISO 13485 quality management standard. Creating an intervention which helped to meet that standard was a key aim for two reasons: it was an important aim for the institute; and (as noted in sub-Chapter 1.6.2) there may be a legal requirement for in-hospital device production to comply with said standard in the medium term. Even if loopholes are created in this new legislation, the design process intervention would still be aiming to help popularise design, clinical, and quality management best-practice – which is no bad result.

Investigations B1 and B2 were geared towards establishing a specification for the proposed design intervention – accommodating current practice improvements in a manner which was complimentary to, and a partial facilitator of, ISO 13485 compliance. They were procedural investigations built around deskwork. Investigation B3 on the other hand, delved deeper than those general procedural levels; to generating specific, granular, and evidenced detailed design considerations for complex patient specific devices. It was built around five more design case studies (thesis case studies 10-14) and extensive fieldwork. Investigation B4 was a prototyping process to assemble the design intervention in document form – encompassing the requirements determined by the data collected in B1-B3.

Crucially, the narrowing of the research focus is visible throughout Investigation B – with the attention targeted towards complex craniofacial implants.

4.5.1. Investigation B1 – Incorporating Solutions to Barriers in Current Practice

This investigation was a simple desk-based exercise of translation and synthesis. The characterisations of current practice from Investigation A were linked to a list of process modifications. Those modifications were conceived to mitigate the problem with, lower the barrier to, or improve the efficiency of, each given factor. Some process modifications were clear and recognisably corrective - by virtue of recommending precisely against problematic aspects of current practice. Others required subjectivity based on professional experience – particularly when multiple possible solutions existed. In order to make such inferences and judgements explicit, the results were presented in a table including a column with a space for overt justification. Generally, where multiple possible solutions existed, the ones impacting current methods the least were favoured – in order to maximise potential adoption and uptake.

4.5.2. Investigation B2 – Accommodating ISO13485 Requirements

This investigation, like investigation B1, was desk-based and revolved primarily around analysis and translation. Here, the aim was to identify the requirements for, and implement a Quality Management System (QMS) which would develop the institute's design activities and ensure they complied with the ISO 13485 standard. This was a commercial aim for the institute and an activity whose external validity was supported by feedback from: two external fabrication-partner audits (one day each, with two assessors); one external pre-certification audit by a notified body (one day, with an auditor and a trainee auditor); and two internal audits by an institute staff member (one half day each, with a staff member trained for internal auditing). This system, like the design intervention in investigation B4, was constrained in scope to the *design* aspect of the patient-specific device production process (with fabrication controls excluded, beyond ensuring the design outputs were suitable for their stated processes).

Each resulting component of the pre-certified QMS was assessed for relevance for inclusion in the design intervention. Relevance here, was defined as those components or functions of the QMS which the framework could reasonably and efficiently replace or co-opt; independent of design tools or design context. Although context independence was a key aim (to have validity beyond the institute), users were necessarily assumed to have competency in using whichever design tools were judged to be most suitable at their institution. This way, tool-independence could be targeted, without making the design intervention an educational, overly prescriptive and incredibly long pro-forma. These judgements and analyses could not claim to contribute to a design intervention which, upon adoption, guaranteed compliance and certification to ISO 13485; because a QMS by definition must be appropriate for, supported by, and specific to its own institution (ISO., 2016). Moreover, the defining feature of ISO 13485 is the very large extent to which it is predicated on a context-specific risk assessment. Judgements about relevance in this investigation were unavoidably made from a baseline of a QMS which had been designed in response to an institute-specific process failure modes effects analysis (FMEA). However, that FMEA was undertaken based on the service models characterised by Investigation A2, and which did not contain any unorthodox methods relative to those described in the literature in Chapter 3. On that basis, it was a sound approach

to use the QMS developed for the institute by the researcher, as a point of departure for abstraction.

To delineate clearly between the institute's commercial aims and activities undertaken for this research, only summary views of the developed QMS were presented and annotated in the results sub-Chapter 6.2. This achieved a balance between communicating sufficient information about the nature, extent, and purpose of the QMS and its components; and maintaining a focus on the analyses and translations of certain relevant aspects for abstraction and generalisation to the design intervention. A table was used as the vehicle for presenting the results of these judgements; with the same opportunities as in the results from Investigation B1 to make the reasons for subjective judgements clear. Once again, this was with a view to improving external validity of the research – and to encourage thorough interrogation of the subjective reasoning, in order to improve or adapt the outcomes wherever the intervention might be implemented as part of future research work for different audiences or contexts.

4.5.3. Investigation B3 – Incorporating Clinical Design Rules / Considerations

This investigation identified and evaluated key design considerations when digitally planning and designing complex craniofacial AM and CNC machined devices. To achieve this, it analysed the literature review from Chapter 3 to collate and consolidate frequently-cited considerations from previous work. Articles were sourced from searches of the PubMed database, and then the searches were expanded to Google Scholar, to ensure that peer-reviewed technical papers were not overlooked. Then abstracts were analysed for relevance and qualifying articles saved for full review. This review covered both complex craniofacial reconstructions and simple reconstructions (where a given issue is generalisable across categories) to establish the current state-of-the-art. Considerations with fewer than three sources were excluded, as were obvious pre-requisites – such as the biocompatibility, good strength, and stiffness of PEEK and titanium.

Then, new data from five primary case study observations (thesis case studies 10-14) were described, analysed, and concluded for analogous and unique considerations.

Those unique considerations were speculative and deserve further research in the future. They emerged from the case studies, but remain as-yet unproven across a wider sample, or in the literature. Incidentally, the term “design considerations” was used in place of “design rules” to reflect the evolving and patient-specific nature of the devices in question – and to allow scope for modifications depending on a patient’s unique needs. Issues of universality and generalisation were a recurring theme in this process. As with Investigation A, the results from these observations and desk-based analyses of the researcher’s own designs are as much about the specific details (i.e. the design considerations) of the processes, as they are about the nature of the designed outputs themselves. As such, specific details about the justification for design decisions are presented in the results for this case series (see sub-Chapter 6.3).

In this investigation, complex craniofacial devices were narrowed in definition as those which replaced the geometry of two or more bony surfaces (or of comminuted defects). Geometrically simpler reconstructions such as many orbital floors or cranioplasty plates would be likely to involve fewer critical design considerations, or be more easily fabricated in a hospital laboratory (Hughes et al., 2003, Bartlett et al., 2009, Peel and Eggbeer, 2016). This investigation’s featured case studies were divided between cases of meningioma and fibrous dysplasia. Each case required disease excision and alloplastic reconstruction in the orbito-temporal region. The cases varied in four key ways: alloplastic reconstruction material; the degree of digital planning which was undertaken; the use (or not) of surgical guides; and naturally, in specific design details. Guides were produced in an epoxy resin via vat photopolymerisation AM. Four AM implants were produced in medical grade titanium Ti6Al4V ELI (grade 23). One implant was produced in PEEK via CNC machining.

The findings from this investigation (in sub-Chapter 6.3.1) were drawn from literature review, from primary-data, or from a combination of both. External validity was supported by a publication in a peer-reviewed journal (Peel et al., 2017). However, key limitations persist and should be highlighted explicitly. The primary data came from a single hospital unit (UHW, Cardiff, UK) and a single surgeon in collaboration with a single implant design service comprising two design-engineers (at the institute). The conclusions drawn from this data have only been shown to

apply in these cases – or in isolated cases within this series. The primary data was skewed towards titanium implants, and the secondary data literature review skewed towards PEEK – reflecting its prevalence in reports. Further work is required in the future on both fronts to address these imbalances and small sample sizes. Surgery duration evaluations from the primary data relied on subjective estimates – future work on health economics within this and other hospital units is required to build a fuller picture. Finally, it should be noted that varied AM titanium surface finishes were selected based on surgeon preference – the implications of these choices provide another avenue for future investigations.

Surgeon-evaluated device performance and clinical results from each case dictated subsequent method modifications. All devices were prescribed and implanted by the same UK maxillofacial surgeon, in the same hospital, with significant input from a multidisciplinary team including neurosurgery and ophthalmology colleagues. All digital planning and design work was undertaken in collaboration with the institute. The researcher was partially responsible for design activity in cases 10 and 11; and fully responsible in case 12. The researcher had no direct involvement in cases 13 and 14, but extensive observational field notes, screen-captures, and photographs were recorded for all cases. In all of those cases, the digital workflow was selected to overcome problems experienced by the maxillofacial surgeon in using conventional and semi-digital techniques in prior complex reconstructions. For example, a meningioma (cancer) patient with failed autologous bone graft reconstruction had undergone revision surgery at the hospital, using titanium mesh which was intra-operatively shaped on an anatomical model. The result was judged only as acceptable - with scope for improvement in aesthetic accuracy, eliminating donor-site morbidity, improving visual functional outcomes, and reducing surgery duration.

The digital workflow involved (to varying degrees) the use of medical models, digital surgical planning, patient-specific guide design, patient-specific implant design, polymer guide fabrication and metallic implant fabrication. Pre-operative Computed Tomography (CT) scanning was utilised for each patient. CT data processing was undertaken by a design engineer at the institute using a standardised procedure and appropriate CE-marked software (Mimics, Materialise, Belgium). All polymer models and guides were fabricated using a form of vat photopolymerisation;

StereoLithography Apparatus (ProJet 6000HD, 3D Systems, USA) in Accura ClearVue resin (3D Systems, USA) which has been tested to USP 23 Class VI – rendering it suitable for sterilisation and for building transient surgical devices when parts are cleaned appropriately. Polymer devices were prepared for fabrication and had support structures added using Magics (Materialise, Belgium).

Device design was undertaken by institute engineers using FreeForm Plus (3D Systems, USA) in all cases - via its haptic PHANTOM interface. Implants in case studies 10-13 were fabricated by a form of powder bed fusion; Laser Melting (LM) Ti6Al4V-ELI (medical grade 23) by an appropriately accredited supplier (3D Systems LayerWise, Belgium). Titanium was selected by the surgical team on the basis of a long track-record of success in the hospital and the wider maxillofacial specialty – in addition to the titanium benefits highlighted in the literature review Chapter. Implant components in thesis case study 14 were fabricated by five-axis CNC of PEEK by a similarly qualified supplier (Synthes, Switzerland). PEEK was selected for this case because of a high-degree of confidence that post-operative radiotherapy would be necessary. PEEK's radiolucency was judged to be important – for post-operative imaging and radiotherapy uninterrupted by scatter or artefacts; important for surveillance and treatment.

4.5.3.1. Case Study [10]

The patient in case study 10 presented with headaches, a drooping eyelid, eye asymmetry, left-eye exophthalmos (protrusion), worsening vision, and diplopia (double vision) on far-left gaze. Following consultation and pre-operative CT imaging, a left spheno-orbital intra-osseous meningioma was diagnosed.

In theatre, a pretracheal approach was used for site exposure – aiming to achieve good post-operative aesthetics by positioning the incision behind the hairline.

4.5.3.2. Case Study [11]

Patient 11 presented with left-eye exophthalmos, headaches, seizures, and decreasing vision. Following consultation and pre-operative CT imaging, a left skull-base meningioma was diagnosed – extending to the temporal bone and posterior orbit.

In theatre, a coronal approach was utilised.

4.5.3.3. Case Study [12]

Patient 12 presented with left-eye exophthalmos, pain, decreasing vision, and a visual field defect. Following consultation and pre-operative CT imaging, fibrous dysplasia was diagnosed in the patient's left cranio-orbital region.

In theatre, a coronal-flap approach was employed for access to the site.

4.5.3.4. Case Study [13]

Patient 13 presented with right-eye exophthalmos. Following consultation and pre-operative CT imaging, a right cranio-temporal-orbital meningioma was diagnosed – with intra-cranial involvement.

In theatre, a coronal approach was used to access the affected area.

4.5.3.5. Case Study [14]

Patient 14 presented with, discharge from the left ear, swelling of the temporal fossa and decreasing vision. Following consultation and pre-operative CT imaging, a left spheno-orbital meningioma was diagnosed – with middle cranial fossa involvement.

In theatre, a coronal approach was used to access the affected area.

4.5.4. Investigation B4 – Constructing a Design Process Intervention

This investigation was undertaken as a desk-based document-design activity. Investigations B1, B2, and B3 had provided clear requirements for a design intervention to better structure and drive the complex craniofacial patient-specific device design process. Primarily, Investigation B1 was designed to improve the fidelity of the user and product requirements list collected at the outset of a new product's development. This link was shown in the refined conceptual framework (Figure 29 from sub-Chapter 4.2.3).

Certain relevant (generalisable) sections from institute QMS documents were copied, adapted, and synthesised into an initial design intervention prototype. Those relevant documents included: a product and customer requirements collection facility; a review of the requirements collected; design considerations for complex craniofacial devices; links to evidence for those considerations; product design activity peer-review facilities; and directions to obtaining high fidelity feedback. This composite prototype was constructed simply, in standard word-processing software with a view towards maximum compatibility (Microsoft Word, Microsoft, USA). Other media were rejected, such as creating an app or a webpage, on that same basis of wide compatibility. Additionally, project resources and focus barred any pursuit of those programming techniques – this research was chiefly concerned with the content and structure of the design intervention, not its interactivity. Attention was paid to the intervention form layout – including clear demarcation of sections for example. Translation of its content to the domain of proprietary software remains a potential avenue for future research.

In total, two prototyped iterations were required until the intervention form satisfied the requirements from B1-B3. The final iteration of the intervention is presented in its corresponding results sub-Chapter (6.5). Annotations point to the document design features and justifications for their inclusion.

4.6. Investigation C Procedure – Design Intervention Impact Verification

Investigation C comprised two sub-investigations; a pilot test with one participant and a refined test with two further participants. It sought to verify the performance of the novel design intervention by identifying and analysing the effects it had on aspects of the device design process for simulated patient cases. Naturally, the contextual focus remained on meningioma of the craniofacial skeleton – reflecting the focus of the evidenced framework from investigation B4. Both quantitative data and qualitative data were collected across the full course of what were, as justified in sub-Chapter 4.3.4, comparative observations. Generally though, the quantitative measures were related to observations of the participant's design activities, while the qualitative measures stemmed from short interviews after the design phase; about subjective reactions to using the framework relative to their reactions to using their own conventional approaches.

Participants were asked to model alloplastic reconstruction solutions to the artificial (but realistic) patient scenarios which are described in sub-Chapter 4.6.1 below. They were asked to design solutions using CAD software. Alternatively, they could have been asked to describe what they would have done using CAD software, or been asked to sketch solutions by hand. Modelling was chosen though, with the aim of affording the opportunity to observe any positive or negative impacts of the framework on real design activities, with which they were certain to be familiar, in real time.

4.6.1. Investigation C1 – Design Intervention Pilot Testing

One participant from the institute was recruited for the pilot test. Participant 1 had three years' experience of designing patient-specific devices using Mimics (Materialise, Belgium) and FreeForm (3D Systems, USA) at the time of the observation. Their daily role included the delivery of the institute's core surgical design consultancy services – using the underlying workflows, and quality control procedures abstracted by Investigation B. The pilot test aimed mainly to evaluate the appropriateness and effectiveness of the planned data collection procedure, and data collection tools. However, given the relatively minor modifications required

between the pilot observation and verification observations, the decision was taken to analyse the pilot data too – particularly in light of the intensity and effort required during data collection.

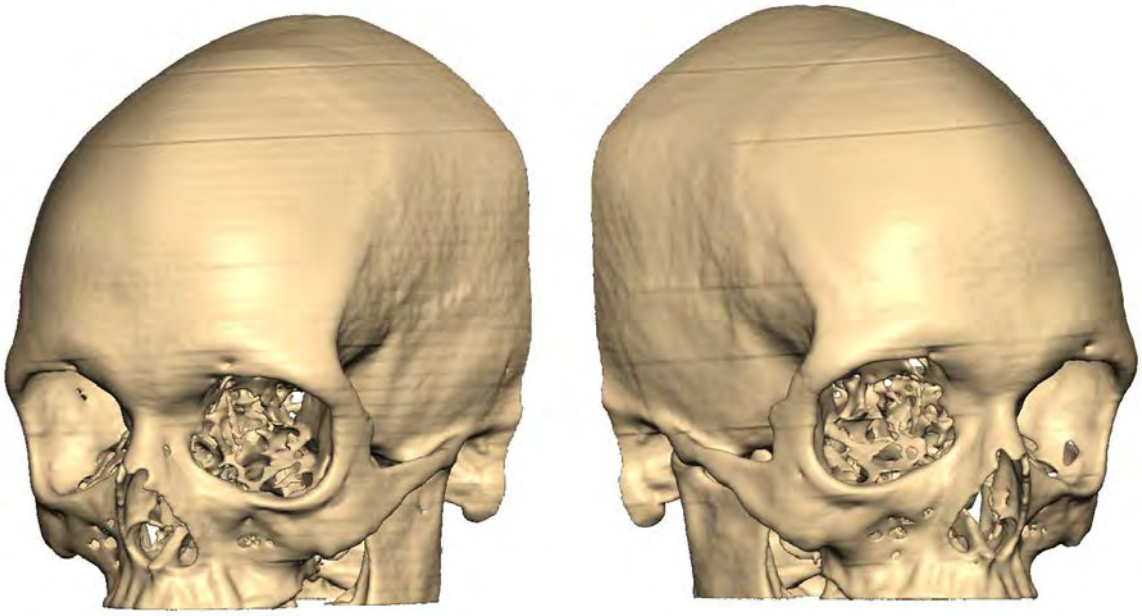


Figure 30 - 3D Virtual Model of Investigation C Scan Data

A simulated patient project was created – by selecting CT scan data from the institute archive. That archive contains those data sets which are stored to meet data handling and record-keeping requirements. Datasets were filtered to find patients with scans encompassing the full cranium, without any existing implants or reconstructive hardware, without visible defects to the skeleton, and with scan data of sufficiently small slice thicknesses and slice distances so as not to result in stepped 3D reconstructions. The chosen dataset (Figure 30) was then anonymised – resulting in all personally identifiable information being removed from the Mimics (Materialise, Leuven, Belgium) file. Scan data is routinely archived by the institute in the more space-efficient and more conveniently reviewable Mimics file format, rather than as larger raw DICOM files.

The CT scan data was segmented for bone by manually fine-tuning a pre-set, built-in Hounsfield value for bone. The manual adjustment minimised artefacts and maximised bone tissue fill. After region-growing the resulting mask, the eraser and local thresholding tools were used (in conjunction with a graphics tablet) to refine the mask by editing across individual slices of the scan. Excess data was cropped away, though a wider margin was left around the region of interest than would

usually be necessary – with a view towards accommodating possible personal modelling preferences of the participants. For example, some may prefer to have a smaller, focused working piece, while others may desire a broader coverage to permit wider aesthetic symmetry judgements. The virtual model of the patient's (healthy) anatomy was exported in the STL format with high quality and moderate smoothing settings, and with shell-reduction switched on – to minimise potential issues with STL file errors.

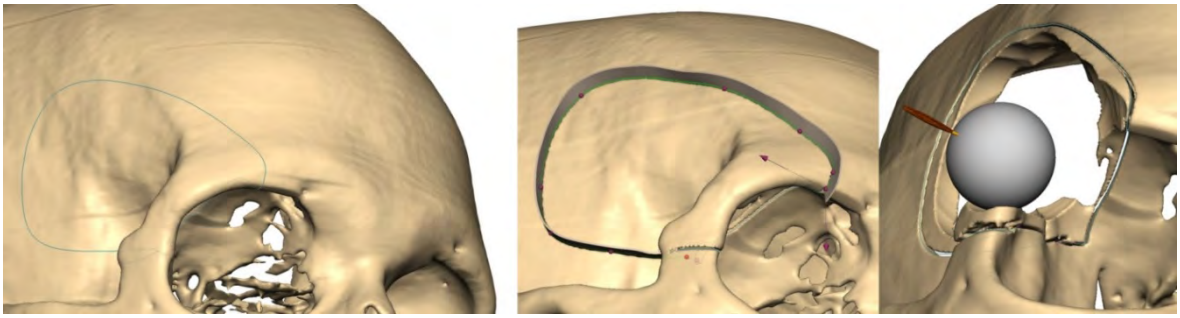


Figure 31 - Modelling Procedure for Model with Right Defect

Verification required comparisons between participant design activity before and after being introduced to the intervention. As such, two design problems were presented to each participant – with a request to solve the first as they would in conventional daily practice, and to solve the second after being introduced to the printed framework. To reduce the time burden on the commercially and clinically loaded participants, the tumour segmentation, margin verification, excision planning, and surgical cutting guide design activities (as described in the case studies in Investigation B3 and its results) were already completed upon presentation of the data to the participants.

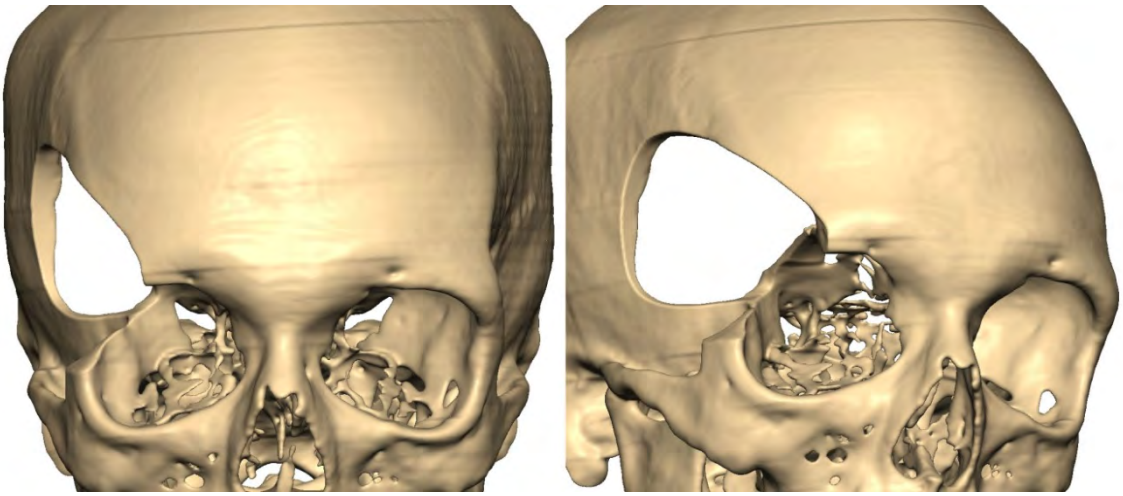


Figure 32 - Model with Right Defect

Two different excision margins were modelled (Figure 31) on separate copies of the virtual patient model by using the 'ridge' function in FreeForm Modelling Plus (3D Systems, USA). After cutting a 0.7mm gap along the sketched profile, manual carving tools were used to remove the simulated disease – which was attached to the "healthy" anatomy by complex internal bone structures. The specific margins were arbitrarily manipulated to span aspects of the temporal, sphenoid, and frontal bones – with a degree of invasion into the superior orbit and rim. Different margins were used for the two models to discourage simple repetition across the two tests the participants would each undertake. However, the margins encompassed the same general areas of the cranium – to permit a degree of comparison between designed outcomes, and not just between the processes and actions employed. One defect was designed into the patient's right (Figure 32), with significant orbital involvement, and a moderate cranium involvement. The other defect was designed into the patient's left (Figure 33), with less orbital involvement, but a larger extent of cranial invasion.

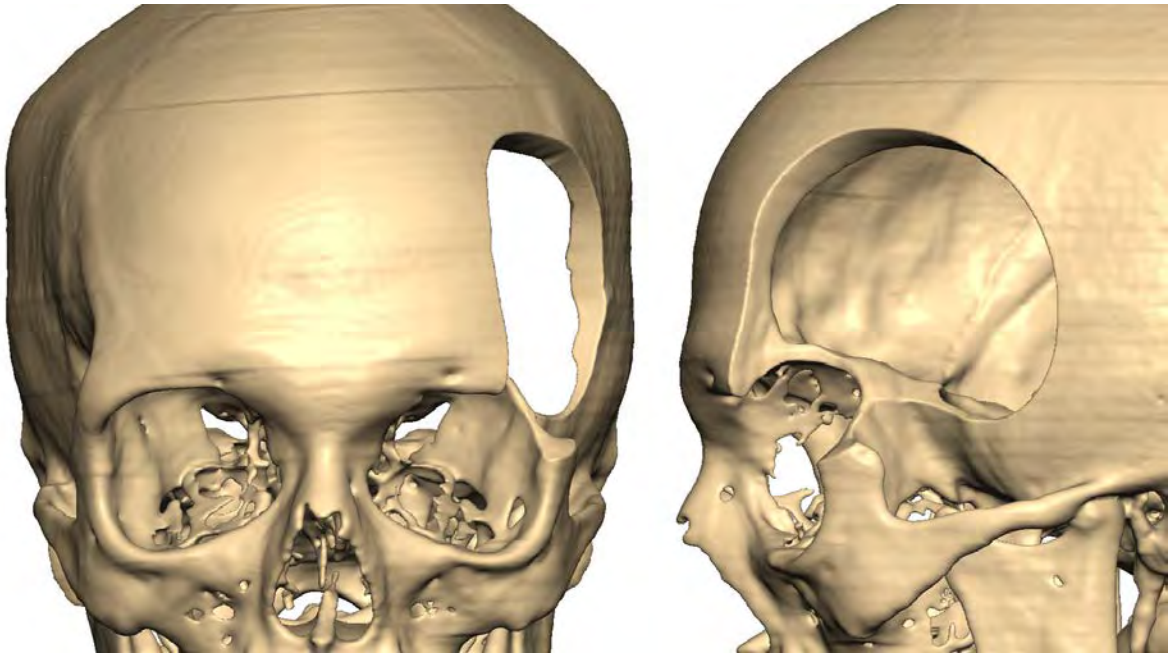


Figure 33 - Model with Left Defect

Two time slots of four hours each were allotted for the pilot participant – totalling eight hours involvement from the one institute staff member. In detail, this

incorporated fifteen minutes for introductions and project set-up, three hours for design activity and forty-five minutes for reflection (via interview). Design activity was defined as establishing requirements, conceptualising solutions, CAD modelling, and informal design review. The latter parts of the design intervention (which included peer review, verification, and feedback) were provided for reference only – and to provide the participant with full design process context. This planned time-breakdown was based on the high skill level of the participant, their experience and familiarity with the software tools and patient-specific implant design, and with an appreciation of their limited availability (as would likely be the case for any clinically active biomedical design engineer).

Some over-running was permitted for the interviews – to the degree of finishing an answer to a question or finishing a topic. Design activity durations were fixed, and not permitted to overrun. This aimed to facilitate a degree of comparison between progress with, and without the framework. Allowances were made for breaks or emergency interruptions – during which, the clock was stopped. Although participants were informed about the time allocated for each portion of the experiments, they were encouraged to work at their normal pace so as not to explicitly or implicitly encourage rushing. Participant 1 (pilot) was asked to reconstruct the model with the right defect first (using their conventional practice) and the model with the left defect second (after being introduced to the printed framework). When the participants were designing according to their conventional practice, they were asked to complete any requisite forms or paperwork or other records as they normally would.

At least two weeks were allowed between the participant's two design sessions. Like the use of two different defect models, this was to discourage self-referencing or simple copying of design decisions across the two separate defects. Essentially, this break between sessions aimed to remove the precise design solutions from the first session from the participant's immediate recall.

The author-researcher acted the role of prescribing and operating surgeon during each design session. This was not necessarily reflective of a typical initial planning session – during which only the excision might be agreed, and a basic design outline approved for downstream offline modelling. However, the ability to simulate a fully

realistic customer-designer relationship (and communication techniques) was out of reach. That could have required staging the design activity over several days and (possibly) working remotely from the participant to respond to emailed proposals or queries. Comparing modelling activities before and after framework use (with realism compromised) sought to maximise the reasonable measurements of framework performance – all within the pragmatic resource constraints of a doctoral thesis project.

Printed information (Appendix 6) was prepared to ensure consistency across the information delivered to each participant about the nature of the experiment and the procedure for data collection. Experience from working commercially in the institute was used to populate the information sheet – with the (relatively small) amount of detail provided by a surgeon in the first instance. The information sheet also included a participant consent form in order to obtain informed consent for the data recording methods and scope of data use. Key answers about design specifics were defined by the researcher before the sessions. This information was recorded by completing relevant fields of a blank copy of the design intervention pro-forma document (completed version in Appendix 7); to ensure that consistent responses to participant questions were immediately at-hand during the experiments. Those notes were used by the researcher by searching through a digital copy of the document on a laptop during the experiments – with the screen pointing away from the participant. Answers were retrieved in this way to disconnect the content of the answers from their physical location in a printed framework; and so mitigate the risk of participants being able to see which fields contained relevant information in which part of the document. As the simulated surgeon, the author-researcher did not volunteer extra information beyond that delivered in the project introduction, or sought via participant questions.

After each observed design exercise, a brief semi-structured interview was undertaken to collect subjective, qualitative feedback about the participant's experience of designing what was, in the context of the projects explored in this thesis, a highly complex device (or devices) – using both their own processes and the framework. The interview questions (or, starting points) in Table 4 were also exploited to gather technical information about the degree to which standards and regulations were accommodated in their setting. Follow-up questions, and

participant responses were recorded in field notes. Where the participant had not finished the design and modelling of the alloplastic implant(s), they were asked to outline how they would have progressed the solutions to completion.

During the observations, the process was recorded in three ways – manual note taking in a pre-prepared pro-forma (Appendix 8), video recording (including audio) of participant modelling activities and interactions, and backup audio recording – to retrieve important quotations accurately in the event of video failure. Participants were encouraged to comment on or otherwise explain their working through simultaneous verbalisation as they progressed through the design sessions. The post-design interview was audio recorded. Video and audio recording were employed with a view towards accurate analysis even during busy periods where the author-researcher was responding to participant questions in the role of prescribing surgeon, providing introductory briefings, or noting other key findings.

The pro-forma was designed to focus attention on those key observations targeted for improvement by the framework. Spaces to note the time at which key observations occurred were designed-in; with a view towards efficient analysis and quotation extraction; as opposed to transcribing eight hours of recordings per participant – which, as justified earlier, would have been unachievable in a reasonable timeframe. The key observations and how they were recorded for Investigation C are summarised in Table 5 below. The key quotes extracted from those key observations had inclusion criteria based on a quote's ability (alone or in a group) to clearly represent a recurring insight or theme, or based on a quote's ability to represent a unique insight or theme.

Table 4 - Investigation C1 Interview Questions

Investigation C – interview questions / starting points:
Please describe your designed solution in the context of the project and product requirements.
Please describe how you would have finished the design, and its key design details.
How do you rate the ease (or difficulty) of the design exercise?

Questions asked in conventional session only:
What is the biggest barrier (or barriers) during everyday design work? *Did that (or they) manifest themselves in this exercise?*
How is quality controlled (if at all) is your design process? *To what degree do you follow these controls?*
How prescriptive is the structure of your design process? *To what degree do you follow this structure? (As you go?)*
How are projects managed? *Including intra-team arrangements?*
What were your emotional reaction(s) to using your conventional processes to work on this exercise?
To what degree, and how, is your regular design process documented and recorded?
To what degree are design procedures supported by evidence? *How? Sources?*
To the degree that any exist, how are disagreements between you and your clients regarding designed solutions resolved?
To what degree are regulatory requirements considered in your regular design work? *Where required?*
How are new design approaches or ideas evaluated and approved? *How often do you try something new?*
How often are you presented with an unusual design problem?
Is feedback on your designed device performance collected? How? *How is this used?*

Questions asked in intervention session only:
Please describe the effects, if any, the framework had on your design process – relative to your conventional methods.
What where your emotional reaction(s) to using the framework in this design exercise?
How, if at all, did section 1 of the framework (project set-up) affect your working?
How, if at all, did section 2 (establishing implant requirements) affect your working?
How, if at all, did section 3 (specific design considerations) affect your working?
Does your conventional practice include an activity analogous to section 4 (peer review)? *How does / could this affect your design work?*
Does your conventional practice include an activity analogous to section 5 (peer review)? *How does / could this affect your design work?*
Does your conventional practice include an activity analogous to section 5 (peer review)? *How does / could this affect your design work?*
What effects, if any, did using the framework have on the success of your designed outputs (or at least the design direction)?

Table 5 - Key Observations for Investigation C

Key Observable Factors	Data Type	Limitations / Controls	Data Recording	Data Analyses	Presented As
Fidelity of the requirements list (or verbal equivalent).	Quant	May be extra requirements not anticipated by framework fields. / Allowed for new directions and requirements to develop.	Live observation. Video recording. Intervention form.	Notes to highlight requirements discussion timestamps. List of participant-generated requirements. Cross-referencing between participant list and ideal list.	Checklist / matrix.
Participant behaviours, durations, orders, and patterns.	Quant	N/A	Live observation. Video recording.	Notes to highlight key behaviour timestamps. Simple behaviour coding.	Longitudinal time-in-motion charts.
Number, nature, and relevance of questions asked by participants.	Qual. & quant	N/A	Live observation. Retrospective video analysis.	Notes to highlight key question timestamps. Cross-referencing between questions asked and framework fields.	Narrative description and analysis. Longitudinal time-in-motion charts.
Participant emotions during the design activity – and towards the framework.	Qual.	-	Live observation. Retrospective video analysis. Interview audio recording.	Notes to highlight key emotion timestamps. Identification of key quotes.	Key quote transcriptions.

Degree of (current, non-framework) process compliance with ISO 13485 requirements.	Quant	-	Retrospective video analysis. Interview audio recording.	Cross referencing with ISO 13485 requirements list from sub-Chapter 2.8.1.	Checklist / matrix.
Degree of design completeness, in the allotted time.	Quant .& qual.	Experience levels were appropriate for the task, but still varied. Framework was always used second – so naturally had an advantage. / Unable to improve under constraints.	Live observation. Interview audio recording. Designed outputs.	Identification of key interview responses regarding remaining work. Assessment of CAD files.	Screen-captures of work achieved. Narrative description and analysis. Key specification points.
Appropriateness of designed solution(s).	Qual. & quant	Impossible to be fully objective. Approaches could also have been limited by modelling ability. / So judged based on requirements list, then specific outcomes.	Live observation. Retrospective video analysis. Designed outputs.	Assessment of CAD files. Notes to highlight key remaining-modelling-activity description timestamps. Cross-referencing between ideal requirements list and both actually modelled, and described design solutions.	Screen-captures of work achieved. Narrative description and analysis.

4.6.2. Investigation C2 – Design Intervention Verification Testing

Following the completion of the pilot test, and subsequent reflection, minor changes were made to the data collection methods to overcome small issues. No changes were necessary to the intervention form itself. Otherwise, the procedures followed were identical to the pilot test. The C2 verification tests took place at Morriston Hospital's Maxillofacial Laboratory. Participant 2 was a maxillofacial laboratory manager and experienced prosthetist. This participant had used digital design tools in their laboratory (Mimics, Materialise, Belgium; and FreeForm, 3D Systems, USA) for fifteen years. Participant 3 was a 3D biomedical technician – using the same tools, as Participant 2 and undertaking fundamentally the same role as Participant 1, but in the laboratory. Participant 3 had two years of patient-specific device design experience.

4.6.2.1. Investigation C2 – Post-Pilot Method Modifications

Investigation C2 had an extra participant relative to C1. As such, some small modifications were required – and extra consideration given to the staging of the observed scenarios. Participant 2 was asked to reconstruct the right defect model first, as previously described for participant 1. Participant 2, on the other hand, was asked to reconstruct the left defect first with their conventional practice, and the right defect second using the framework; with the aim of minimising the influence of the precise nature of the defect on being able to evaluate framework performance.

Fatigue towards the end of the CAD modelling session, and throughout the interview, was a small problem in the pilot test – for both participant and researcher. The pilot test CAD modelling time was therefore reduced for the verification tests from 180 minutes to 150 minutes, and the break between modelling and the interview was increased from 15 minutes to 30 minutes. To the limited degree that it was possible to draw conclusions on the subject, 150 minutes was shown by the pilot test to represent ample time to establish a clear characterisation of the participant's finished device designs. This insight was

used as an indicator that reducing the modelling time was unlikely to negatively affect the observed phenomena.

4.7. Research Ethics

In order to satisfy general and institutional ethics requirements, three main strategies were deployed through this research work. Firstly, the institute's IT and data-handling policies (Appendix 9) were followed at all times. This means that no personally identifiable information (visual or otherwise) was included in this research for any patient. It also resulted in the data which had been generated by this study or co-opted for analysis within it, being kept on a secure server, with password protected access and a limited, justified core group of users. Physical security measures were also in-place throughout the work, such as physical data and artefacts being stored in a locked room, in a building requiring swipe-card access.

Where professionals were observed, interviewed, or recorded in any way, where they would otherwise not have been during normal institute service provision, informed consent was always obtained. This was in the form of participant information sheets, including spaces for signatures to indicate acceptance (Appendices 4, 6). Said forms always reminded the participant that they were able to stop the observation and withdraw from the study at any time. Additionally, permission was sought and obtained from individual patients (via their clinicians) for using images taken in theatre.

Institutional ethics concerns were addressed by navigating the University and NHS Trust ethics approval pathway, and (from Investigation A2 onwards) by becoming an honorary member of design and research staff within Morriston Hospital; and by virtue of that fact, within NHS Wales as a whole. University ethics approval documents are provided in Appendix 10. NHS ethics approval documents are provided in Appendix 11. Or rather, in the case of the NHS, correspondence is attached to document how the activities being undertaken in Investigations A1, A2, and B3 were not defined as clinical research. Instead, these activities were classified as service evaluations of current practice and as such, required no special approvals – beyond those described above. Furthermore, Appendix 15 shows the results of using the Medical Research Council (MRC) online assessment tool. This further confirmed the non-clinical-research status at a national

level. Associate membership of the IMPT (Appendix 13) added an additional layer of approval. Honorary employment with the NHS (Appendix 12) further lowered barriers to observation; permitting access to operating theatres and to hospital departments whenever agreed. The same best-practice precautions were taken for observing these contexts, but with special consideration given to operating theatre visits by maintaining as low a profile as permitted by the observation requirements. Instructions were always followed in-theatre – and permission requested prior to entering the space, or engaging with staff. Clearly, these extra measures were important in such a sensitive environment.

All data collection in Investigations A and B refrained from interfering in or modifying the current practice of designers or clinicians. The only time this did occur was in Investigation C – when a simulated patient case was created; to completely remove the risk of negatively impacting patient treatment. Participants were instructed to name the CAD files clearly (reflecting their non-clinical status) and to store them separately to their usual casework.

4.8. Chapter 4 Summary

In summary, Chapter 4 has:

- defined the research structure (Chapter 4.2.1), and constraints (4.1);
- located the research in its methodological context (4.2.5);
- introduced, refined, and justified a list of refined research questions (4.2.2 – 4.2.4);
- introduced, refined, and justified a conceptual framework (4.2.3);
- demonstrated how data collection activities related to the research questions and conceptual framework (throughout);
- justified the choices of data collection tools by linking their strengths and limitations to investigations A, B, and C (4.3);

- described the data collection procedures to permit interrogation and repetition (4.4 – 4.6);

- described and justified the steps taken to ensure research ethics compliance (4.7);

- and has through these activities, contributed significantly to objectives 2, 3, and 4 from Chapter 1.9.

5. Investigation A Results – Characterising Current UK Practices

This Chapter (Figure 34) presents the results of participation in, or observation of, simple and complex implant production processes. The nature of the processes were the key data from this investigation; obtained by recording actions, aims, tools, materials, human resources, success measures, design decisions, process durations, and overall costs to the NHS of each process. It contributes to meeting objective 2 from Chapter 1.9 and to answering research questions 1, 2, and 3.2 from Chapter 4.2.4.

5.1. Investigation A1 Results – Simple Routine Implants

5.1.1. Case Study [1] Results: Observed Conventional Cranioplasty Process

The 'conventional' cranioplasty implant fabrication method (photographic flowchart in Figure 35) was performed by a Consultant Maxillofacial Prosthetist and a Principal Maxillofacial Prosthetist and utilised a bilateral medical model of the craniotomy defect. To create the model, the researcher imported Digital Imaging Communication in Medicine (DICOM) format CT data into Mimics version 14.11 (Materialise, Leuven, Belgium) and segmented for bone. Region-grow tools were used after each editing stage to discard unattached pixels. Then, the close morphology tool was used to ensure completely-bounded regions of bone wherever possible; with a view to creating solid volumes of resin during fabrication. After cropping and editing to remove the excess inferior data aspect, the result was exported in the STereoLithography (STL) format for building. High quality export settings were used – including 2 smoothing iterations per established institute practice. This also aimed to assist with a successful vat photopolymerisation AM build; by mitigating risks associated with small points across the surface of the anatomy. The SLA model was fabricated using a 3D Systems SLA250, with Watershed XC11122 resin (Somos, USA). This resin was used for all SLA builds at the institute owing to its transparency (for visibility of anatomical structures) and its testing to USP Class VI standards; permitting transient contact with a patient in surgery – after proper clean-up.

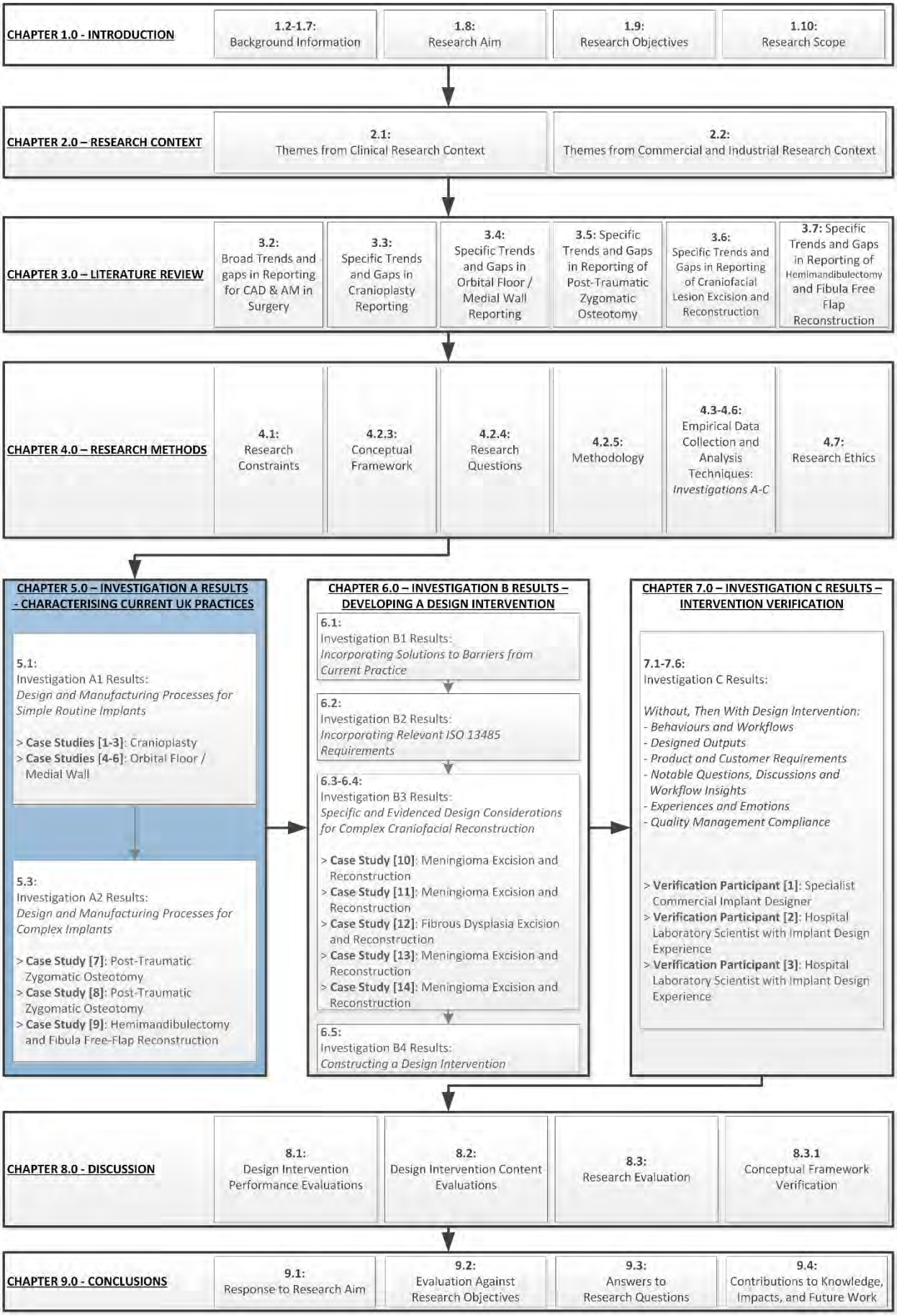


Figure 34 - Thesis Overview, With Current Location Highlighted (Chapter 5)

The prosthetist removed clay from its packaging and partially heated it in an oven to soften it into a workable state. Once the defect was filled with clay, the desired symmetrical contour was gradually carved using knives, the prosthetists fingers, and lighter fluid (via cotton wool) to smooth the surface. After drying to a solid state, an impression was taken of the reconstruction and surrounding area in plaster – this formed the female half of the press tool. Pouring plaster onto this half (with a separator coating) completed the fabrication of the male half of the tool.

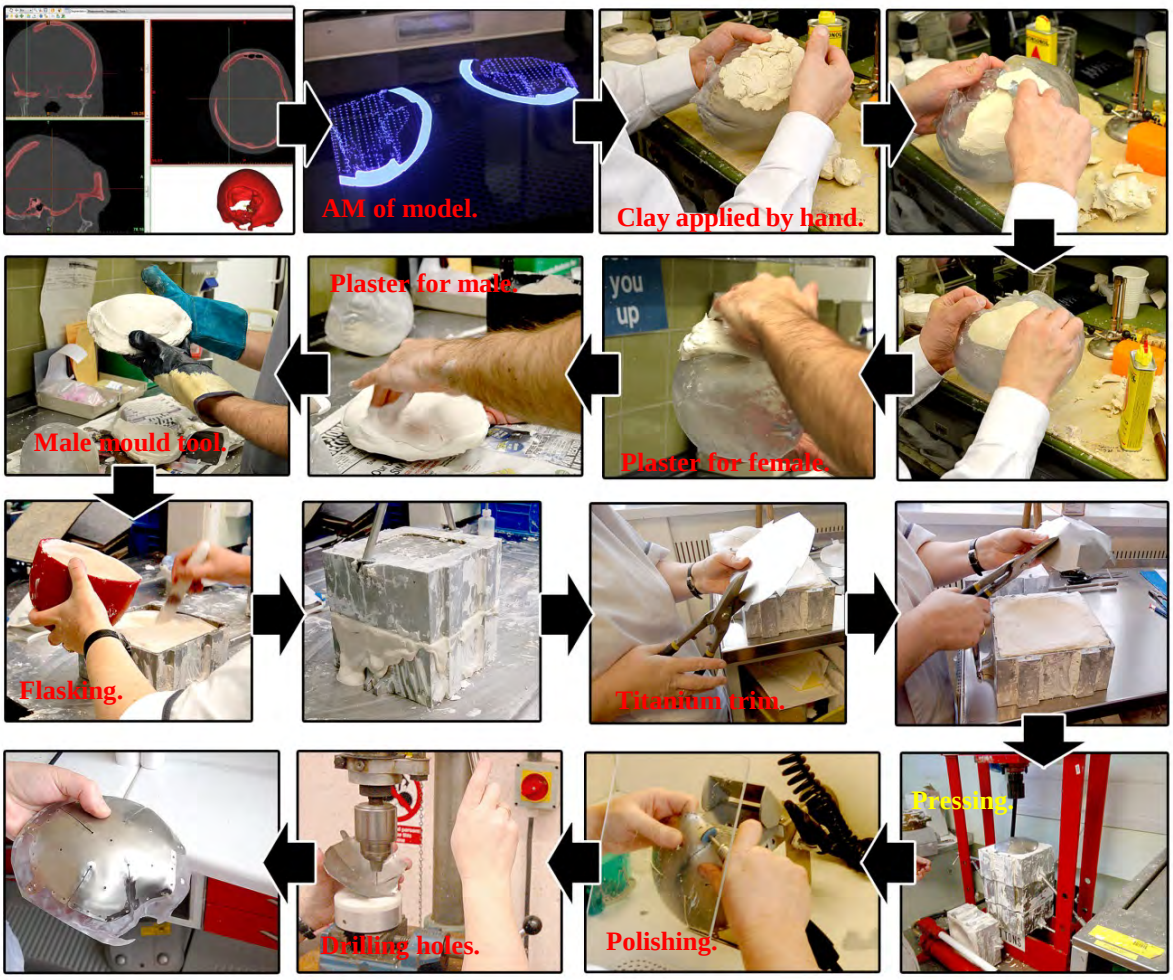


Figure 35 - Conventional Cranioplasty Design & Fabrication

Once the plaster tool had set fully, 0.5mm thickness titanium sheet was cut roughly to size and swaged in a press. Metal cutters were used to remove creases. After a further swage-check cycle, the plate remained in the press overnight. Next, burrs were removed from the edges of the plate and the surfaces were polished using rubber wheel tools. 2mm diameter holes were drilled around the edge of the plate (for

fixation) and arbitrarily spaced holes drilled throughout the main plate area for fluid transfer. A unique identifier was laser-engraved to the outer surface.

5.1.2. Case Study [2] Results: Observed Semi-Digital Cranioplasty Process

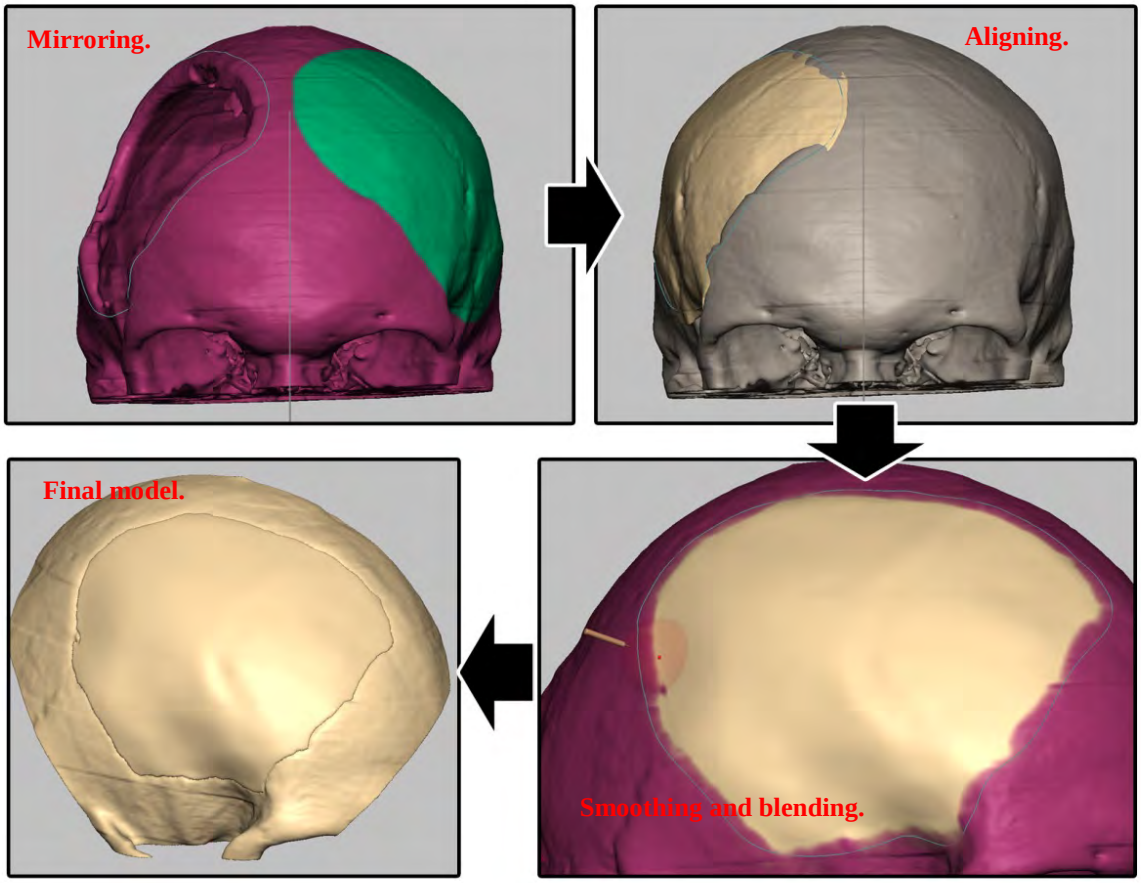


Figure 36 - Additional CAD Steps (Prior to SLA Model Fabrication) for Semi-Digital Cranioplasty Jig Design

The 'semi-digital' cranioplasty implant fabrication method was performed by an Orthodontic Laboratory Technologist and utilised a unilateral digitally reconstructed medical model of the craniotomy defect. The researcher undertook near-identical processes as for the conventional method to the point of STL export from Mimics. This file was subsequently imported into Freeform Modelling Plus version 12 (3D Systems, USA) and the defect reconstructed subjectively and visually using mirroring, deformation, and blending tools. Final adjustments were made after checking symmetry with a digital on-screen ruler. The researcher's interpretation of

a suitable defect reconstruction was signed-off by the ordering surgeon prior to building.

The technologist undertook near-identical processes to form the press tool, and to fabricate the implant as the prosthetist had for the conventional method, but with some key exceptions. The manual clay carving was not necessary because of the digital reconstruction (Figure 36). The impression was taken for the female mould half directly from the medical model. Additionally, a larger number of fixation holes were drilled around the full rim of the plate to provide additional fixation options.

5.1.3. Case Study [3] Results: Recorded Digital Cranioplasty Process

Figure 37 - Additional CAD Steps for Fully-Digital Cranioplasty Design

The 'digital' cranioplasty implant fabrication method (Figure 37) was performed by the researcher, after an enquiry by a maxillofacial surgeon responsible for prescribing (but not operating with) the implant. After a conversation to discuss the design possibilities afforded by CAD and AM, the researcher and surgeon agreed upon a plate which would fit inside the defect. This aimed to avoid an overly bulbous appearance, to minimise palpability of the bone-implant interface through the skin, and to reduce the pressure on the skin flap sutures. Further collaborative decisions were made to establish: a 2mm thickness (a conservative subjective choice to cautiously over-engineer); a diamond pattern mesh structure across the main area (for fluid transfer); and selection of the Electron Beam Melting (EBM) (Arcam AB, Mölndal, Sweden) form of the powder bed fusion process (because of its better suitability for large parts, and lower cost compared to SLM). Fixation was to be provided using 0.5mm thick tabs at the top, bottom, left and right extremes of the

plate – which would overlap onto the existing anatomy with 2mm diameter screw holes. Again, mitigating palpability was the aim, along with avoiding implant exposure.

The researcher undertook identical processes as for the semi-digital approach up to the point of reconstructing the defect. The plate thickness was realised using offset and Boolean subtraction functions, with a further subtraction ensuring a 0.5mm clearance between the edge of the plate and the bone of the defect edge. This aimed to guarantee a passive fit inside of the defect. The agreed diamond mesh was applied using an area-emboss tool (leaving an unmeshed rim of 5mm around the plate edge to create uninterrupted regions for tab attachment and a uniform boundary). Finally, a unique text identifier was embossed onto the surface, and the file exported in the STL format for building (which commenced only after the ordering surgeon had reviewed numerous images in a design verification document). It was built as part of a batch of three devices. A small reference medical model was built as a jig to validate the accuracy of the AM implant at the surgeon's request – rather than rely on the CAD software alone.

5.1.4. Case Study [4] Results: Observed Conventional Orbital Implant Process

The 'conventional' orbit implant fabrication method (Figure 38) was performed by a Consultant Maxillofacial Prosthetist, Consultant Maxillofacial Surgeon, and a Principal Maxillofacial Prosthetist. They utilised a bilateral medical model of the orbits prepared by the researcher at the institute. To create the model, DICOM format CT data was imported into Mimics and segmented for bone. After cropping and editing to remove the excess data aspects, and identical build-failure mitigation steps as for the cranioplasty, local detailed segmentation of the delicate medial wall and orbital floor structures was undertaken manually on a layer-by-layer basis. Thresholding with a brush tool set to around 110 HU, and ensuring that all available bone was captured by the active layer mask, aimed to maximise the accuracy of the model and subsequent reconstruction. The finished layer mask of the patient's properly processed anatomy was exported in the STL format for building.

A short discussion between the Principal Prosthetist and Consultant Surgeon, using the physical anatomical model as a reference, determined the target implant size and fixation points. This represented an easy decision – thanks to a clearly defined defect. The prosthetist removed clay from its packaging and filled the defect. The desired symmetrical contour was gradually achieved using his fingers and small flame-heated dental tools to smooth the surface. A brief conversation with the Consultant Prosthetist followed; to confirm the suitability of the evolving reconstruction, and the proposed implant extents. Notably, a brief check was undertaken in Mimics using the patient's anatomy and a virtual model of a stock reconstruction plate – to rule out its viability as an alternative strategy. This would have eliminated the time investment of the prosthetists at a busy point of the working week. The stock plates were already routinely available in the operating theatres and would not have incurred an extra cost to the maxillofacial unit. It was quickly determined that the required height of the implant at the medial aspect of the orbit meant that a truly custom implant was worth pursuing for its improved contour accuracy.

After drying to a solid state, an impression was taken of the reconstructed area and the immediately adjacent regions in putty. This was repeated after the first attempt did not extend far-enough posteriorly. The impression was placed (defect side down) into plaster. After drying, removal of the impression putty from the plaster, and sanding the result, this female mould tool half was flasked by placing it into a metal container which had been filled with wet plaster. After drying, separator liquid was brushed onto the surface of the female mould half. Then the male upper tool half was filled with plaster and placed on top. The tool halves were left in a press to dry in order to guarantee a consistent split line. Then, a layer of wax (of negligible thickness) was melted over the mould tool surfaces to insure against undercuts and to assist downstream – in opening the tool.

With the wax layer hardened, 0.25mm thick titanium sheet (standard practice in this lab) was cut roughly to size and swaged in the press. Metal cutters were used in conjunction with a metal grinding disc tool to remove obvious excess material around the edge of the implant. The implant was pressed again for 1 hour. Afterwards, 2 holes of 1mm diameter were drilled for fixation (following centre-punched guide marks in the intended locations) and 6 arbitrarily-spaced holes of 2mm diameter were

drilled across the main surface to permit fluid transfer. Burrs were removed from the implant edges using a rubber wheel multi-tool attachment, and from the drilled holes and main implant surface area using a "Kenda Queen" polishing attachment. Finally, a polishing wheel with titanium oxide polish was used to finish the surfaces to a high shine. The implant was left in the press until required (3 weeks in this case – with a stated minimum final pressing time of 24 hours, in more urgent cases).

Figure 38 - Conventional Orbital Floor Design & Fabrication

5.1.5. Case Study [5] Results: Observed Semi-Digital Orbital Implant Process

The 'semi-digital' orbital implant fabrication method was performed by a Principal Maxillofacial Prosthetist, a Consultant Maxillofacial Surgeon and utilised a unilateral digitally reconstructed medical model of the orbital floor defect. The researcher undertook near-identical CAD processes as for the conventional method to the point of STL export from Mimics. The major difference was the export of a second STL file – with the 'missing' anatomy of the healthy orbit drawn-in manually to provide a "perfect" basis for mirroring. This drawing was performed on a layer-by-layer basis, using a graphics tablet, and a small brush size in Mimics. The drawn-in elements were subjectively extrapolated from the adjacent bony regions. This STL file was imported into Freeform Modelling Plus and the defect reconstructed using the same mirroring, deformation, and blending tools as were used for the semi-digital cranioplasty.

The designer's interpretation of a suitable defect reconstruction was again signed-off by the ordering clinician prior to building. In this instance, the ordering clinician was the prosthetist who would be responsible for downstream implant fabrication in the laboratory. They has discussed the extents, fixation, and drainage hole design features with the operating surgeon; as was usual for their particular unit's practice. Both the reconstructed floor, and the original (unaltered) version of the anatomy were printed. The latter was requested for visual reference and for verification trial-fitting of the completed implant.

The prosthetist undertook near-identical processes to form the press tool and fabricate the implant as for the conventional method with a key exception. The manual clay carving was not necessary because of the digital reconstruction (Figure 39). The medical model was flasked in clay and pressed against directly.

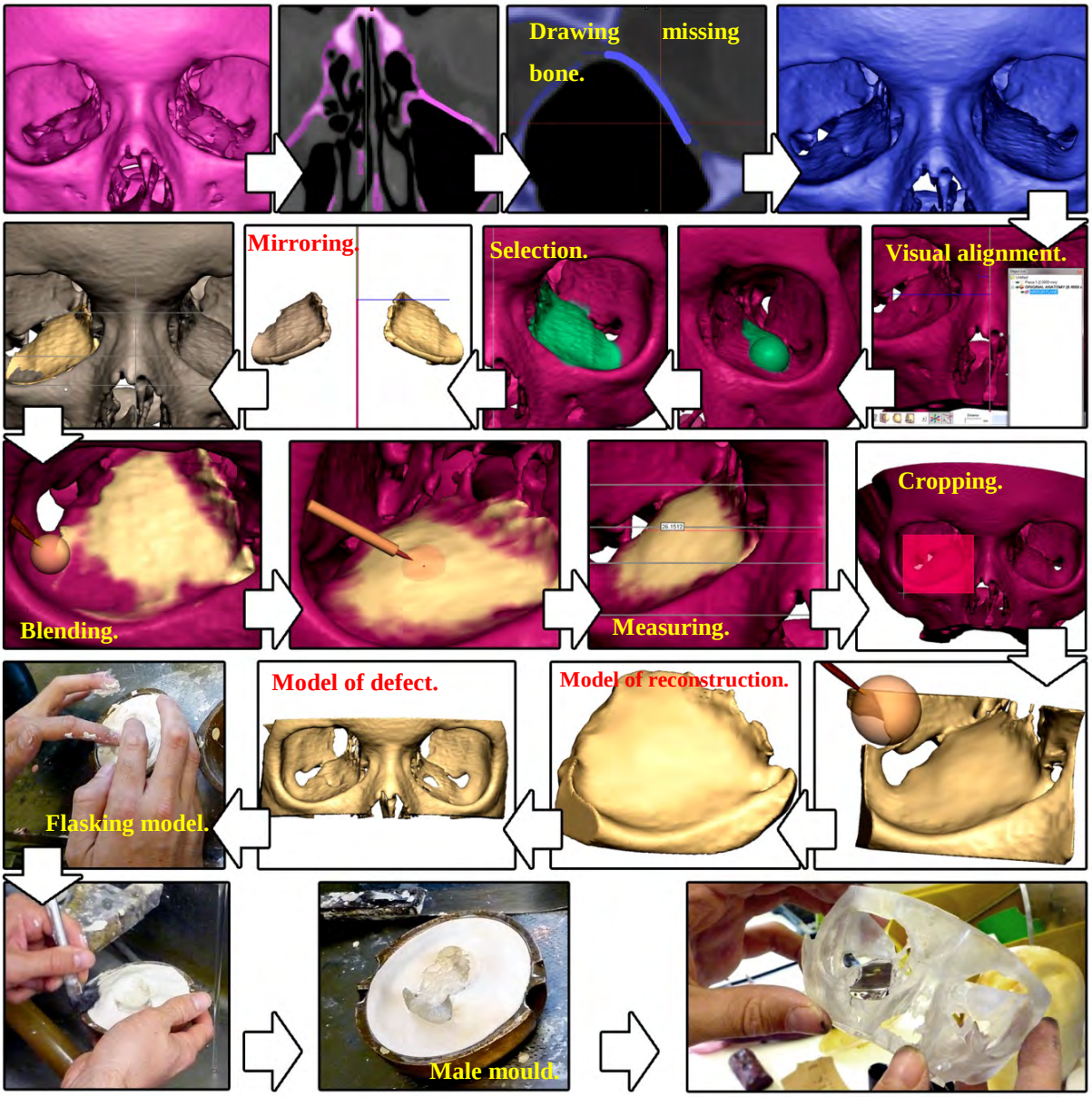


Figure 39 - Additional or Different Steps during Semi-Digital Orbital Floor Implant Production

5.1.6. *Case Study [6] Results: Recorded Digital Orbital Implant Process*

The 'digital' orbital implant method (Figure 40) was performed by the researcher/design-engineer at the institute, in response to an enquiry by a Consultant Maxillofacial Surgeon. After an in-person conversation to discuss the design possibilities afforded by CAD and AM, the designer and surgeon agreed upon a two-part plate which would restore the orbital floor shape and be cantilevered against the inferior orbital rim (in the absence of a posterior bone 'shelf' to rest against). The second piece would restore the medial wall – and fixed in a similar location on the

orbital rim as the first part to minimise the required exposure. The two-part design aimed to facilitate easy insertion, given the particularly large size of the defect and implant. Further collaborative decisions were made to establish a 0.5mm thickness (based on the surgeon's previous experience with stock plates), fluid transfer holes across the main area, and the SLM (3DSystems LayerWise, Belgium) powder bed fusion AM process. A polished upper surface was specified; this decision was based on the surgeon's previous experience.

The design engineer undertook identical processes as for the semi-digital approach up to the point of reconstructing the defect using the FreeForm CAD software. The drawn-in healthy anatomy was used as the basis for the mirroring operation; and therefore formed the main basis of the reconstruction. Then, the deformation and blending tools completed the virtual defect recontouring. The implant thickness was realised using surface-offset functions, with a split line (to separate the implant into the medial and lateral components) being constructed and iterated using a curve, then cut. The file was exported for building (which commenced only after the ordering surgeon had reviewed numerous images in a design sign-off form and quotation document). At the surgeon's request, a small reference medical model was again built as a visual reference, and as a means to verify the accuracy of the AM implant.

5.1.7. Case Studies [1-6] Results: Process Costs and Times-In-Motion

As shown in the top row of Figure 41, the best-case conventional process cranioplasty implant was ready for sterilisation after seven working days. Raw materials including the medical model cost £687. NHS staff costs for hands-on-activities were £118. The combined cost to the NHS of producing this implant was £805. The device was implanted successfully. Raw data and calculations can be found in Appendix 5.

As shown in the middle row of Figure 41, the best-case semi-digital process implant was ready for sterilisation after seven working days. Raw materials (including the medical model) cost £607. NHS staff costs for hands-on-activities were £53. The combined cost to the NHS of producing this implant was £660. The device was implanted successfully.

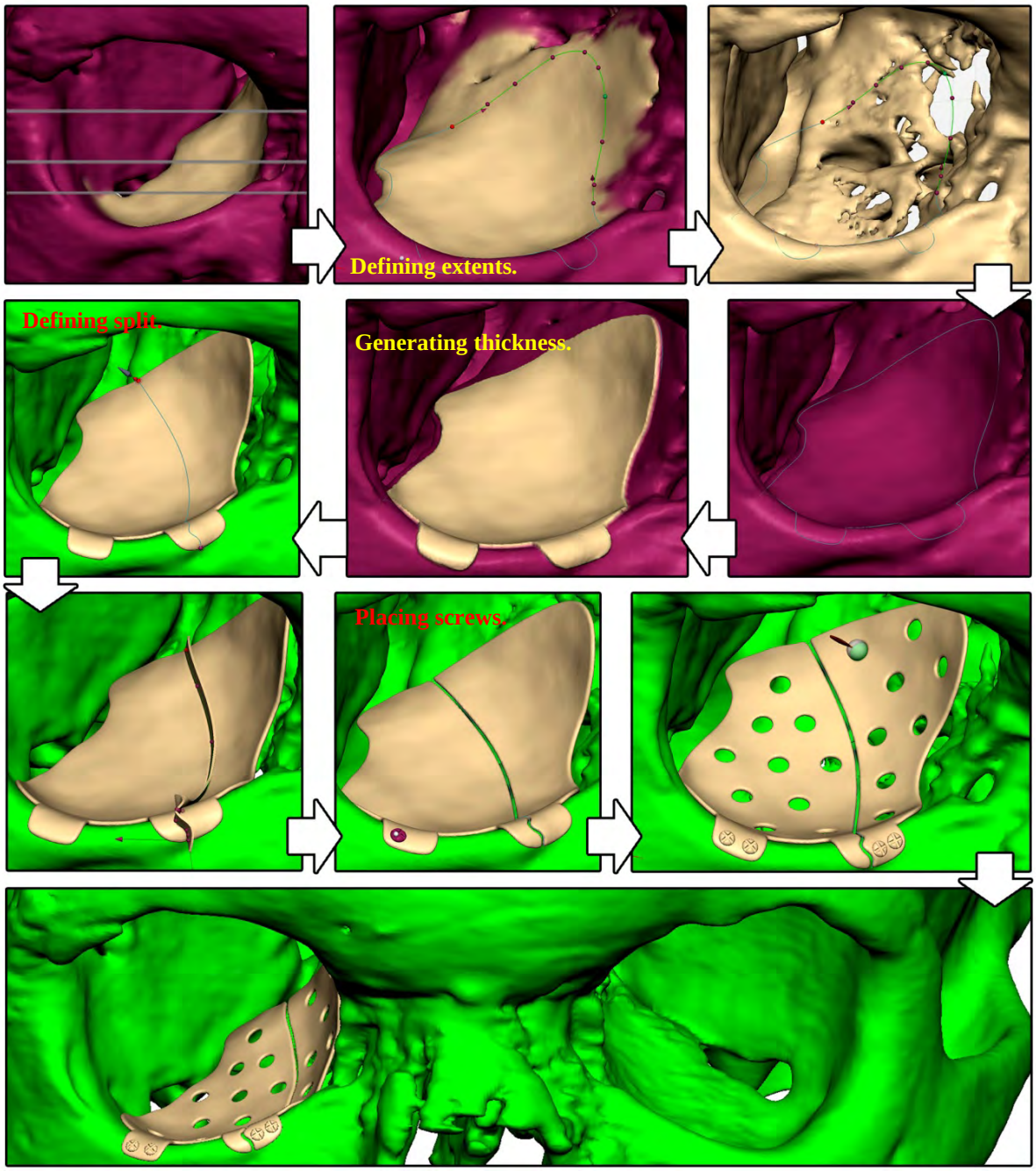


Figure 40 - Additional CAD Steps during Fully-Digital Orbital Floor Implant Production

As shown in the bottom row of Figure 41, the best-case digital process implant was ready for sterilisation after seven working days. Raw materials (including the medical model) cost £1748. NHS staff time-in-motion costs were £34. The combined cost to the NHS of producing this implant was £1782. The device could not be implanted successfully (analysed in sub-Chapter 6.1) and a backup semi-digital plate was used which had been prepared for the surgery.

The digital method was 2.7 times the cost of the semi-digital method – driven primarily by the price of metal fabrication and secondarily by the cost of the design time (CAD work).

As shown in the top row of Figure 42, the best-case conventional process orbital implant production time (ready for sterilisation) was 5 working days. Raw materials including the medical model cost £193. NHS staff costs for hands-on-activities were £48. The combined cost to the NHS of producing this implant was £241. The device was implanted successfully.

As shown in the middle row of Figure 42, the best-case semi-digital process orbital implant production time (ready for sterilisation) was 5 working days. Raw materials (including the medical models and reconstruction service) cost £319. NHS staff costs for hands-on-activities were £18. The combined cost to the NHS of producing this implant was £337. The device was implanted successfully.

As shown in the bottom row of Figure 42, the best-case fully-digital process orbital implant production time (ready for sterilisation) was 9 working days. Raw materials and the design service (including the medical model) cost £794. NHS staff time-in-motion costs are £19. The combined cost to the NHS of producing this implant was £813. The surgery was cancelled for this case – as the patient had decided against further surgery. The surgeon had though, fully verified the appropriateness of the design.

The digital method was 3.4 times the cost of the conventional method – driven primarily by the price of metal fabrication and secondarily by the cost of the design time (CAD work).

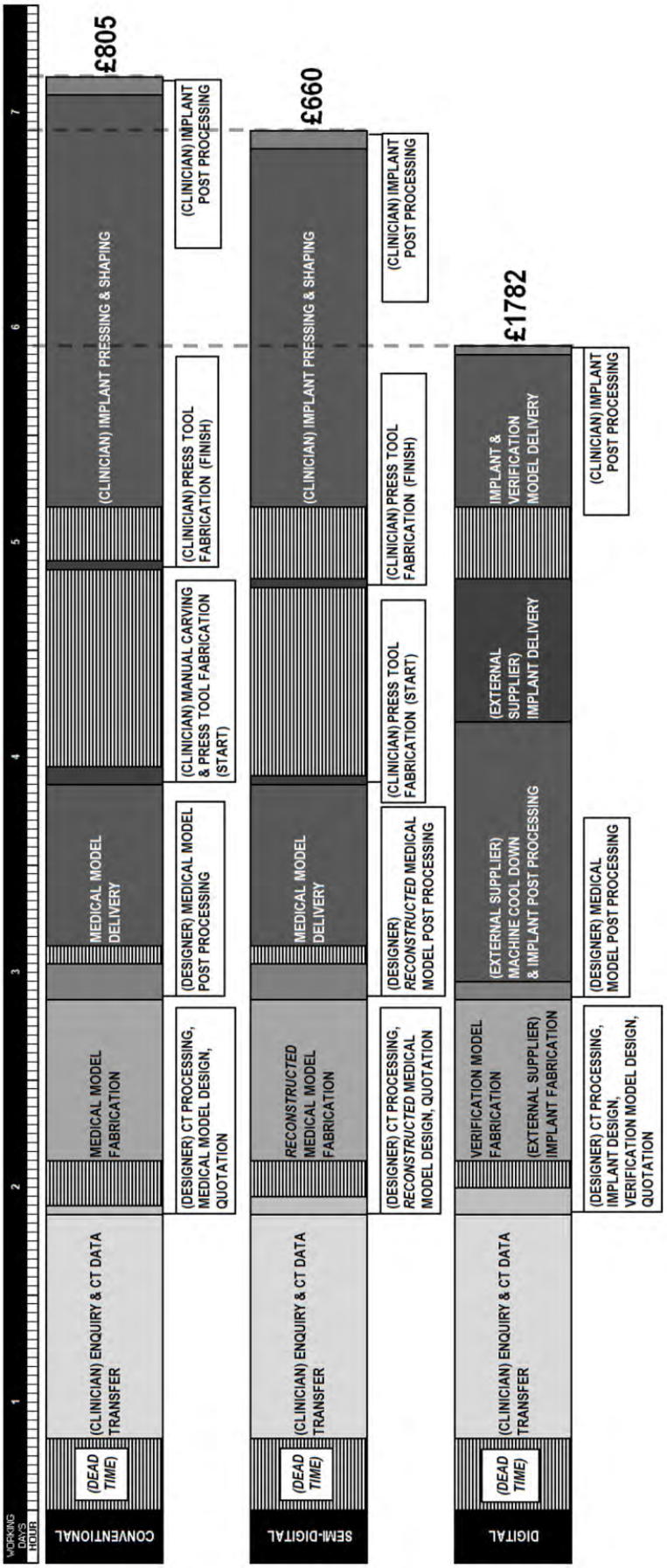


Figure 41 - Costs and Task Durations for 3x Cranioplasty Production Methods

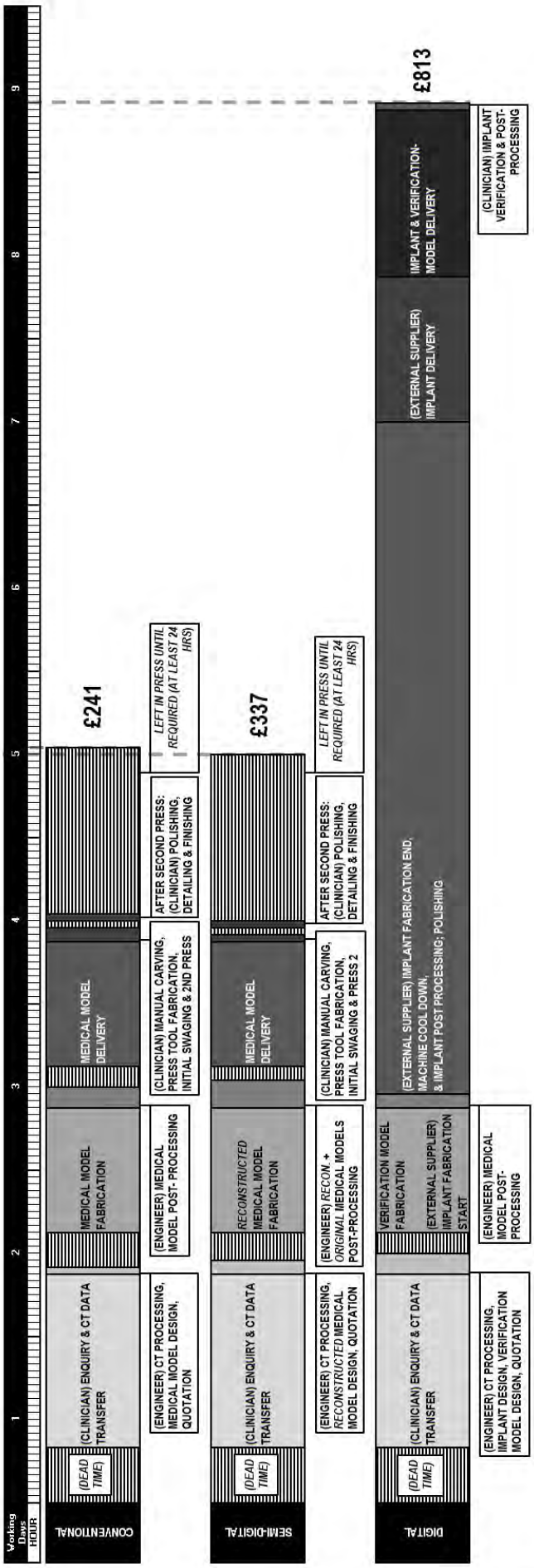


Figure 42 - Costs and Task Durations for 3x Orbital Floor Production Methods

5.2. Investigation A1 Results – Routine Implants - Analysis

Based on the cost to the NHS, CAD/AM cranioplasty plates were not yet viable for routine use according to the cases presented (albeit they were relatively normal defects and were not driven by a need to fully exploit the abilities of CAD/AM). A semi-digital approach represented the least expensive option and achieved the same functional result as the conventional method. The major factors in determining the semi-digital value were a less expensive medical model and lower NHS staff costs (since manual carving was unnecessary).

Based on the cost to the NHS, CAD/AM orbital implants were not yet viable for routine use according to the cases presented (albeit they were relatively normal defects and were not driven by a need to fully exploit the abilities of CAD/AM). A conventional approach represented the least expensive option and achieved the same functional result as the conventional method. The major factors in determining the value of the conventional method were a less expensive medical model (enough to offset slightly higher NHS staff costs thanks to the requirement for manual carving).

5.2.1. Results Analysis: Process Factors

Both conventional and semi-digital cranioplasty implant production methods produced successful plates (as judged by the patient's follow-up) – they were fitted quickly and fulfilled their morphological and mechanical functions. Additionally, these processes have been regularly used by their respective hospitals for many years and so offered very high familiarity to surgeons. Conventional and semi-digital orbital implant production methods also produced successful plates. Furthermore, given the thorough review of the digital orbital implant design by the operating surgeon, it is reasonable to expect that the implant would have been entirely successful too.

The digital cranioplasty process output (EBM plate) did not fit the defect site which had been scanned 7 months prior to the surgery. More urgent operations had taken precedent in the queue for the stretched resources of the hospital's operating theatres. As a result, the patient's temporalis muscle had fused to the meninges of their brain.

Fitting the AM implant would have required the neurosurgeon to meticulously separate the muscle – judged to be an unnecessary risk. If this issue had been raised during the design stage, a solution would have been found before presenting an erroneous design to the ordering surgeon for verification. The chances of the issue being raised were reduced by the ordering surgeon not being the same person as the operating surgeon. They were from different departments because of the hospital commissioning structure.

This was not a problem for the patient – as a backup plate produced using the semi-digital method was used. This was produced because of the embryonic nature of the digital process for the particular hospital. The fused muscle was left in position and a segment of the semi-digital plate was manually bent up and over the muscle obstacle by the surgeon. This adjustment was easy and quick thanks to the cuts in the plate – which were made in areas where creases formed during initial swaging. Therefore, the location of these cuts was entirely fortuitous – not the result of a conscious design decision. Still, the inherent malleability of the material (when compared to the digital case study device) could have conceivably permitted numerous in-theatre modifications of this sort.

5.2.2. Results Analysis: Key Design Factors

For cranioplasty implants, the featured conventional and semi-digital case studies suggested that laboratory fabrication occurred through an ill-defined series of iterative actions sometimes in the absence of fully realised design intent (albeit with an incredibly rich variety of skills and uniquely specialised experience to draw upon). Customary actions were repeated for each case – without any communication between technician and surgeon about the individual patient.

Consultation and communication with the operating surgeon was more extensive for the conventional and semi-digital orbital implants than for cranioplasty. Consultation occurred at the beginning of the design process; with many small decisions (such as the precise positioning of the fixation screw holes) being determined ‘on-the-fly’ by the prosthetist or technologist based on their experience. Indeed, it is important to highlight that the design responsibility was split variously

between design engineers at the institute, ordering surgeons, prescribing surgeons, technologists, and prosthetists. This dispersed and blurred authority contributed to the digital cranioplasty design failure.

For that digital cranioplasty case study, the key factors behind the design's failure were related to the fidelity of both the shared knowledge of the surgical plan (between researcher and operating surgeon) and therefore the fidelity of the product requirements list. Tangible examples to improve fidelity include increasing the number of information fields (describing each surgical step), and improving the richness of the collected and discussed information (important contextual details such as the temporalis muscle limiting access to the defect edge).

5.3. Investigation A2 Results – Complex Implants

5.3.1. Case Study [7] Results: Recorded Process and Design Outcomes for Revision Post-Traumatic Zygomatic Osteotomy

The patient was involved in a road traffic accident 13 months prior to the project beginning, which had resulted in bilateral arm fractures, right lower limb injuries, and multiple facial fractures. The immediate reduction and repair of the facial fractures (amidst life-saving surgery) had been carried out with minimum invasion in order to preserve the sight of the left eye. 12 months later, the patient's concerns involved the appearance of the affected cheekbone and orbit, and the sinking-in of his left eye which necessitated turning his head to see clearly to his left side. He was unable to fully close the eye without using his hand, and was self-conscious enough about his appearance to wear a hat and clear-lensed glasses as a matter of routine. He lacked confidence to walk around in public.

The primary risk from the proposed corrective revision surgery related to sawing and moving bone in the region of the optic nerve; and implanting an orbital floor component in the same critical area. As such, the potentially large increase in

Figure 43 - Medical Model of Original Anatomy

accuracy afforded by digital planning and custom AM devices was deemed appropriate by the operating maxillofacial surgeon.

The patient underwent a CT scan using a Toshiba Aquillon with a 0.5mm slice thickness. The DICOM format data was imported into Mimics version 15 (Materialise, Belgium) and segmented for bone using the software's default threshold Hounsfield values. Existing metalwork from the primary reconstruction was erased manually on each CT slice. A 'Region-Grow' operation was undertaken after each stage of the process to remove unattached pixels. Delicate bony structures around the orbital floors and medial walls required local thresholding using a small brush and Hounsfield values between 90 and 110. Once completed, the most recent 'Original Anatomy' mask was exported in the STL file format. This file was fabricated using an SLA 250 (3D Systems, Rock Hill, USA) vat photopolymerisation process with Accura Xtreme resin (3D Systems, USA) for detailed visual and physical review (Figure 43).

In order to provide a robust basis for downstream mirror-based reconstruction of the damaged left orbital floor, a second STL file was exported of the right orbital floor, with areas of absent bone manually drawn-in.

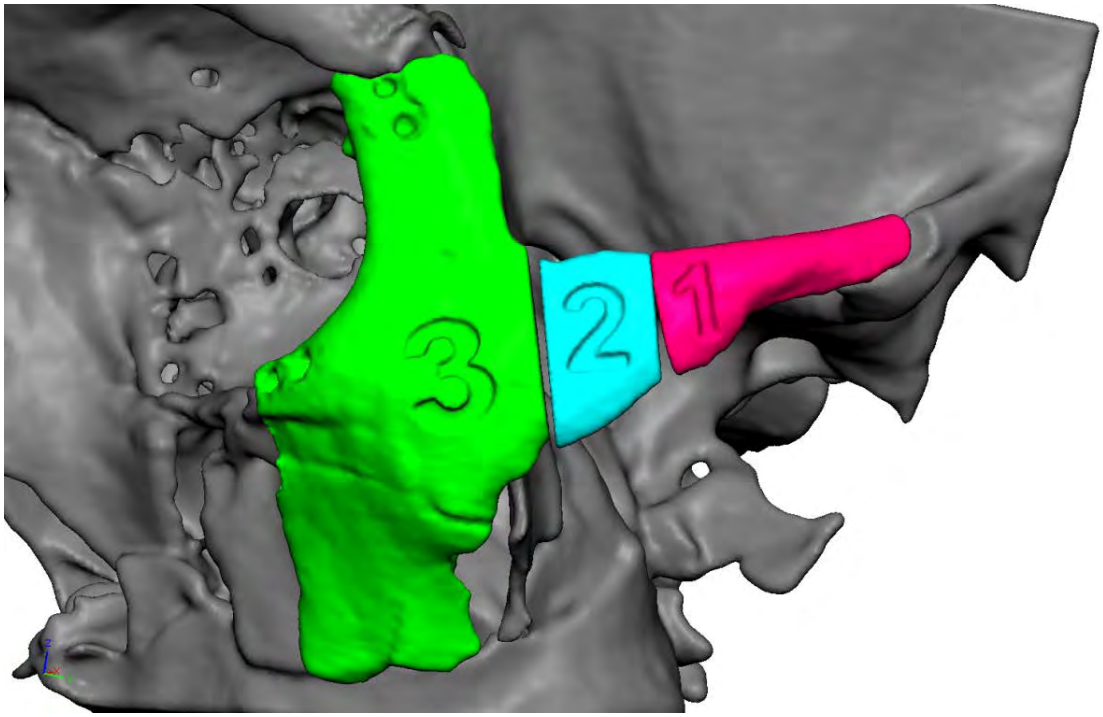


Figure 44 – Planned Osteotomies, Mobilised Bone Segments, and New Positions

Both resulting STL files were imported into FreeForm Modelling Plus version 13 (3D Systems, USA) and an initial collaborative meeting established between surgeon, prosthetist and design engineer (researcher). A translucent overlay mirror of the patient's right-side onto the damaged left-side was setup to act as an ideal-outcome reference. The optimum bone cutting locations were prescribed (three bone fragments were deemed necessary to attain the desired shape). The cuts were made virtually and the bones repositioned according to the surgeon's instructions (Figure 41). Numbers were assigned to each piece as shown – to simplify intra-team communication. These individual pieces were set as unmodifiable 'Buck' parts to protect their condition for the remainder of the process. Each bone fragment was assigned a bright, contrasting colour and number to assist in communication between clinical and engineering specialities. The extreme contrasts assisted the surgeon, who was colour blind. When a model of the planned re-position was built for team review, a full-colour Z-Corp 510 (3D Systems, USA) machine was selected for its ability to maintain the virtual colouring on the physical model (Figure 42), and based on its availability at the institute. This is a binder jetting AM process whereby a coloured 'glue' is deposited on a layer-by-layer basis to stick a plaster-like build material together. Similarly, a model was built with the separated bone fragments as loose, individual pieces – to facilitate repositioning rehearsal.

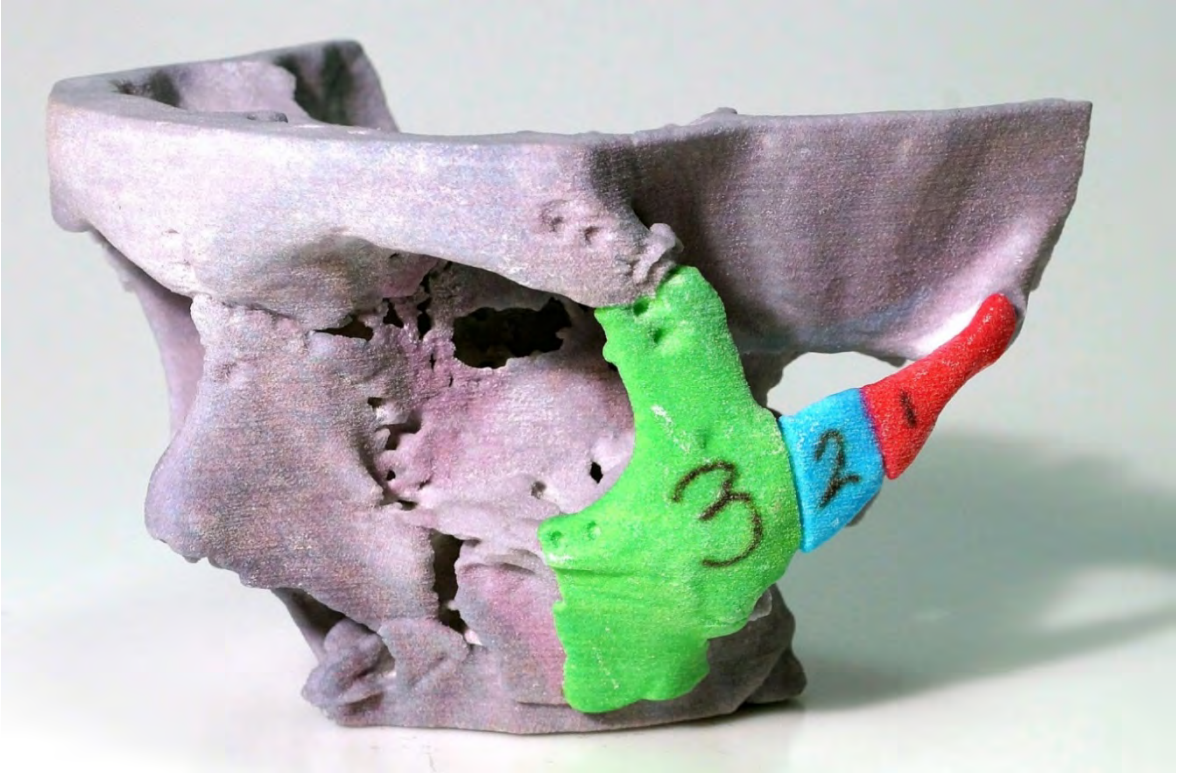


Figure 45 - Colour Medical Model

Preliminary specifications were agreed for a single-part repositioning guide and implant – targeting simplicity and low fabrication costs. After two exploratory concepts were rapidly iterated in FreeForm (using the 'Layer' function), prototypes (Figure 46) were fabricated by a ProJet HD3000 Plus (3D Systems, USA) material jetting AM machine using VisiJet EX200 (3D Systems, USA) acrylate build material. Upon handling these prototypes with the anatomical models, the combined guide / implant approach was judged unsuitable by the surgeon. The competing requirements to have a large-surface-area (for the guide function) and minimal volume (for the long-term implant function) were judged to be incompatible in this instance. The prototypes were difficult-to-handle, and too-small to accurately guarantee correct placement in a robust, repeatable fashion. New concepts with separate guides and implants were reviewed by the surgeon with feedback and alteration requests drawn directly onto the parts in pen – for clear, quick communication (Figure 47). The same process was exploited to design a cutting guide; with only two iterations required to establish a final design (Figure 48) thanks to simpler requirements (locate securely onto the existing bone, and clearly dictate the saw cutting vectors). Screw holes were added throughout each guide to prevent movement during cutting, or implant insertion and fixation.

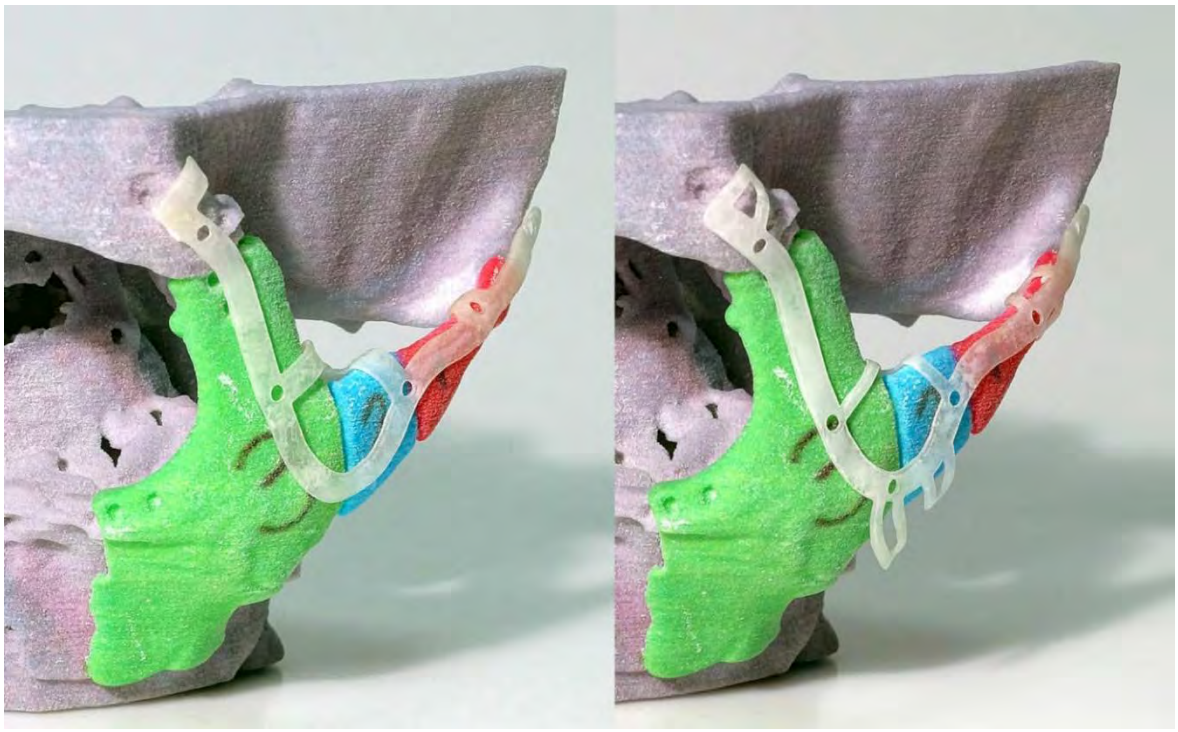


Figure 46 - Early Combined-Device Prototypes

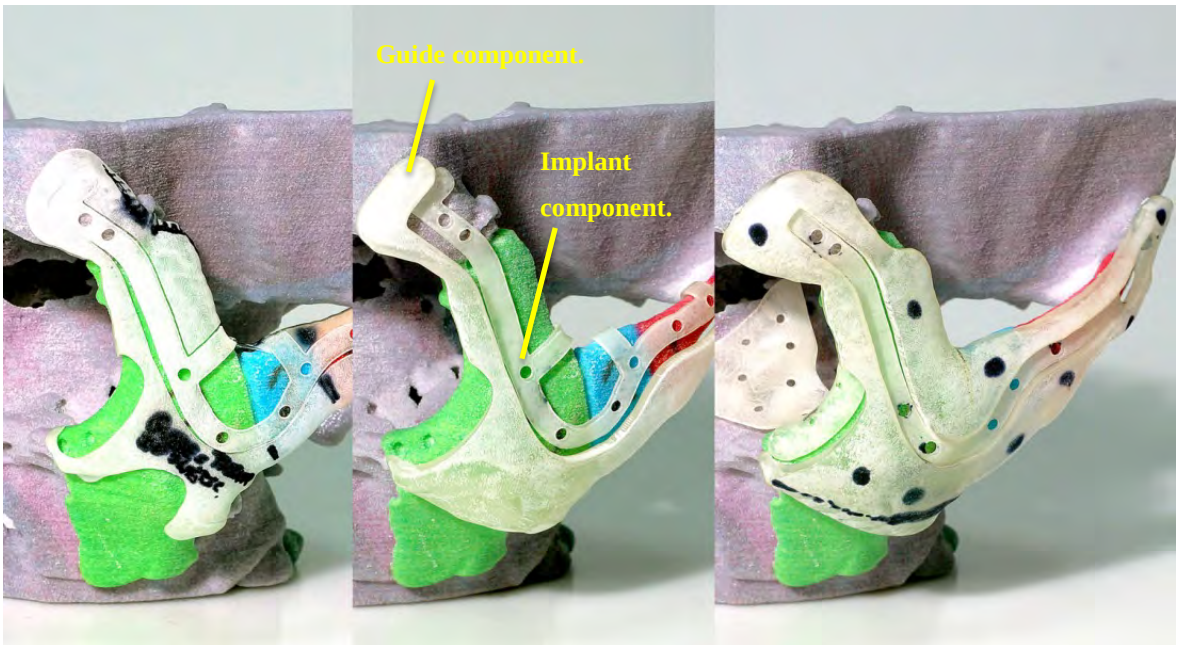


Figure 47 - Early Separate-Device Prototypes

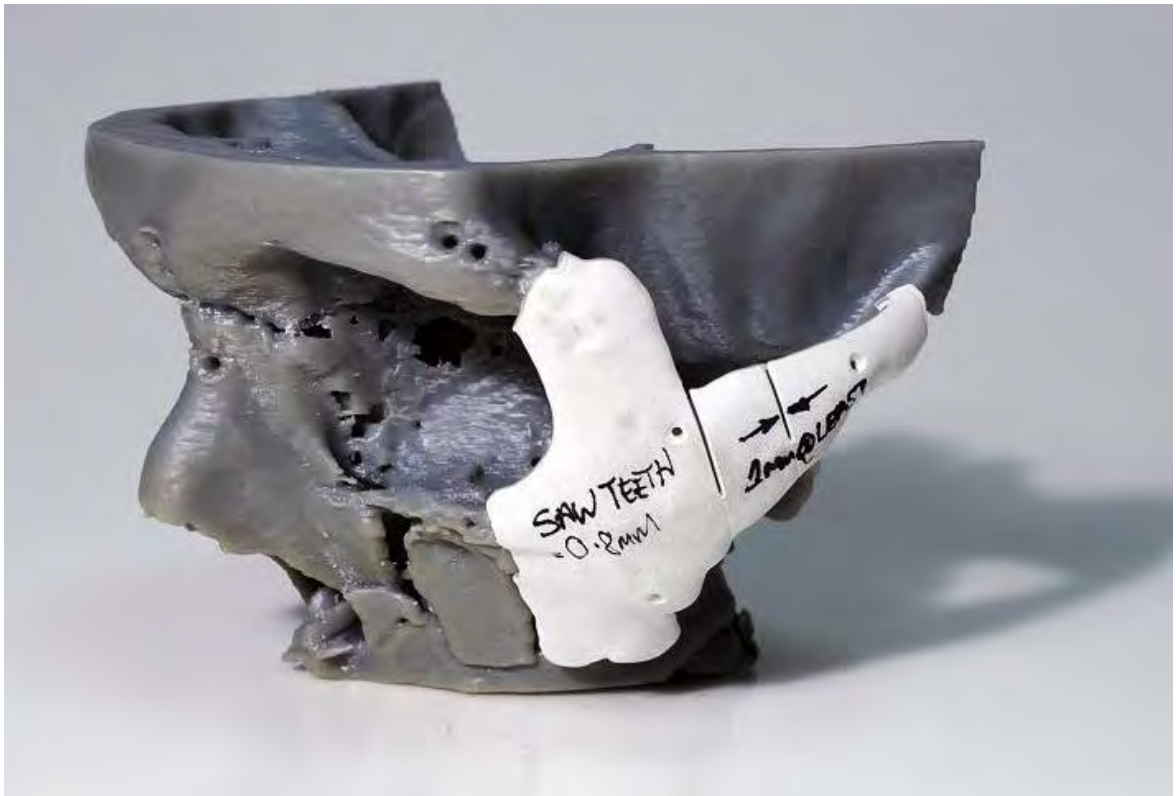


Figure 48 - Cutting Guide Prototype

Here, the orbital floor reconstruction was undertaken digitally – based on mirroring the right side to the left utilising the drawn-in STL as the basis. It was positioned to achieve a visual match with the healthy floor and then validated by digital measurements. Under the prosthetists supervision, using the 'Tug' function, relief was provided to account for the plate thickness – slightly compromising a perfect mirrored match to ensure the plate edges rested on existing anatomy where possible. The plate form was realised using the software's 'Emboss With Curve' command.

The designs were approved by the team for fabrication by external ISO 13485 accredited manufacturers. The zygomatic implant (Figure 49) was built using the SLM powder bed fusion process (3D Systems LayerWise, Belgium) with a 0.7mm thickness and with designed-in countersunk screw holes. A basic support-removal and grit-blasted finish was requested. Grade 23 Ti6Al4 ELI was specified as the build material on the basis of its biocompatibility. The orbital floor implant (0.5mm thickness) was built using the same process and same finish on the inferior surface. The superior surface was polished (Figure 50). All holes used for fixation were of 1.2mm diameter – intended for 1mm screws. Post reaming was undertaken as a precautionary measure in the hospital lab upon delivery. This was also undertaken for the guides – which were built using the Laser Sintering (LS) powder bed fusion

process (Renishaw, UK). Cobalt Chrome was specified as the build material owing to its compatibility for in-vivo use as a transient device and a lower cost relative to titanium in this instance. The guides were designed with a 2.5mm thickness because of the surgeon's preferences for security of handling, strength, and stiffness to resist tool forces.

Figure 49 - Zygomatic Implant

Figure 50 - Orbital Floor Implant

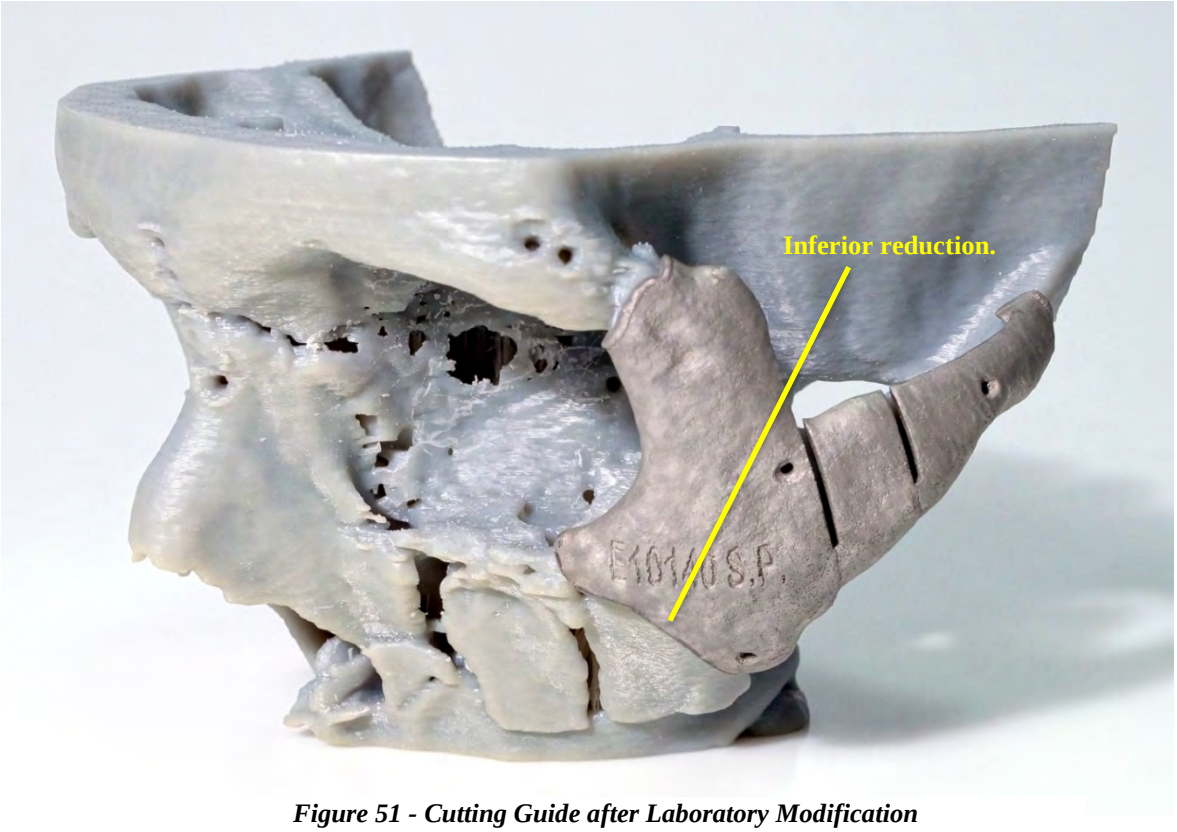


Figure 51 - Cutting Guide after Laboratory Modification

After manufacture and handling by the surgeon, the cutting guide was considered to be too large inferiorly – requiring unnecessary extra dissection and exposure of the defect site. Material deemed excessive was ground away in the hospital lab (Figure 51). For the repositioning guide, extra posterior anatomical engagement was deemed necessary for increased location security. Additional holes were also added to the CAD file – to improve the bone fragment retention during implant fixation. The final design following those modifications was exported from FreeForm and the new repositioning guide manufactured (Figure 52).

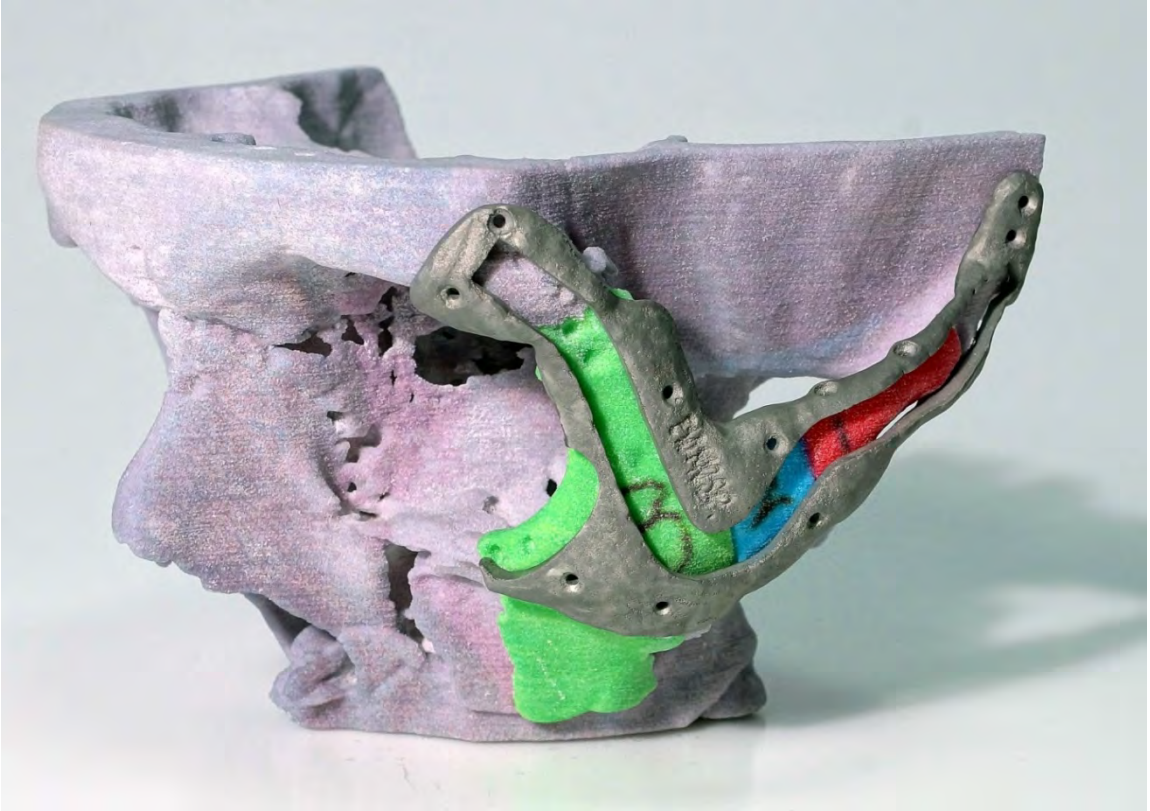


Figure 52 - Repositioning Guide

In preparation for surgery, a group of 30 images were colour printed at A3 size to offer in-theatre reference to the virtual plan. This included four images illustrating the results of a Boolean subtraction function between the separate bone segments in FreeForm. This illustrated areas where small pieces of ossified bone (from after the initial surgery) were to be ground away to permit the three segments to contact each other cleanly. Furthermore, a new set of anatomical models were fabricated using vat photopolymerisation SLA and Accura ClearVue resin (3D Systems, USA) which has been tested to USP 23 Class VI – rendering it suitable for sterilisation and handling by the scrubbed team in-theatre when the models are cleaned appropriately.

The researcher observed the surgery directly and presented images to the surgeon on request – which illustrated key aspects of the previously defined surgical plan; such as planned bone burring locations. The operation was carried out using 2 surgical incisions in previous scars; a coronal incision in the hair line, and one through the lower eyelid (a planned intra-oral incision was not required). Once exposed, all the previous plates and screws in the facial bones were removed. The two incisions allowed the zygomatic bone to be sectioned into 3 pieces using the cutting guide

(Figure 53). The resulting mobilisation allowed access to the orbit to facilitate retrieval of soft tissue which had herniated through the orbital floor fracture.

Figure 53 - Cutting Guide In-Use

The repositioning guide was fixed to the immobile anatomy - allowing the osteotomised bone pieces to be placed into the guide and temporarily fixed using 1.5mm diameter screws. The zygomatic implant was then located into the positioning guide recess and screwed permanently into position using 1.5mm diameter screws (Figure 54). Two screws were used per bone-piece to prevent rotation. The damaged orbital floor was manipulated into position using the orbital floor plate which was located as planned by using the recess in the repositioning guide. The orbital floor implant was fixed with 1mm screws (as selected during the planning phase by the consultant surgeon).

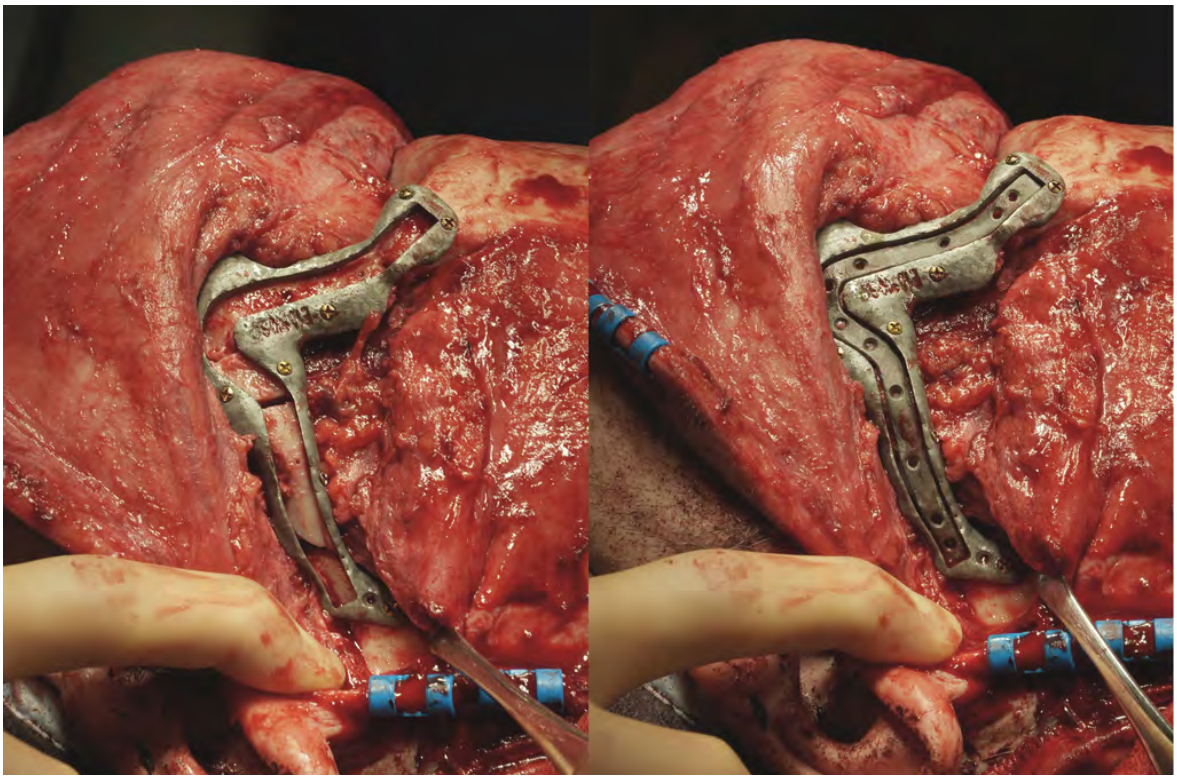


Figure 54 - Repositioning Guide In-Use

The screws temporarily fixing the repositioning guide were removed and the guide lifted away from the bone; leaving the zygomatic implant and orbital floor implant (Figure 55) in place.

The time from enquiry to final device dispatch was 8 months. If quoted commercially at the time of writing, with a minimum number of polymer models, the cost to the NHS of the institute's services would be around £1900.00. The cost of the metal guides and metal implants would be around £2000.00 (based on similar device prices).

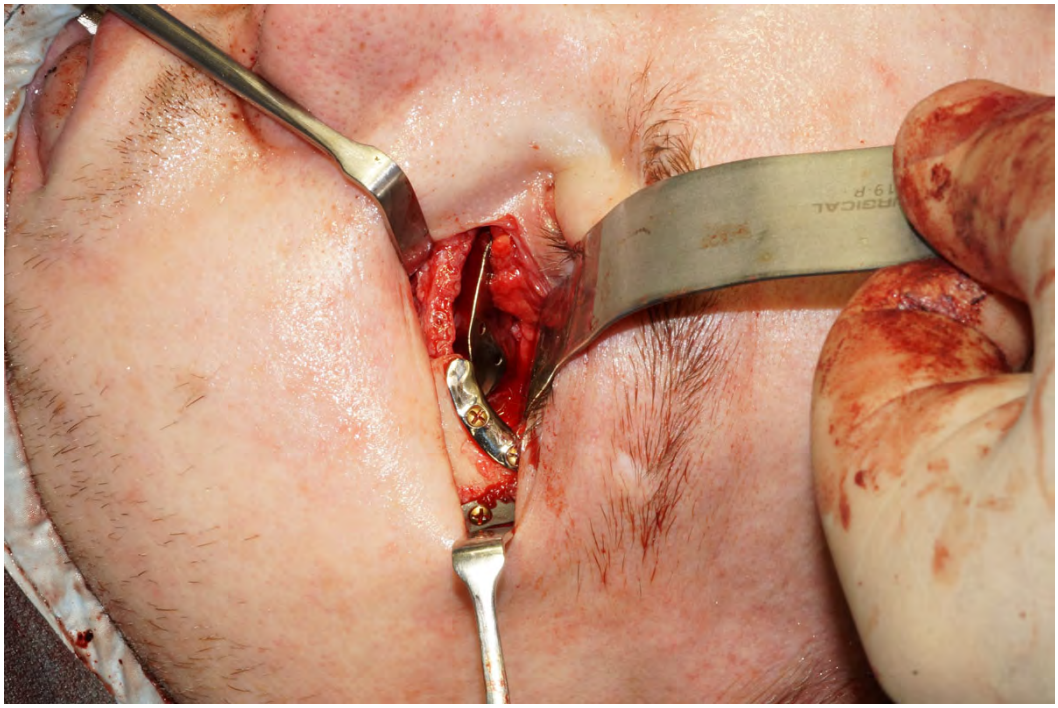


Figure 55 - Orbital Floor Implant In-Situ

5.3.2. Case Study [7] Results: Clinical Outcomes

Clinical outcomes from the surgery were judged by the surgeon to be excellent. The patient's facial asymmetry was aesthetically corrected and his confidence improved. He no longer wore a hat and glasses to disguise his face. His globe was repositioned to a suitable height and depth to attain good vision without the need to turn his head – as well as being able to close his eyelid fully without using a hand to pull the lid down.

A post-operative CT scan was processed using the same protocols as previously described (in the newer Mimics Version 16) to the point of generating a 3D reconstruction of the bone tissue. The pre-operative plan STL (including zygomatic and orbital floor implants) was imported into this workspace and aligned with the post-operative scan using the 'STL Registration' function. Subsequently, contours from the plan-STL were overlaid on top of the post-operative scan slices to enable visual comparisons between the two, as well as digital measurements.

Figure 56 shows the areas of largest deviation from the plan (red) for the zygomatic implant and bone pieces (white) in the axial plane. In the left image, a deviation of

3.65mm is shown for the posterior aspect of bone piece 3. The piece is also around 1mm more lateral than intended in the plan. The zygomatic implant, predictably, exhibits the same deviations. In the right image (taken from a slice towards the superior aspect of the orbitozygomatic complex) the lateral deviation is less pronounced, though the posterior shift is around 5mm for the zygomatic implant location.

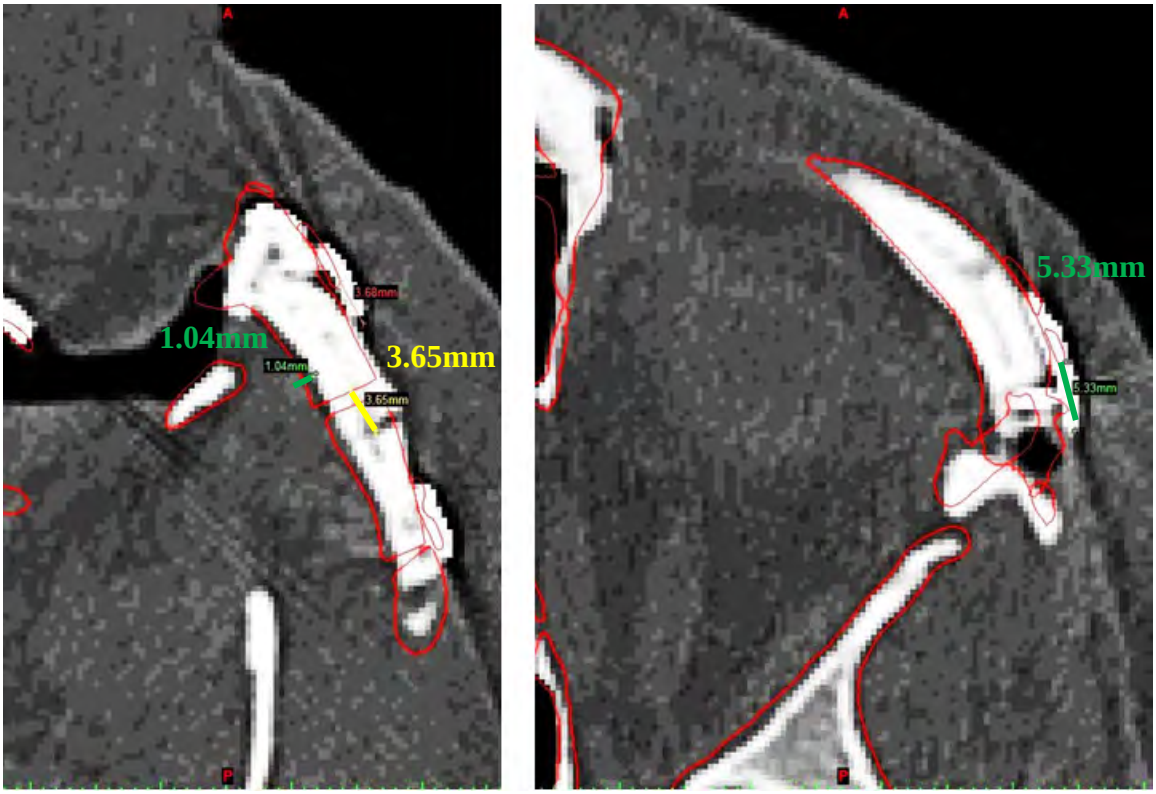


Figure 56 - Post-Operative Scan (Axial View) with Digital Plan Overlay

Figure 57 shows the effect the deviations from the plan had on the position of the orbital floor implant. The left image demonstrates the largest difference of 4.4mm between the planned position of the superior surface of the orbital floor implant (red) and the actual location (white). This is towards the anterior-medial aspect of the plate. The difference steadily reduces to zero towards the posterior and lateral portions. The right-image indicates correct seating of the implant against the bone – signifying that the deviations from the plan can be attributed to the bone piece positioning, rather than incorrect implant fit.

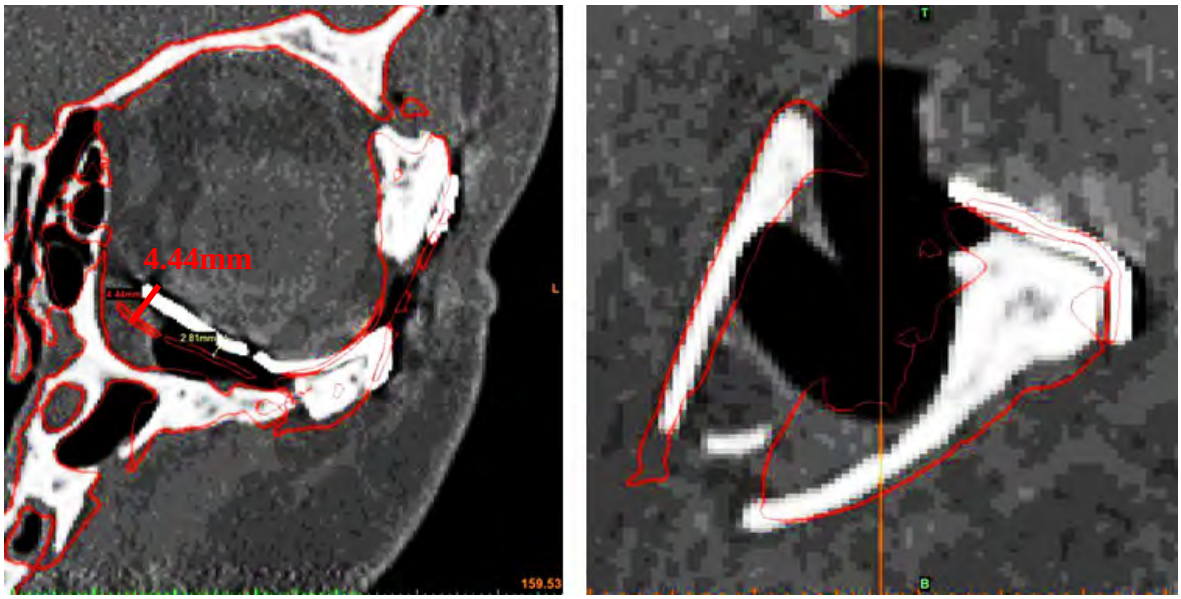


Figure 57 - Post-Operative Scan (Coronal and Sagittal Views) With Digital Plan Overlay

To verify the above comparisons, the registered STL files were imported into Artec Studio Version 9 (Artec Group, Luxembourg) and a 'Surface Distance Measurement' analysis undertaken. Figure 58 shows the result – with green indicating no deviation, blue indicating that the plan is deeper than the outcome and red indicating that the plan is superficial to the outcome. Aside from the post-operative bone pieces and zygomatic implant being inferior to the plan on the whole, there are two indications provided by the comparison. Firstly, the Mimics alignment ('STL Registration') is largely validated (given the overwhelming majority of green areas). Secondly, bone piece 3 has rotated – with the anterior edge being superficial to the plan and the posterior edge being deeper than the plan.

According to the qualitative opinions of the surgical team, the surgery time was reduced relative to a conventional approach by approximately 2 hours. However, a precise, quantitative comparison cannot be made.

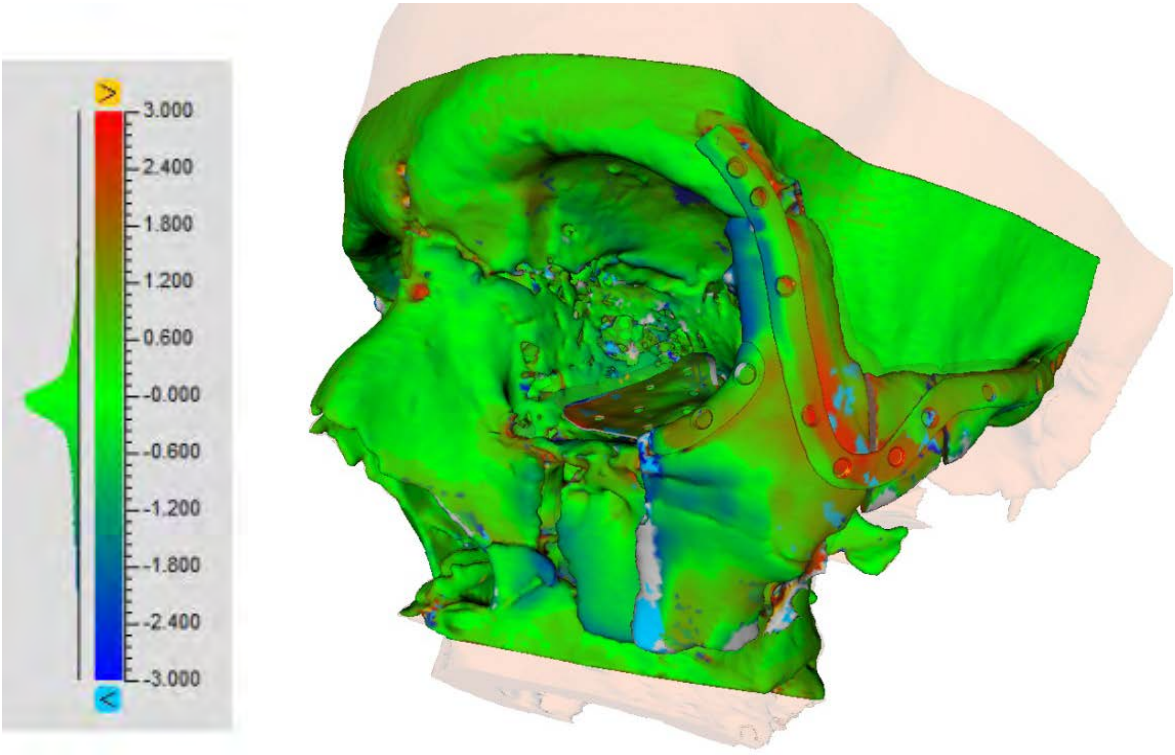


Figure 58 - Post Op Scan Vs Plan Overlay

5.3.3. <u>Case Study [7] Results Analysis</u>

In use, both of the guides largely fulfilled their functional and usability requirements. The cutting guide fitted onto the existing anatomy securely. The saw was guided with an appropriate clearance either side of the blade (0.3mm). However, extra in-theatre clarification and discussion was required (referencing the print-outs) to properly define the saw angle for the cuts around the outer edges of the guide. A cutting ledge of greater thickness than the main body of the guide was deemed likely to mitigate this delay in future cases by physically indicating the intended angled cutting edge against which the blade should rest.

The repositioning guide fitted securely and accommodated each bone segment robustly. During the process of fitting the smaller bone segments into the repositioning guide though, their anteroposterior locations had to be cross-referenced with the planning imagery; they retained some freedom to move even with the guide in place. This could not be solved mechanically without endangering the guide's ability to interface with the pieces (short of introducing undercut complications). A

promising solution for future cases was agreed to be indicating the intended end-point of each bone piece using embossed markings on the surface of the guide.

Bone piece 3 was identified as having rotated in the post-operative scan relative to the planned position. The ideal solution would have been to employ a larger area of contact between the interfacing surfaces, to better control the bone's position in the guide. However, this would have been problematic (or even impossible) owing to this method risking undercuts and hampering the ability of the bone to slide in and out of the guide. An alternative approach could have been to extend the guide to constrain the inferior portion of the bone piece – and have the guide engage immobile anatomy in the same area. However, this would have required considerably greater exposure of the bone which was not desirable. Perhaps then, this slightly sub-optimal position represented the best outcome, given these physical limitations of the technique.

Whilst a successful clinical outcome was achieved, the process as described was extremely time and cost inefficient; the collaborative design process was long and required a high number of device prototypes and anatomical models. Team members agreed that it would be a reasonable assumption that efficiency would improve dramatically in future similar cases - since the device design specifications were then more thoroughly understood.

5.3.4. Case Study [8] Results: Observed Process and Design Outcomes for Revision Post Traumatic Zygomatic Osteotomy and Recontouring

This patient suffered severe facial trauma following a road traffic accident abroad. Like case study 7, emergency surgery had been undertaken. However, the surgery was in an under-equipped hospital in a developing country and had been performed by less-experienced surgeons. As such, CAD and AM supported revision surgery was pursued by the UK consultant maxillofacial surgeon, tasked with improving the patient's aesthetic and functional state. The sight could not be saved in the affected right eye in the original surgery – so this aspect exhibited lower risk than case study 7.

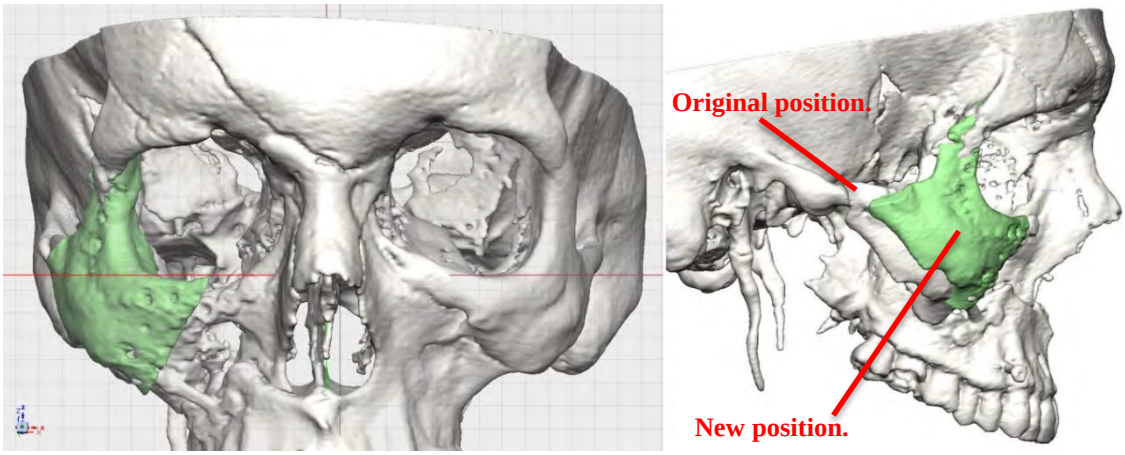


Figure 59 - Digitally Planned Bone Movements

The aim remained though, to restore the correct position of the globe. Surgical planning and device design was undertaken in collaboration with an experienced design engineer at the institute (not the researcher, in this instance). In general, a refined version of the workflow developed for case study 7 was adapted and compressed into a timeframe of 4 weeks, as opposed to that developmental project which spanned several months. The same software tools were used. A new-to-the-institute vat photopolymerisation SLA machine was used for model fabrication – a ProJet 6000HD (3D Systems, USA). The surgical devices were all fabricated by Renishaw (UK), using their AM 250 machines and Ti6Al4V build material.

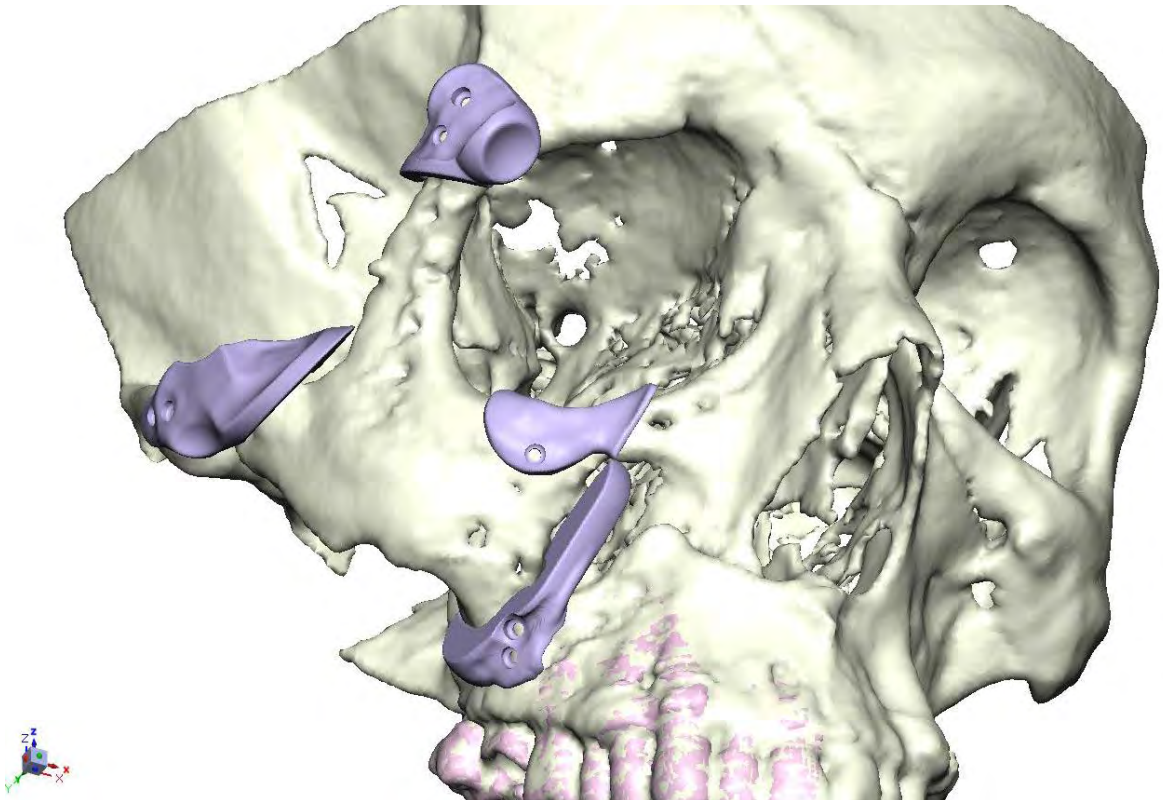


Figure 60 - Digitally Designed Cutting Guides

A medical model of the patient's scan data was used by the surgeon to identify which of the existing screws to remove. Then, a single piece of mobilised bone was deemed necessary to achieve sufficient remodelling. During an in-person surgical planning meeting between engineer and surgeon, the target position of the bone piece was agreed (Figure 59) and small cutting guides designed to translate the osteotomy vectors into theatre accurately (Figure 60). Multiple components were used at the direction of the surgeon, instead of a single piece guide. This approach aimed to mitigate access limitations, guarantee proper anatomical engagement of a wide area, minimise the size of the surgical exposure, and enable an intraoral approach for the medial-most cuts.

Having agreed the fundamental characteristics (thickness, extents, fixation methods) of a repositioning guide and five implants, the design engineer modelled, refined, and detailed the devices after the planning meeting (Figure 61). This permitted the surgeon to return to in-hospital work and represented the usual method of working between the two parties. The repositioning guide took advantage of titanium's strength and stiffness, relative to polymers, even with minimal thickness (1.5mm) to target a sliding-motion insertion path beneath soft tissues at the edges of the exposure site. Cut-outs in the positioning guide aimed to locate and align the implants during fixation, before the guide was removed and the implants were left in place (Figure 62). Three implants (nominal thicknesses of 0.5mm) aimed to hold

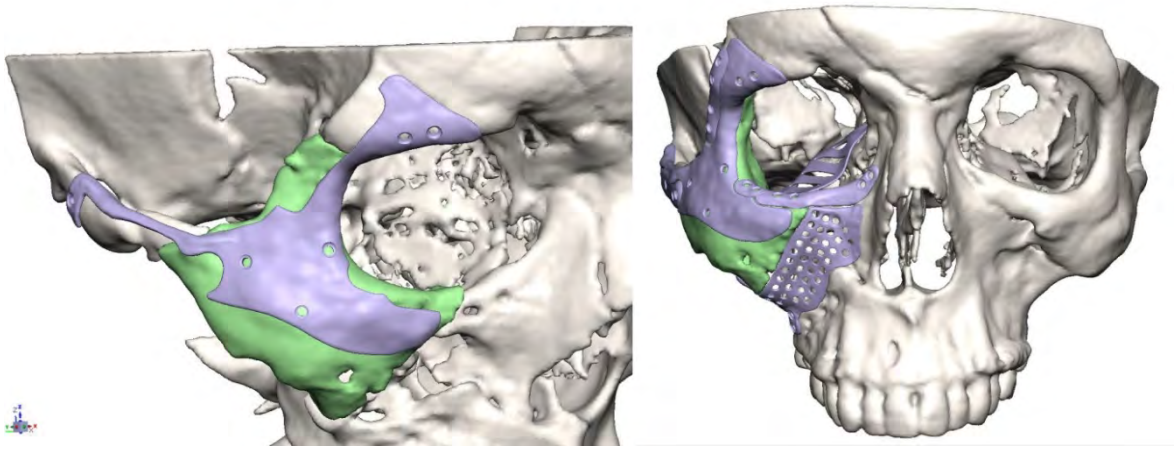


Figure 61 - Repositioning Guide and Implant Designs

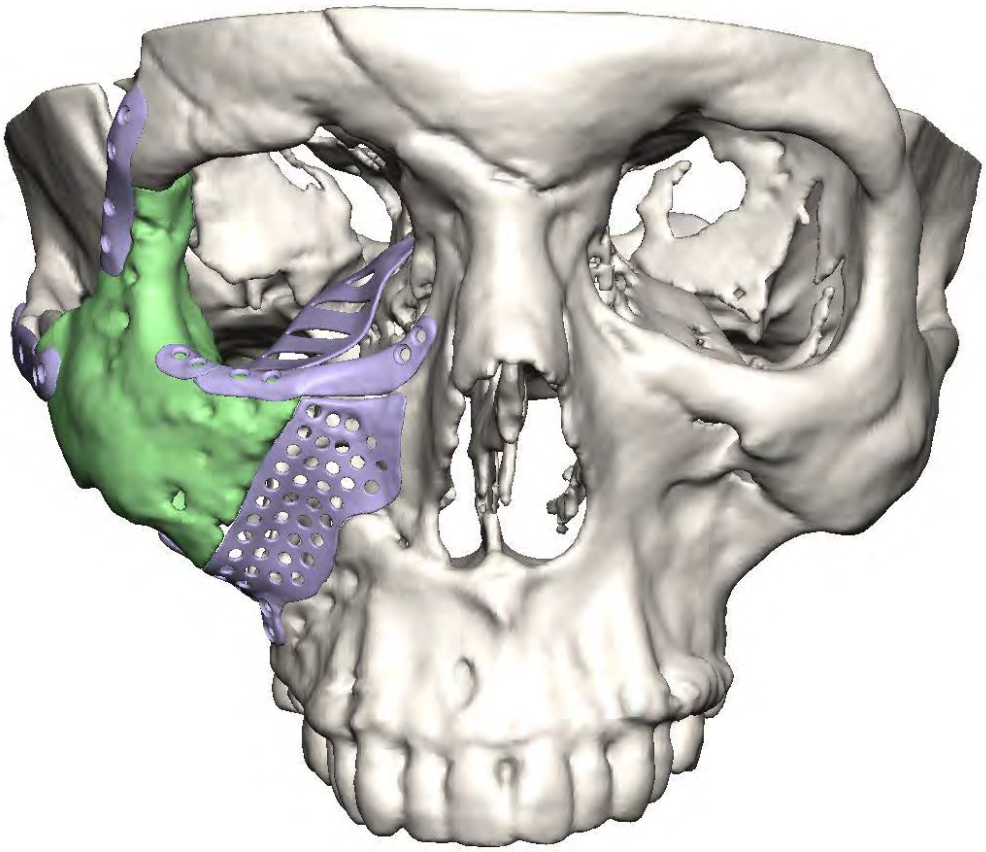


Figure 62 - Implant Plan after Repositioning Guide Removal

the zygoma in position. One implant aimed to reconstruct the orbital floor. One implant aimed to reconstruct an area of missing bone at the maxilla. Fluid transfer holes were added to each of these components. The surgeon verified the designs prior to fabrication, specified a polished finish for the implants (to make removal easier, if required), and a grit-blasted finish for the guides (to minimise cost). Printed images and the new models of the plan were delivered for visual reference in theatre.

The researcher did not observe the surgery directly in this instance. Feedback was obtained from another institute design engineer who was present, and from the lead surgeon. Figure 63 shows intra-operative views of the cutting guides being used in-situ. Areas where previous stock fixation plates had been removed can be seen clearly in the lower-right image. The new implants were designed to avoid these holes. Intra-oral access for one of the cuts is also clearly visible. Figure 64 offers views of the repositioning guide, zygoma implants, orbital rim implants, and orbital floor implant prior to repositioning guide removal.

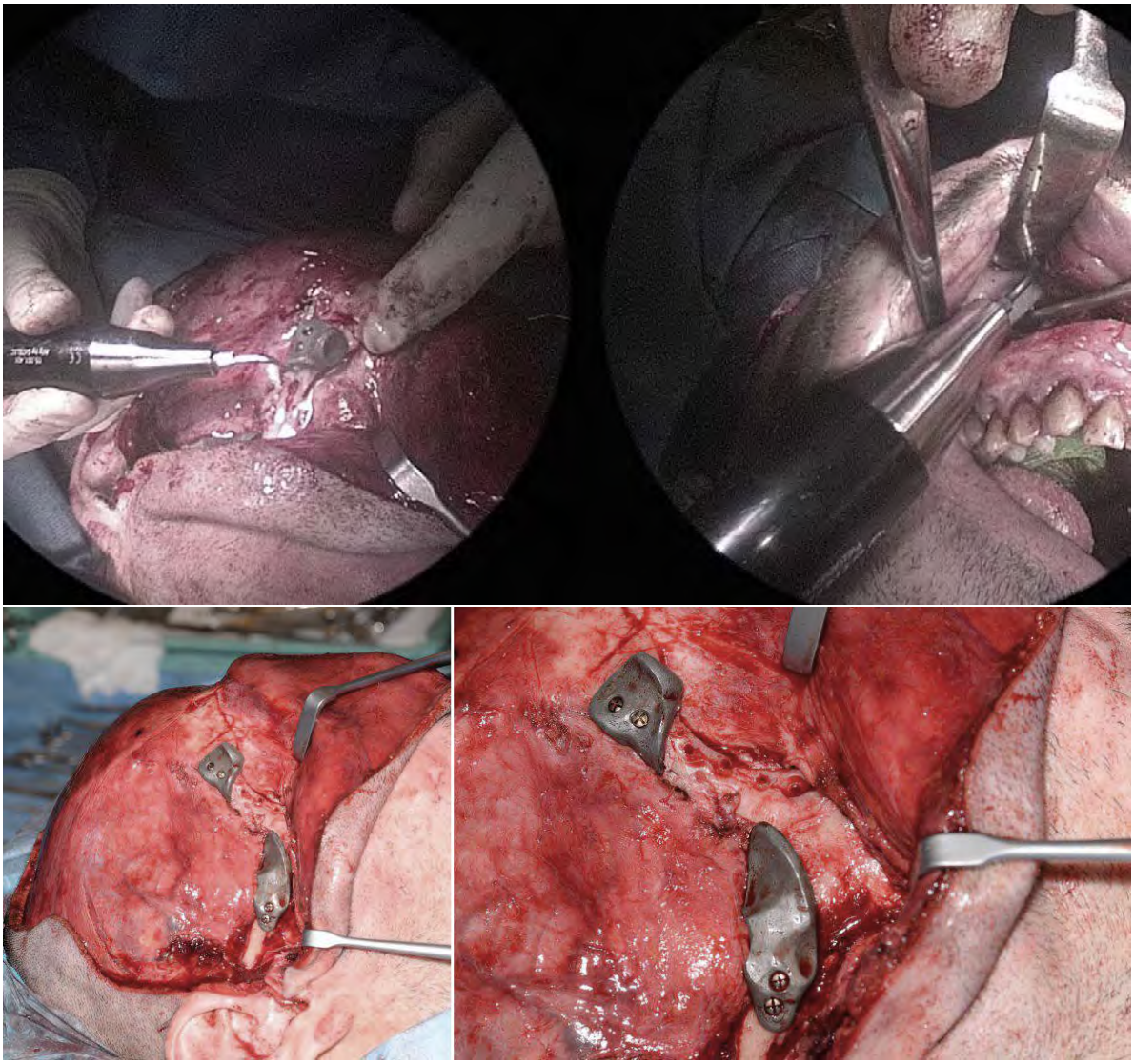


Figure 63 - Cutting Guides In-Use (Images Courtesy Mr S. F. Mustafa, Prince Charles Hospital, South Wales, UK)

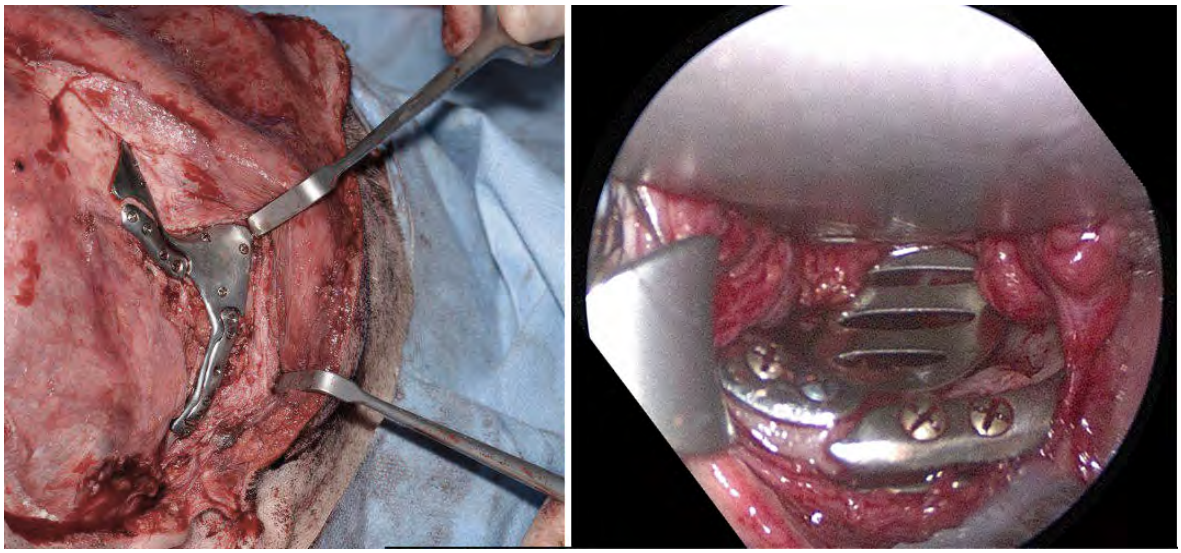


Figure 64 - Repositioning Guide and Implants In-Use (Images Courtesy Mr S. F. Mustafa, Prince Charles Hospital, South Wales, UK)

The time from enquiry to final device dispatch was 1 month. If quoted commercially at the time of writing, with a minimum number of polymer models, the cost to the NHS of the institute's services would be around £1900.00. The cost of the metal guides and metal implants would be around £3000.00 (based on similar device prices).

5.3.5. Case Study [8] Results: Clinical Outcomes

During the surgery, a small triangle of bone was cut away medially to allow the orbital rim implant to be seated more securely. This had been acknowledged as a possible step during the planning meeting, it was an uneventful and safe diversion from the surgical plan. On the other hand, during surgery an unexpectedly large mass of soft tissues (containing the infra-orbital neurovascular bundle) was noted to be emerging from the anterior surface of the maxilla. These soft tissues had, in the surgeon's opinion, likely been displaced following the injury and initial surgery. Their presence obstructed, and would have partially been covered by, the maxilla implant (the inferior-most implant in Figure 62). As such, an intra-operative decision was made to discard that component. Otherwise, the procedure adhered to the digital surgical plan.

Clinical post-operative assessment was positive – despite the omission of an implant. The primary clinical objectives were achieved with no significant compromise. The patient's aesthetics were improved through better symmetry, and the globe was restored to its original height and projection. Like for case study 7, a post-operative scan was available to better quantify the outcomes. Figure 65 shows the post-operative scan aligned with the pre-operative plan (minus the discarded implant). The position of the bone piece was very good – with the differential map on the right side suggesting only a small variation from the plan. The inferior aspect of the repositioned bone piece was rotated medially by 2mm. Consequently, the superior-most aspects were rotated laterally by the same amount. Overall, the accuracy appeared to be comparable to case study 7.

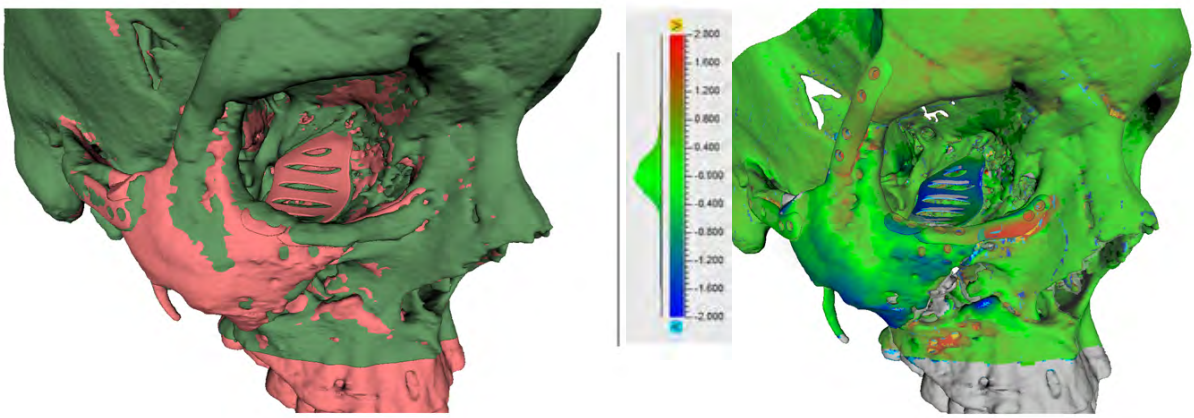


Figure 65 - Overlays Comparing the Pre-Operative Plan and the Post-Operative Scan

5.3.6. <u>Case Study [8] Results Analysis</u>

This case demonstrated a normalised version of the case study 7 workflow – following much shorter, more usual timeframes. This compression was afforded by shortcuts resulting from existing knowledge of: the need for separate guide and implant components; the need for at least two screws in the retention of each device to their respective bone pieces; and the need to design for a minimised exposure of the defect site. With these key design considerations known, time consuming and expensive prototyping stages were eliminated; along with several iterations of the surgical plan. The surgical planning meeting was undertaken in one sitting of approximately one hour.

Negatively, the nerve bundle was not anticipated by the surgeon, nor known as a possibility by the design engineer. Therefore, the surgeon could also not be prompted to consider it. Furthermore, the procedure was of a lower-risk than case study 7 because the sight had already been lost from the right eye. However, this case was at least as successful as case 7 in its clinical aims, and was delivered in a fraction of the time.

5.3.7. Case Study [9] Results: Recorded Process and Design Outcomes for Hemimandibulectomy and Primary Fibula Free-Flap Reconstruction

This surgical planning and device design procedure was well-known to the institute. The researcher had defined and refined a standard-operating-procedure following previous instances of intra-team workload sharing. It aimed to ensure a consistent approach to delivering what had become a routine, but still highly complex design service product. This project was undertaken using the same software tools as for case studies 7 and 8. It used the same fundamental process stages as those; to generate virtual models of the mandible and the fibula from which a bone graft would be harvested.

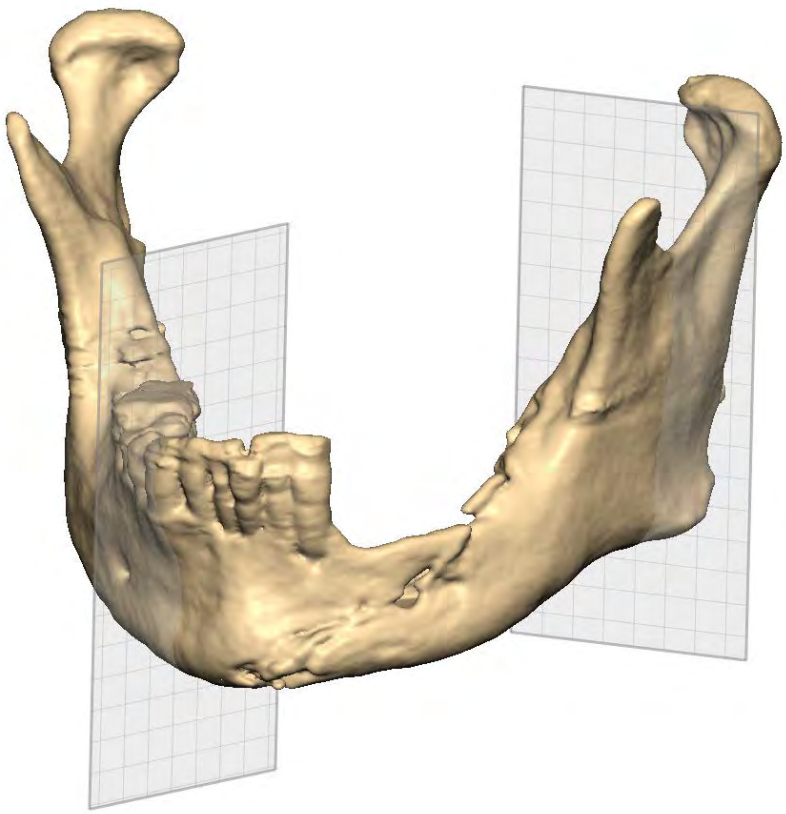


Figure 66 - Virtual Model of Diseased Mandible (With Agreed Cutting Planes)

This patient had a tumour of the left hemi-mandible (Figure 66) which would be excised and replaced with a vascularised bone flap from the right fibula; in a primary, single-stage procedure. The tumour was malignant, so speed of planning, design, and fabrication was essential. In this instance, the surgeon also requested guided dental implant placement in the fibula graft – to commence immediate dental

rehabilitation and if possible, eliminate the need for future procedures. An in-person surgical-planning meeting was arranged between the Consultant maxillofacial surgeon and a design engineer at the institute (researcher). The institute provided a virtual plan, physical models, and designs for two mandible cutting and drilling guides, one fibula cutting and drilling guide, and one mandible implant.

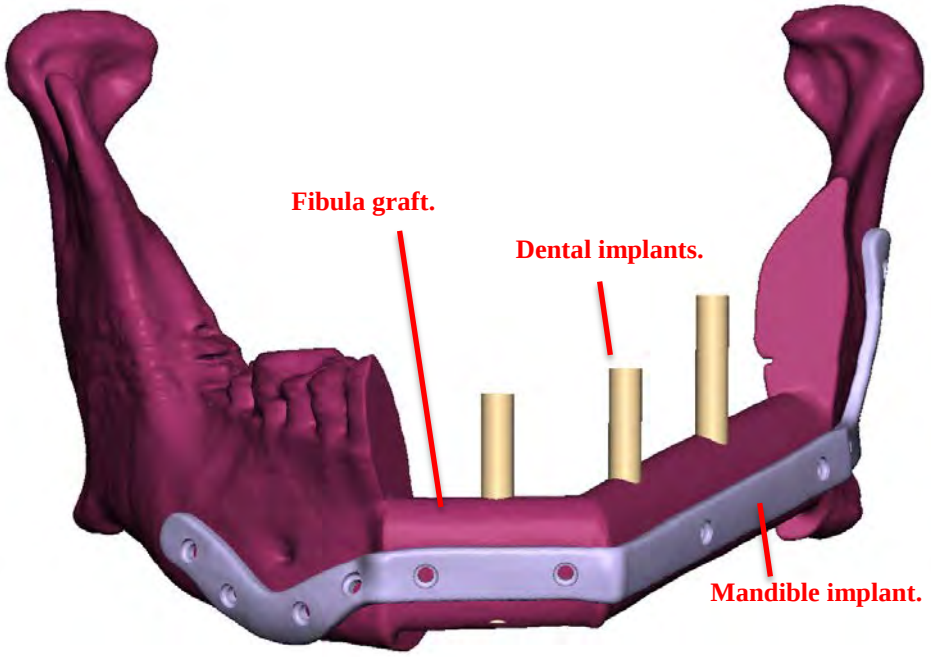


Figure 67 - Planned Fibula Grafts, Mandible Implant, and Dental Implants

During this short meeting (45 minutes), the excision margins on the mandible were described by the surgeon, and interpreted by the researcher. Additionally, the precise segments of fibula for the grafted reconstruction (Figure 67) were iterated, agreed, and visually assessed, then digitally measured for appropriateness. The fibula remodelling was assisted by rendering a translucent overlay of the healthy, contralateral mandible and adjusting the virtual bone graft to best-match. Here, the surgeon aimed primarily to reconstruct the inferior border of the mandible, whilst maximising the contact area between residual mandible and grafted bone, and achieving sufficient height for supporting the dental implants. Also in the meeting, key details about the custom devices were discussed and explicitly agreed: the implant extents and fixation; the screws to be used (2mm diameter); the location and diameter of the proposed dental implants; the path of the custom mandible implant (avoid the mental nerve); and the basic extents and aims of the cutting guides (Figure 68).

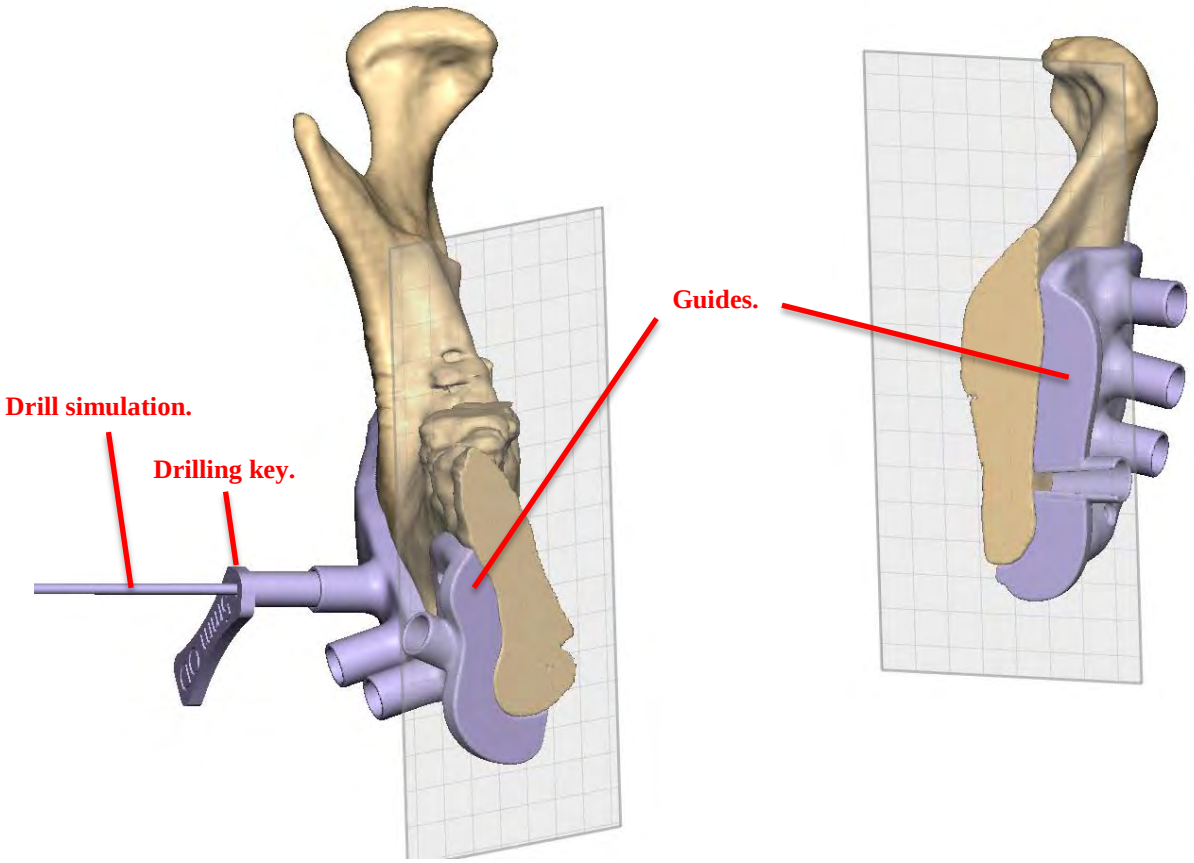


Figure 68 - Virtually Excised Mandible with Cutting Guides, and Drilling Guidance Keys

Finally for the initial meeting, certain rules developed for the standard operating procedures, through learning from previous cases, were reviewed by the surgeon and confirmed for application to this particular case. Then, the intricate modelling was completed 'offline' – without the busy surgeon's presence. Outcomes were checked against the approved rules. When virtually harvesting the fibula, precautions were taken to ensure the first segment began at least 80mm from the distal aspect. This aimed to ensure a good blood supply. For the same reason, no individual graft segment was permitted to measure under 20mm in length. Slight relief was modelled between the implant, and each of the bone-to-bone joints; with the aim of creating some flexibility to accommodate small deviations from the planned contour. The implant was designed with a rectangular cross section of 7x2mm to reflect the dimensions of the stock plates which would otherwise have been used in this type of procedure. This reflected a cautious approach in the absence of any published evidence favouring alternatives. Countersinks were modelled at the screw sites to

ensure proper screw seating; and so minimise palpability of screw heads through the skin. Precautions were taken to ensure 0.3mm of material was left at the base of the countersinks (the minimum recommended thickness from the manufacturing entity). The surgeon arbitrarily requested a polished mandible implant. The metal AM manufacturer in this case (Renishaw, UK) confirmed internal procedures to automatically add 0.3mm compensatory thickness to the part; permitting the same amount to be lost during polishing without compromising the design.

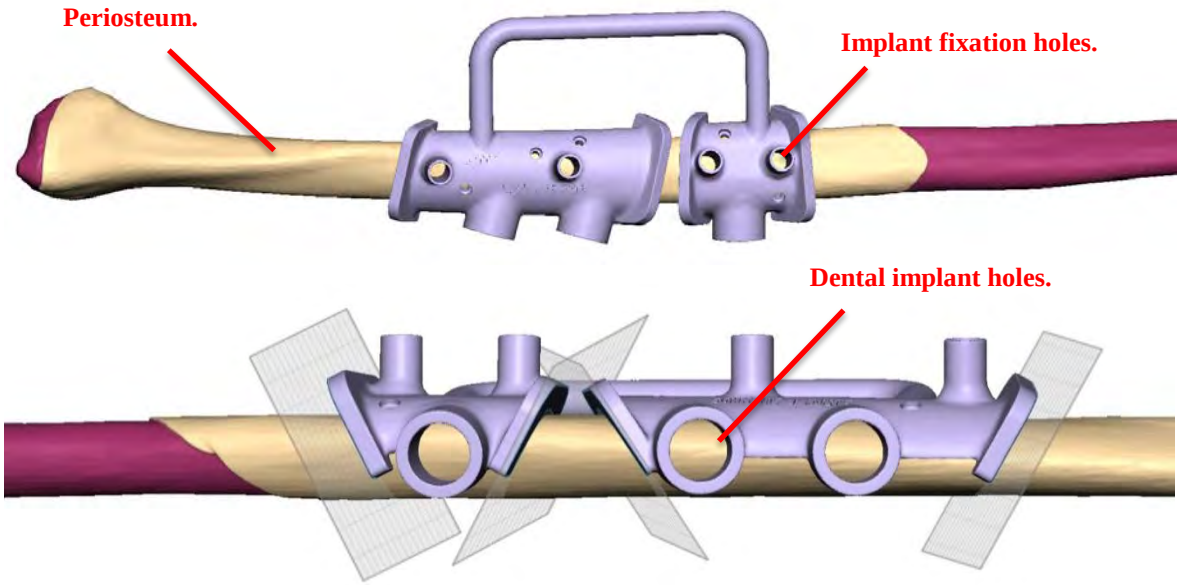


Figure 69 - Lateral and Superior Views of Fibula Cutting and Drilling Guide Design

The fibula guide (Figure 69) was directed to interface with the lateral aspect of the fibula; a less contoured area deemed more suited to creating the lateral aspect of the mandible reconstruction. Because of this smooth contour, and lack of distinctive landmarks, a positioning guide for the fibula was designed (Figure 70) to locate on the irregular distal aspect, and butt-up against the fibula cutting guide. This aimed to ensure correct location of the guide, and also improve the surgeon's confidence by providing feedback of such. A 0.6mm thick layer of simulated periosteum was added to the fibula (Figure 69) to improve the realism of the virtual bone-device interface.

Drilling guide holes were modelled on the mandible and fibula guides at the precise locations of the eventual implant fixation screw holes. This aimed to further guarantee accuracy; by confirming to the surgeon that the implant was not only fixed to the correct size and shape of graft, but was fixed in the correct location on the

graft. Drilling 'keys' (small metal AM jigs) were designed to slide into the drilling collars. This was based on standard institute practice, which had been validated by (O'Malley, 2016). They aimed to fully constrain the axis angles of the pilot hole drill; by extending the length of the constrained shaft area. Furthermore, the triangular shape of the guide hole aimed to improve irrigation to the bone – to improve cooling and therefore maintain bone viability. Finally, general design-for-AM best practice was followed, by ensuring that there were no sharp corners, or sudden thickness variations which could cause issues with deformation on cooling. The surgeon verified the proposed designs by reviewing a document. This approved fabrication.

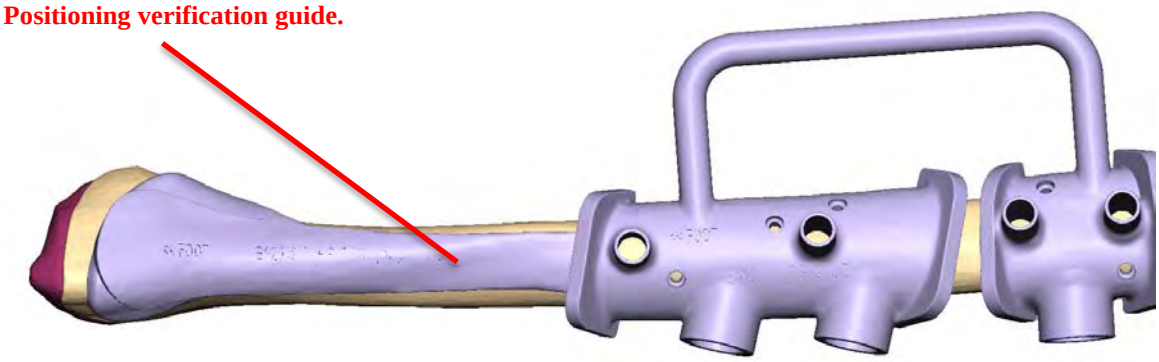


Figure 70 - Positioning Verification Guide and Main Fibula Cutting / Drilling Guide

The time from enquiry to final device dispatch was 15 working days. If quoted commercially at the time of writing, with a minimum number of polymer models, the cost to the NHS of the institute's services would be around £2000.00. The cost of the metal guides and metal implants would be around £1700.00 (based on similar device prices).

5.3.8. Case Study [9] Results: Clinical Outcomes

Again, the researcher did not observe the surgery directly. Feedback was obtained from another institute design engineer who was present, and from the lead surgeon. The procedure progressed largely as planned. However, in the interests of ensuring bone graft viability, the surgeon decided to omit the immediate insertion of dental

implants. Perioperative assessments of bone quality prompted a conservative approach; with the main aim being to ensure good vascularisation of the fibula at the mandible defect site. Otherwise, clinical outcomes were deemed to be excellent – with good aesthetics and a robust foundation for rehabilitation. The surgical team were impressed by a decrease in surgical time (self-reported and lacking specific figures), the improved predictability of the outcome, and the simplification of what would otherwise have been an iterative, highly skill-dependent procedure, undertaken by manual remodelling of bone.

5.3.9. Case Study [9] Results Analysis

This case study adhered to well-developed, high fidelity processes which were specific to the surgery in question. There was a clear requirements list which made the process simple and quick for all of the stakeholders. The time from enquiry to delivery of the parts was well within the surgeon's deadline to ensure safe tumour excision. This differed from the exploratory nature of case study 7 and the only partially-refined processes used in case study 8. Every designed and fabricated device worked perfectly – to the degree that they were used (i.e. no attempt was made to drill the dental implant pilot holes).

The clearest illustration of the success of this case (and those like it, for this hospital) was the uniform adoption of this technique by the unit in question. As much as this was indicative of the reliable and routine delivery of such complex design services, it cannot be taken as a business-case endorsement of in-hospital planning and design software. The equipment was uniquely gifted to the hospital for political and promotional reasons. The success of the hospital-designed parts (in terms of taking advantage of the benefits of CAD and AM) remains unclear.

5.4. Chapter 5 Summary

In summary, Chapter 5 has:

- described, illustrated, and costed three different design and fabrication processes for simple and routine UK NHS cranioplasty implant and orbital implant production (Chapters 5.1.1 – 5.1.7);

- described and illustrated three different design processes for complex implants ranging from first-of-their-kind to routine (5.3.1 – 5.3.9);

- identified that when available, the semi-digital approach to cranioplasty implant production was the least expensive, with an acceptable clinical outcome (5.2);

- identified that when available, the conventional approach to orbital floor or medial wall implant fabrication was the least expensive, with an acceptable clinical outcome (5.2);

- concluded that, at least for the featured complex cases, fully digital CAD and AM devices were justified in terms of making procedures viable, improving predictability, and improving (subjectively assessed) clinical outcomes (5.3.3, 5.3.6, and 5.3.9);

- shown that the success of the complex cases increased in parallel with the fidelity of the product and user requirements list, and the standard operating procedures 5.3.4 – 5.3.9);

- highlighted the importance of several other key factors throughout the patient-specific device design process including: the gap between ordering and prescribing surgeons, the number of relevant discussion prompts during planning, the amount of justification or evidence for a design decision, the number of iterations of a design, and the number of anticipated surgical problems (5.2.1 – 5.2.2);

- and in doing these things, has contributed to meeting objective 2 from Chapter 1.9 and to answering research question s 1, 2, and 3.2 from Chapter 4.2.4.

6. Investigation B Results – Developing a Design Intervention

This Chapter (Figure 71) identifies, justifies, and presents the assembly of a new patient-specific device design intervention. It contributes to meeting objective 3 from Chapter 1.9 and to answering research questions 3.1 and 3.2 from Chapter 4.2.4.

The framework was paper-based, and targeted both in-hospital and external commercial design contexts. It sought to create a standard structure for the patient-specific device design process, independent of specific software tools, fabrication tools, users, and immediate design contexts. It sought to do this in a way which was conducive to the successful and efficient implementation of a quality management system for design control; in light of the quality and regulatory burdens identified in Chapter 1.6. This was not, and could not, be a ready-made 'drag-and-drop' QMS. This was on account of the essential requirement that any QMS should be innately tailored to its organisation, and be able to demonstrate support from top management. Instead, the framework aimed to incorporate the most generalisable aspects of a design QMS; grouped around specific surgical interventions, and supported by evidence.

Sub-Chapter 6.1 presents the specific solutions developed for the intervention, to address the problems with existing procedures, as identified throughout Chapters 2, 3, and 5. Sub-Chapter 6.2 summarises the complete QMS developed by the researcher (for the institute context), then isolates and justifies the generalisable functions used in the framework. Sub-Chapter 6.3 identifies new, evidenced, specific design considerations for complex craniofacial reconstruction; with a view to solving some of the problems with the existing literature identified throughout Chapter 3. It does this by systematically reviewing the complex craniofacial reconstruction literature for design rules or design considerations. Then, it contributes new considerations from a case series of five similar institute design projects. Sub-Chapter 6.4 presents and justifies the collated design intervention document.

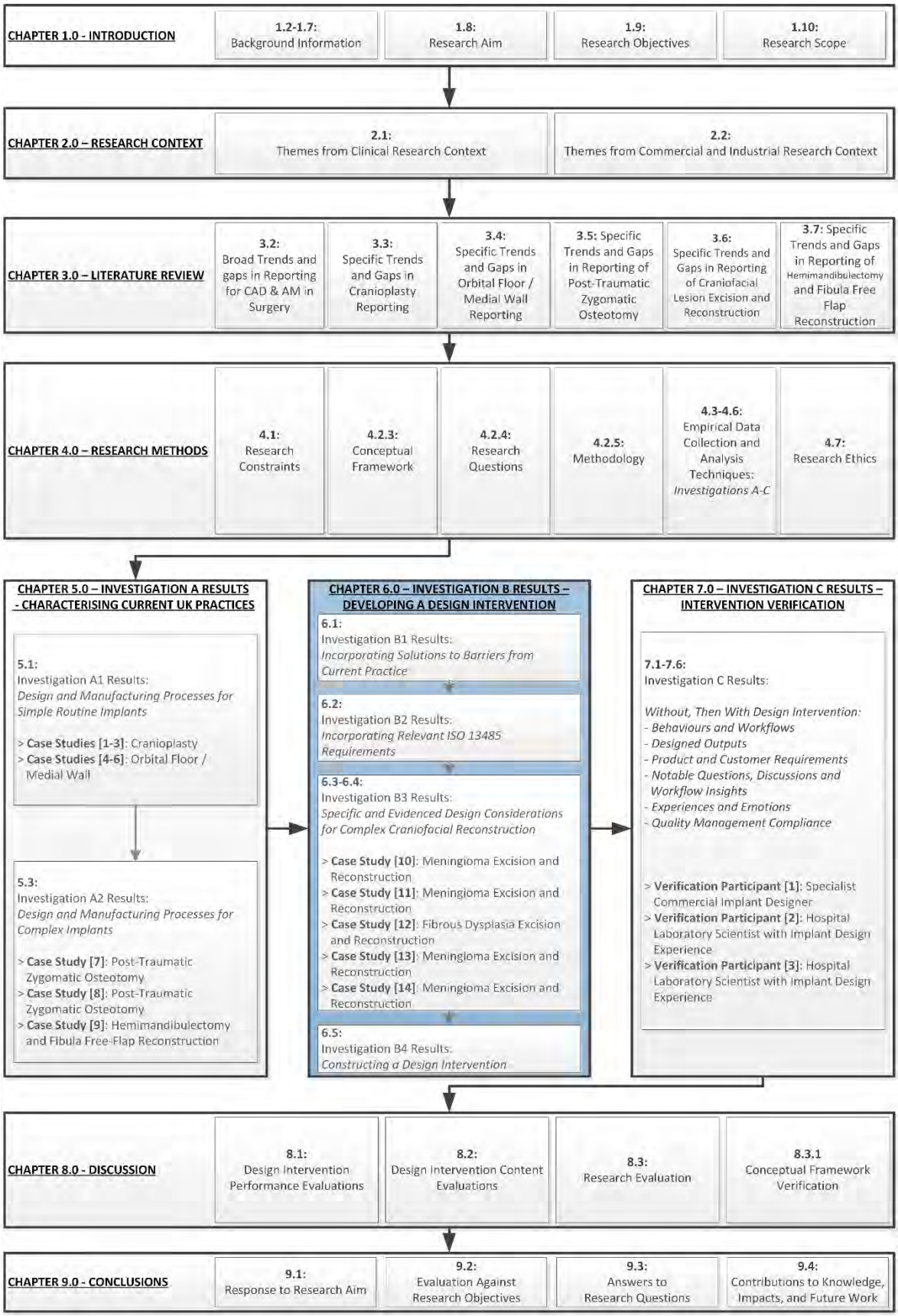


Figure 71 - Thesis Overview, With Current Location Highlighted (Chapter 6)

6.1. Investigation B1 Results – Incorporating Solutions to Barriers from Current Practice

Table 6 describes the identified barriers to routine adoption of CAD / AM / CAM devices, the sources from this research, and the methods by which the intervention aims to overcome them. The final column acted, in effect, as a contributor to the design intervention specification.

Table 6 – Problems Identified from Current Practice Evidence; with Proposed Design Intervention

Current Context / Practice Barrier	Source(s)	Aim to Mitigate in Design Intervention by:
CAD/AM/CAM can be difficult to justify compared to conventional devices; in the context of downward cost pressures on the NHS.	Chapter 2, Chapter 5	Creating a low-cost, paper-based intervention; for use across design processes or procurement processes. Minimising the number of design iterations required, through structuring the up-front gathering of explicit product requirements.
In-hospital device production not subject to same quality controls as commercial devices. Likely future 'corrections' of this.	Chapter 1, Chapter 3	Incorporating the most generalisable aspects of an ISO 13485-compliant QMS; to prompt and provide a framework for the development of a hospital's (or commercial entity's) own QMS.
Service model fragmentation / variation.	Chapter 2, Chapter 3	Creating a low-cost, paper-based intervention; generalisable across software tools, or external services.
Knowledge gaps between specialities.	Chapter 2, Chapter 3, Chapter 5	Prompting explicit identification of key details and concepts from a top to a granular level; including details of: the surgical problem, surgical plan, ideal devices, technical constraints, shape and material characteristics, and individual design features.
Literature often omits key details for enabling reproduction of methods; making adoption of successful techniques more difficult.	Chapter 3	Encouraging acting designer to clarify assumptions, solve misunderstandings, and record explicit specific aspects of the design decision-making and design characteristics. Future development of publications can draw on that pseudo design file.

Literature rarely reports on design or CAD modelling details.	Chapter 3	Prompting structured, detailed feedback.
Design decisions are rarely justified in full (or at all) by the ordering or operating surgeon.	Chapter 2, Chapter 3, Chapter 5	Prompting publication of given patient case; as case study, case series, or larger review (wherever worthy).
Default, general lack of evidence supporting CAD/AM design decisions.	Chapter 3	Making evidenced recommendations for a specific patient-specific device category (at first); and referencing the source for the recommendation to permit surgeon review. Framing recommendations as “considerations” not “rules” to reflect the tentative nature of the conclusions; and to acknowledge the flexibility required to modify approaches across unique cases.
Ill-defined and ill-justified conventional practice gold-standards.	Chapter 3	Prompting explicit, conscious, and public documentation of justifications for overall approach or design detail decisions.
CAD/AM complex workflow efficiency (and success) can increase in parallel with the fidelity of the product / user requirements list, and the fidelity of the standard operating procedures.	Chapter 5	Prompting discussion across key product and user requirement categories drawn from context, literature, and research case studies. Remaining flexible by not specifying procedural SOP’s for particular software packages.
Fidelity of the product and user requirements list can increase in parallel with the number of anticipated potential surgical problems, and the shared understanding of the surgical plan.	Chapter 5, Chapter 3	Prompting consideration of specific plan factors; especially about factors which have demonstrably been overlooked by previous designers.
Risk of design process failure increases, in line with the number of intermediaries between acting designer and operating surgeon.	Chapter 5	Encouraging interaction between acting designer and operating surgeon wherever possible. Mandating verification by the operating surgeon.

6.2. Investigation B2 Results – Accommodating ISO13485 Requirements

6.2.1. Results: Components of a Full QMS

ISO 13485 is not prescriptive in terms of *how* an organisation intends to satisfy its requirements – only that its chosen *methods*, do in fact, result in it meeting those requirements. To make one set of relevant possible methods tangible, insofar as they could be represented in documented formats, the requirements of the standard were interpreted to create a QMS for the institute. Then, the documents comprising that QMS (Figure 72), and the manner in which they were designed to be used in product realisation (Figure 73) were analysed (Table 7) on the basis of suitability for being co-opted into the design intervention proposed by this research (presented in sub-Chapter 6.5).

The QMS created by the researcher aimed to control the *design and development* of patient-specific, maxillofacial, non-weight bearing, non-articulating devices. Its outputs were STL files of verified patient specific guide, and patient-specific implant designs. Production of the end-use physical devices by AM or CNC machining was not controlled; because these aspects were outside of the stated scope of this research. After the design QMS was completed, it was assessed (Appendix 14) as being suitable for progressing to a full audit (pending certain highlighted modifications) by an accredited body (British Standards Institute, UK). Following modifications to address the potential nonconformities, the QMS was certified through internal audit as being compliant.

Although the product realisation workflow (Figure 73) directed the use of many of the QMS documents (Figure 72); others did not feature in the workflow at all. This was because they were related to creating a sustainable environment for good design (such as procedures for ensuring management responsibility) or were related to certain routine tasks to ensure a robust context for design activity (e.g. procedures for purchasing new tools). Table 7 clearly identifies those less-generalisable QMS aspects which were too-highly dependent on their context for inclusion in the intervention.

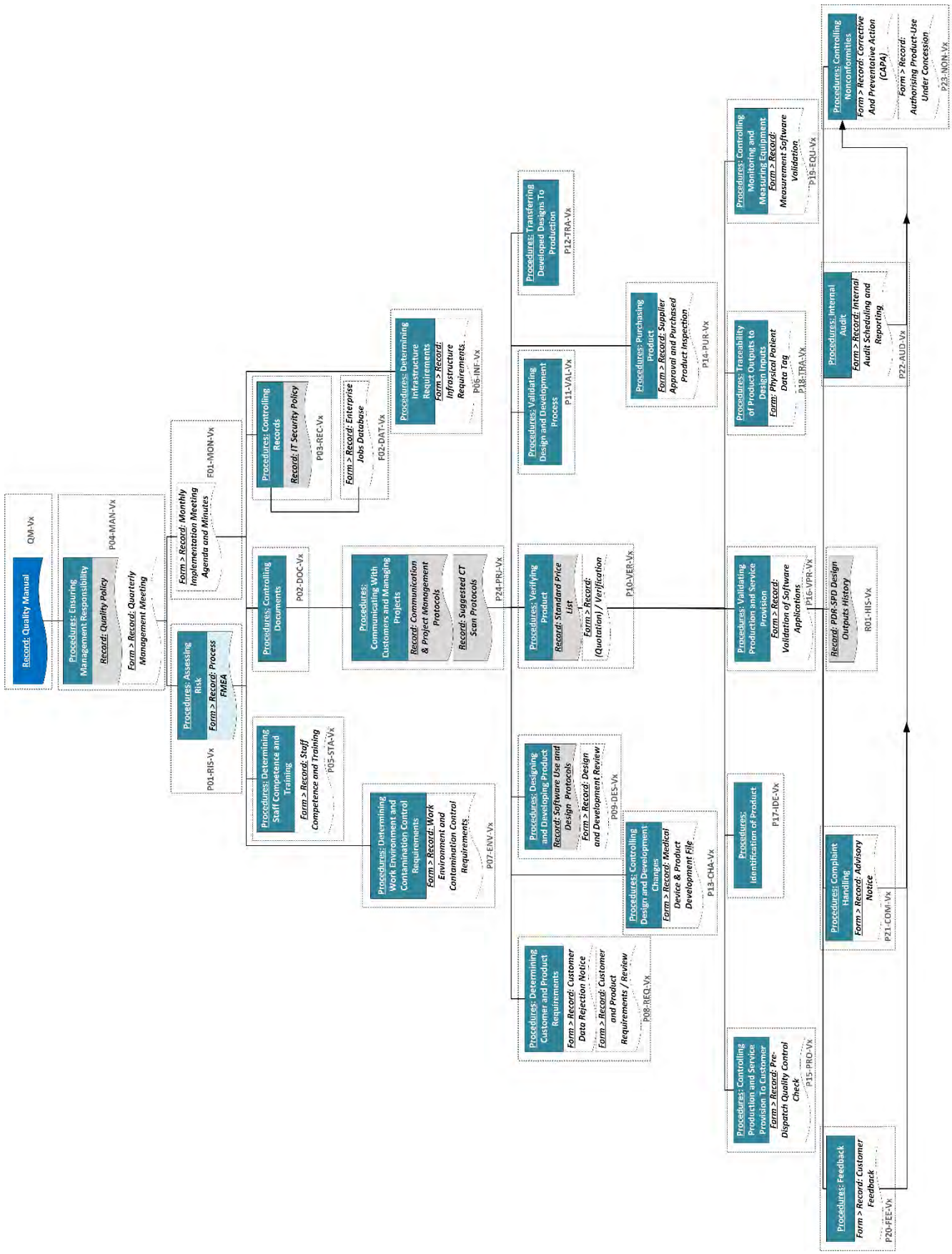
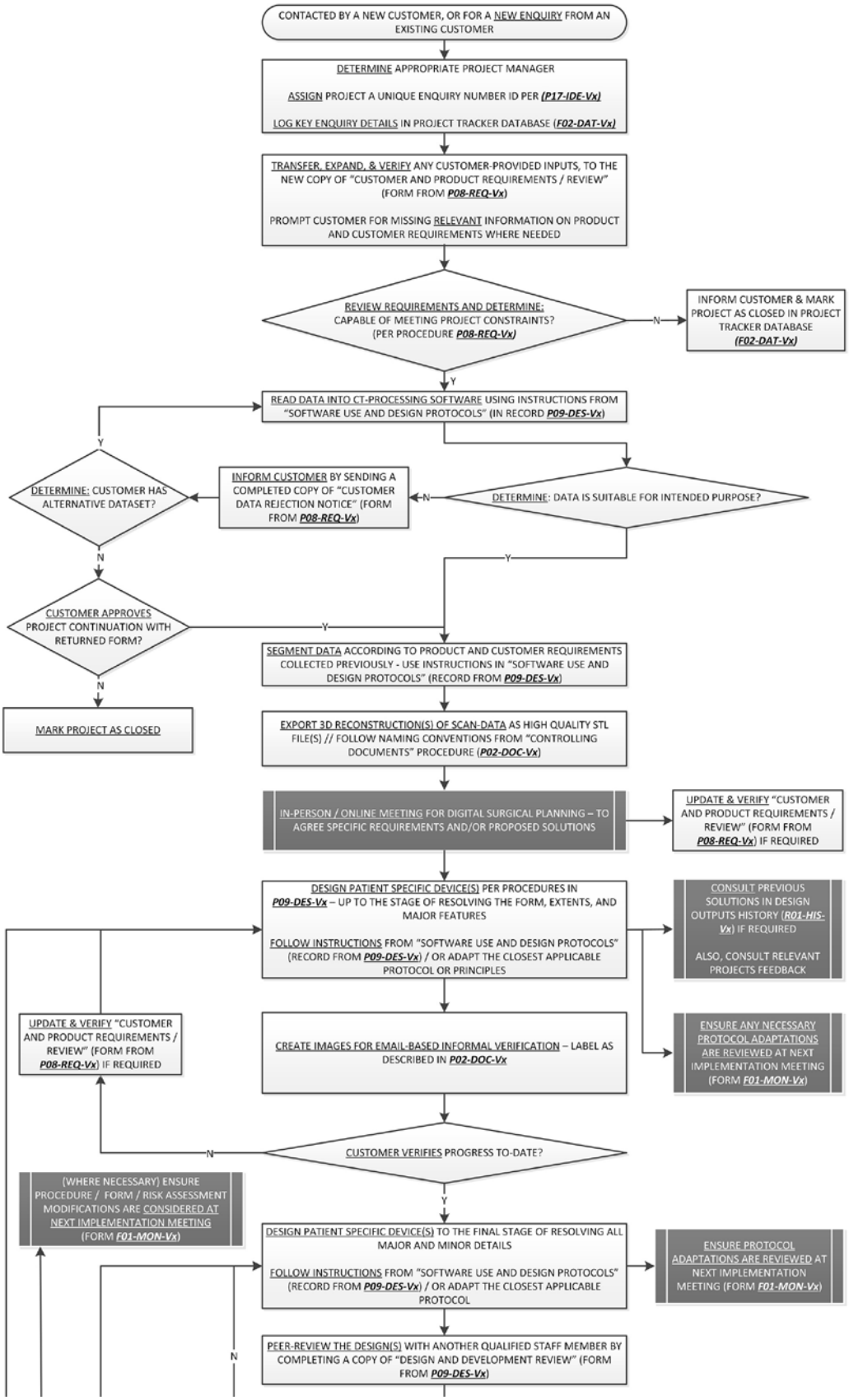
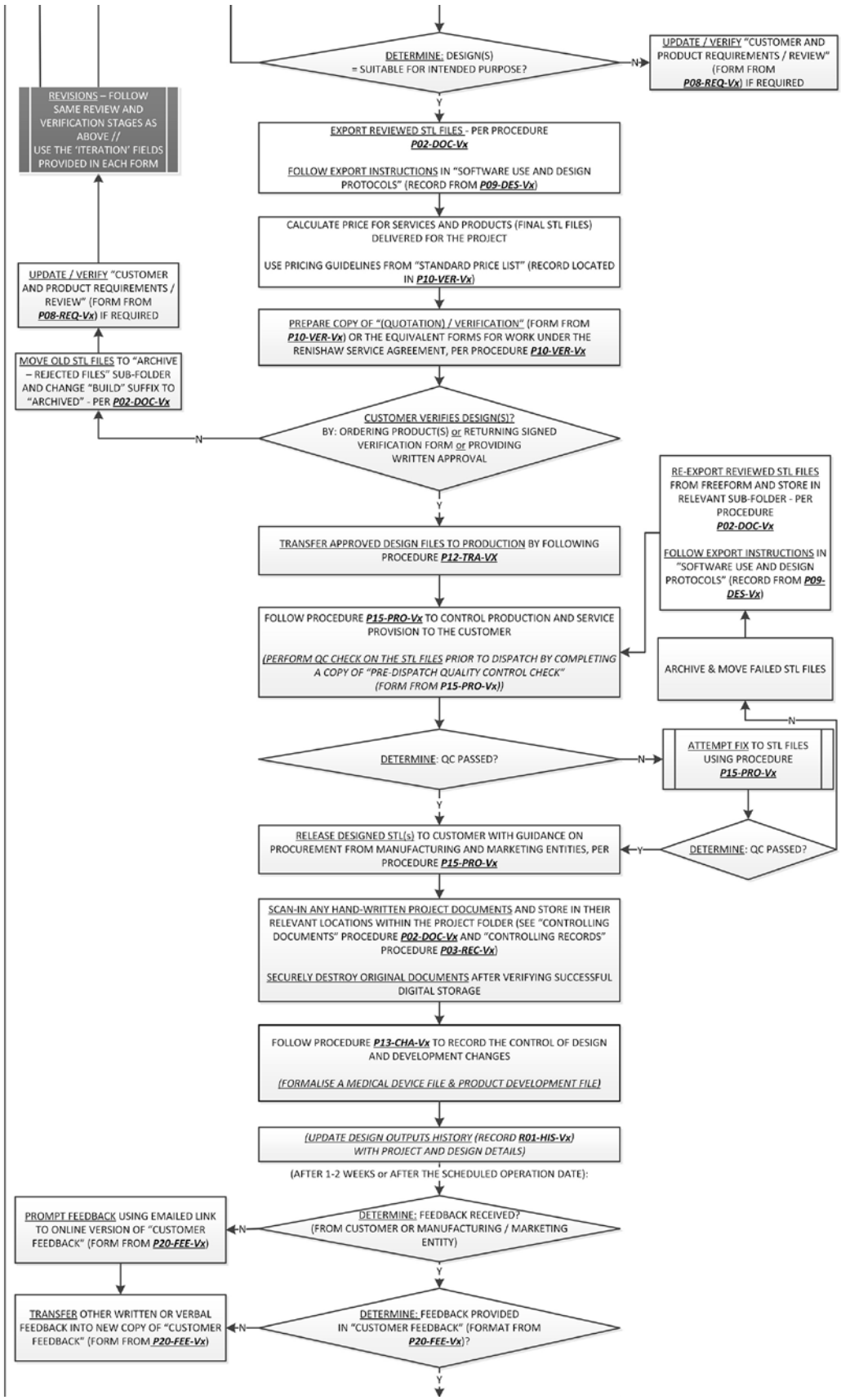


Figure 72 - Document Structure for Complete QMS


CONTACTED BY A NEW CUSTOMER, OR FOR A NEW ENQUIRY FROM AN EXISTING CUSTOMER
DETERMINE APPROPRIATE PROJECT MANAGER
ASSIGN PROJECT A UNIQUE ENQUIRY NUMBER ID PER (P17-IDE-Vx)
LOG KEY ENQUIRY DETAILS IN PROJECT TRACKER DATABASE (F02-DAT-Vx)
TRANSFER, EXPAND, & VERIFY ANY CUSTOMER-PROVIDED INPUTS, TO THE NEW COPY OF "CUSTOMER AND PRODUCT REQUIREMENTS / REVIEW" (FORM FROM P08-REQ-Vx)
PROMPT CUSTOMER FOR MISSING RELEVANT INFORMATION ON PRODUCT AND CUSTOMER REQUIREMENTS WHERE NEEDED
REVIEW REQUIREMENTS AND DETERMINE: CAPABLE OF MEETING PROJECT CONSTRAINTS? (PER PROCEDURE P08-REQ-Vx)
N
INFORM CUSTOMER & MARK PROJECT AS CLOSED IN PROJECT TRACKER DATABASE (F02-DAT-Vx)
Y
READ DATA INTO CT-PROCESSING SOFTWARE USING INSTRUCTIONS FROM "SOFTWARE USE AND DESIGN PROTOCOLS" (IN RECORD P09-DES-Vx)
DETERMINE: DATA IS SUITABLE FOR INTENDED PURPOSE?
N
INFORM CUSTOMER BY SENDING A COMPLETED COPY OF "CUSTOMER DATA REJECTION NOTICE" (FORM FROM P08-REQ-Vx)
DETERMINE: CUSTOMER HAS ALTERNATIVE DATASET?
Y
N
CUSTOMER APPROVES PROJECT CONTINUATION WITH RETURNED FORM?
Y
N
MARK PROJECT AS CLOSED
Y
SEGMENT DATA ACCORDING TO PRODUCT AND CUSTOMER REQUIREMENTS COLLECTED PREVIOUSLY - USE INSTRUCTIONS IN "SOFTWARE USE AND DESIGN PROTOCOLS" (RECORD FROM P09-DES-Vx)
EXPORT 3D RECONSTRUCTION(S) OF SCAN-DATA AS HIGH QUALITY STL FILE(S) // FOLLOW NAMING CONVENTIONS FROM "CONTROLLING DOCUMENTS" PROCEDURE (P02-DOC-Vx)
IN-PERSON / ONLINE MEETING FOR DIGITAL SURGICAL PLANNING – TO AGREE SPECIFIC REQUIREMENTS AND/OR PROPOSED SOLUTIONS
UPDATE & VERIFY "CUSTOMER AND PRODUCT REQUIREMENTS / REVIEW" (FORM FROM P08-REQ-Vx) IF REQUIRED
DESIGN PATIENT SPECIFIC DEVICE(S) PER PROCEDURES IN P09-DES-Vx – UP TO THE STAGE OF RESOLVING THE FORM, EXTENTS, AND MAJOR FEATURES
FOLLOW INSTRUCTIONS FROM "SOFTWARE USE AND DESIGN PROTOCOLS" (RECORD FROM P09-DES-Vx) / OR ADAPT THE CLOSEST APPLICABLE PROTOCOL OR PRINCIPLES
CONSULT PREVIOUS SOLUTIONS IN DESIGN OUTPUTS HISTORY (R01-HIS-Vx) IF REQUIRED
ALSO, CONSULT RELEVANT PROJECTS FEEDBACK
UPDATE & VERIFY "CUSTOMER AND PRODUCT REQUIREMENTS / REVIEW" (FORM FROM P08-REQ-Vx) IF REQUIRED
CREATE IMAGES FOR EMAIL-BASED INFORMAL VERIFICATION – LABEL AS DESCRIBED IN P02-DOC-Vx
ENSURE ANY NECESSARY PROTOCOL ADAPTATIONS ARE REVIEWED AT NEXT IMPLEMENTATION MEETING (FORM F01-MON-Vx)
CUSTOMER VERIFIES PROGRESS TO-DATE?
N
(WHERE NECESSARY) ENSURE PROCEDURE / FORM / RISK ASSESSMENT MODIFICATIONS ARE CONSIDERED AT NEXT IMPLEMENTATION MEETING (FORM F01-MON-Vx)
Y
DESIGN PATIENT SPECIFIC DEVICE(S) TO THE FINAL STAGE OF RESOLVING ALL MAJOR AND MINOR DETAILS
FOLLOW INSTRUCTIONS FROM "SOFTWARE USE AND DESIGN PROTOCOLS" (RECORD FROM P09-DES-Vx) / OR ADAPT THE CLOSEST APPLICABLE PROTOCOL
ENSURE PROTOCOL ADAPTATIONS ARE REVIEWED AT NEXT IMPLEMENTATION MEETING (FORM F01-MON-Vx)
N
PEER-REVIEW THE DESIGN(S) WITH ANOTHER QUALIFIED STAFF MEMBER BY COMPLETING A COPY OF "DESIGN AND DEVELOPMENT REVIEW" (FORM FROM P09-DES-Vx)


DETERMINE: DESIGN(S) = SUITABLE FOR INTENDED PURPOSE?
N
UPDATE / VERIFY "CUSTOMER AND PRODUCT REQUIREMENTS / REVIEW" (FORM FROM P08-REQ-Vx) IF REQUIRED
Y
EXPORT REVIEWED STL FILES - PER PROCEDURE P02-DOC-Vx
FOLLOW EXPORT INSTRUCTIONS IN "SOFTWARE USE AND DESIGN PROTOCOLS" (RECORD FROM P09-DES-Vx)
CALCULATE PRICE FOR SERVICES AND PRODUCTS (FINAL STL FILES) DELIVERED FOR THE PROJECT
USE PRICING GUIDELINES FROM "STANDARD PRICE LIST" (RECORD LOCATED IN P10-VER-Vx)
PREPARE COPY OF "(QUOTATION) / VERIFICATION" (FORM FROM P10-VER-Vx) OR THE EQUIVALENT FORMS FOR WORK UNDER THE RENISHAW SERVICE AGREEMENT, PER PROCEDURE P10-VER-Vx
CUSTOMER VERIFIES DESIGN(S)? BY: ORDERING PRODUCT(S) or RETURNING SIGNED VERIFICATION FORM or PROVIDING WRITTEN APPROVAL
N
MOVE OLD STL FILES TO "ARCHIVE – REJECTED FILES" SUB-FOLDER AND CHANGE "BUILD" SUFFIX TO "ARCHIVED" - PER P02-DOC-Vx
UPDATE / VERIFY "CUSTOMER AND PRODUCT REQUIREMENTS / REVIEW" (FORM FROM P08-REQ-Vx) IF REQUIRED
REVISIONS – FOLLOW SAME REVIEW AND VERIFICATION STAGES AS ABOVE // USE THE 'ITERATION' FIELDS PROVIDED IN EACH FORM
Y
TRANSFER APPROVED DESIGN FILES TO PRODUCTION BY FOLLOWING PROCEDURE P12-TRA-VX
FOLLOW PROCEDURE P15-PRO-Vx TO CONTROL PRODUCTION AND SERVICE PROVISION TO THE CUSTOMER
(PERFORM QC CHECK ON THE STL FILES PRIOR TO DISPATCH BY COMPLETING A COPY OF "PRE-DISPATCH QUALITY CONTROL CHECK" (FORM FROM P15-PRO-Vx))
RE-EXPORT REVIEWED STL FILES FROM FREEFORM AND STORE IN RELEVANT SUB-FOLDER - PER PROCEDURE P02-DOC-Vx
FOLLOW EXPORT INSTRUCTIONS IN "SOFTWARE USE AND DESIGN PROTOCOLS" (RECORD FROM P09-DES-Vx)
ARCHIVE & MOVE FAILED STL FILES
N
DETERMINE: QC PASSED?
N
ATTEMPT FIX TO STL FILES USING PROCEDURE P15-PRO-Vx
Y
DETERMINE: QC PASSED?
Y
RELEASE DESIGNED STL(s) TO CUSTOMER WITH GUIDANCE ON PROCUREMENT FROM MANUFACTURING AND MARKETING ENTITIES, PER PROCEDURE P15-PRO-Vx
SCAN-IN ANY HAND-WRITTEN PROJECT DOCUMENTS AND STORE IN THEIR RELEVANT LOCATIONS WITHIN THE PROJECT FOLDER (SEE "CONTROLLING DOCUMENTS" PROCEDURE P02-DOC-Vx AND "CONTROLLING RECORDS" PROCEDURE P03-REC-Vx)
SECURELY DESTROY ORIGINAL DOCUMENTS AFTER VERIFYING SUCCESSFUL DIGITAL STORAGE
FOLLOW PROCEDURE P13-CHA-Vx TO RECORD THE CONTROL OF DESIGN AND DEVELOPMENT CHANGES
(FORMALISE A MEDICAL DEVICE FILE & PRODUCT DEVELOPMENT FILE)
(UPDATE DESIGN OUTPUTS HISTORY (RECORD R01-HIS-Vx) WITH PROJECT AND DESIGN DETAILS)
(AFTER 1-2 WEEKS or AFTER THE SCHEDULED OPERATION DATE):
DETERMINE: FEEDBACK RECEIVED? (FROM CUSTOMER OR MANUFACTURING / MARKETING ENTITY)
N
PROMPT FEEDBACK USING EMAILED LINK TO ONLINE VERSION OF "CUSTOMER FEEDBACK" (FORM FROM P20-FEE-Vx)
Y
DETERMINE: FEEDBACK PROVIDED IN "CUSTOMER FEEDBACK" (FORMAT FROM P20-FEE-Vx)?
N
TRANSFER OTHER WRITTEN OR VERBAL FEEDBACK INTO NEW COPY OF "CUSTOMER FEEDBACK" (FORM FROM P20-FEE-Vx)
Y

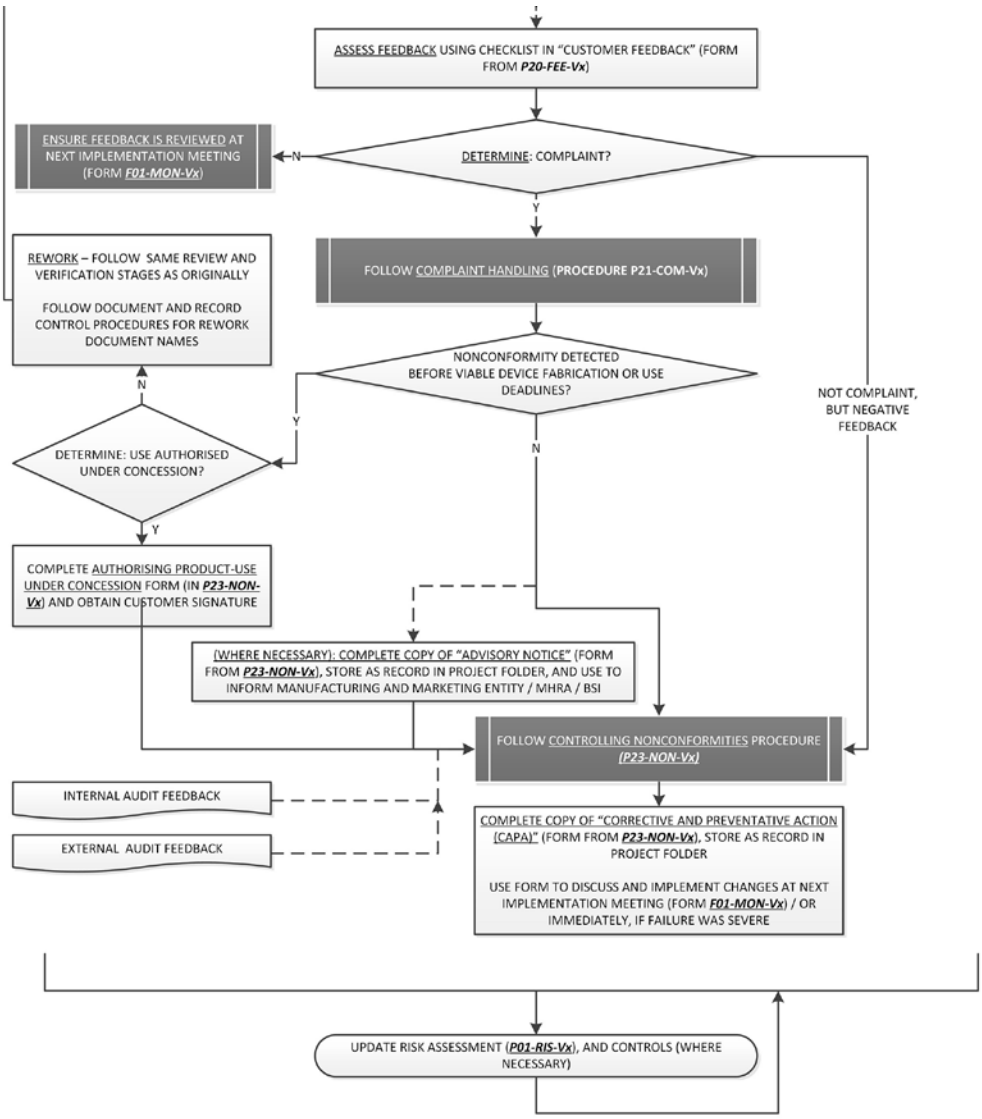


Figure 73 - QMS Design Control Workflow Developed for Institute

6.2.2. Results: Relevant and Generalisable QMS Components

Table 7 describes which QMS procedures and elements were deemed to be independent-enough of their organisational context for generalisation and translation across to the design intervention. The methods by which the functions were intended to be realised in the framework were specified in the final column. This acted, in effect, as a partial contribution to the specification for the creation of the intervention itself.

Table 7 – Generalisable Aspects of QMS Functionality

QMS Procedure / Element	Translatable / Generalisable Functionality for Intervention?	Aiming to Achieve Translation by…
Quality Manual	N – Because context dependent, and not a practical document.	N/A
Ensuring Management Responsibility	N – Because highly dependent on the particular organisation for compliant introduction.	N/A
Assessing Risk	Partially.	Providing a structure for the design and development process to adapt, then analyse for risks in their particular organisation.
Determining Staff Competence and Training	N – Too dependent on context.	N/A
Controlling Documents	Partially.	Providing a document revision control space, and clear identification in the footer.
Controlling Records	N – Because highly dependent on specific IT infrastructure of individual organisation.	N/A
Determining Work Environment and Contamination Control Requirements	N – Too dependent on context.	N/A
Communicating With Customers and Managing Projects	Y.	Defining a clear order and discrete sections for the design process structure; to encourage communicating in finite bursts with clear goals. Encouraging communication with, and mandating verification by the operating surgeon themselves. Generating a high fidelity requirements list up-front; to aim for minimal disruptions to the structured process.
Determining Infrastructure Requirements	N – Too dependent on context.	N/A

Determining Customer and Product Requirements	Y – Almost fully.	Prompting requirements gathering for all relevant fields – based on the results of this research.
Designing and Developing Product	Partially.	Avoiding generalising the software use protocols; to maintain flexibility across tools. Providing evidenced prompts for detailed design decisions in complex craniofacial reconstruction. Facilitating design peer-review.
Verifying Product	Y.	Structuring the workflow to only permit the progression of verified designs.
Validating Design and Development Process	Partially.	Recording changes to requirements and outputs. Encouraging recording of detailed feedback. Statistical synthesis and process evaluation is highly-specific to the organisation.
Transferring Developed Designs to Production	N – software-specific.	N/A
Controlling Design and Development Changes	Partially.	Recording changes to requirements and outputs; which can be referenced by a full design file.
Purchasing Product	N – Too dependent on context.	N/A
Controlling Production and Service Provision to Customer	N - Too dependent on context and tools (for QC check).	N/A
Identification of Product	Partially.	Prompting for a clear statement of the project ID at the outset.
Validating Production and Service Provision	N – Too dependent on context.	N/A
Traceability of Product Outputs to Design Inputs	N – Too dependent on context.	N/A

Controlling Monitoring and Measuring Equipment	N – Too dependent on specific infrastructure.	N/A
Feedback	Partially.	Prompting for feedback after key events and timeframes.
Complaint Handling	Partially.	Prompting the identification of negative feedback qualifying as complaints. Complaints procedure is context-dependent.
Internal Audit	N – Too dependent on specific, tailored QMS.	N/A
Controlling Nonconformities	Partially.	Precluding project progress until mini-CAPA processes have been completed and approved.

6.3. Investigation B3 Results – Specific & Evidenced Design Considerations

Five complex design case studies gradually became available for study – either through project managing and designing, or as observer and peer-reviewer. These meningioma and fibrous dysplasia cases were similar in diagnosis and location, but still demonstrated a sufficient diversity for the generation of new design considerations in each instance.

6.3.1. Results: Specific & Evidenced Design Considerations from Literature

Table 8 collates and summarises the complex craniofacial reconstruction design considerations sourced from existing literature; identified by explicit statement or clear inference. Each included consideration was highlighted by three or more researchers.

Table 8 - Collated and Consolidated Design Considerations from Literature

ID	Design considerations from literature	Considered in
	CAD / AM / CAM justification:	
A	Consider **overall treatment cost Vs. up-front devices cost.** *High upfront costs can be offset by savings from reduced surgery time, hospital stays, and revision surgeries.*	(Manrique et al., 2015), (Eolchiyan, 2014), (Singare et al., 2009), (Stieglitz et al., 2015), (Lethaus et al., 2014)
B	Consider the CAD / AM / CAM approach when there is a desire to **improve the accuracy of the cosmetic outcome.** *Relative to conventional methods.*	(Marbacher et al., 2011), (Rudman et al., 2011), (Gerbino et al., 2013), (Alonso-Rodriguez et al., 2015), (Goodson et al., 2012), (Eolchiyan, 2014), (Scolozzi et al., 2007), (Manrique et al., 2015), (Stoor et al., 2014), (Rotaru et al., 2015), (Jalbert et al., 2014), (Rosen et al., 2008), (Patel and Duckworth, 2015), (Pritz and Burgett, 2009), (Mertens et al., 2013), (Derand et al., 2012), (Salmi et al., 2012), (Li et al., 2013b), (Jardini et al., 2014)
C	Consider the CAD / AM / CAM approach when the defective anatomy is **large and / or geometrically complex.**	(Marbacher et al., 2011), (Kim et al., 2009), (Watson et al., 2014), (Manrique et al., 2015), (Rudman et al., 2011), (Gerbino et al., 2013), (Alonso-Rodriguez et al., 2015), (Jalbert et al., 2014), (Patel and Duckworth, 2015), (Pritz and Burgett, 2009), (Singare et al., 2009)
D	Consider the CAD / AM / CAM approach for **reducing operative time.**	(Kim et al., 2009), (Manrique et al., 2015), (Stoor et al., 2014), (Rudman et al., 2011), (Gerbino et al., 2013), (Goodson et al., 2012), (Adetayo et al., 2015), (Eolchiyan, 2014), (Scolozzi et al., 2007), (Rotaru et al., 2015), (Jalbert et al., 2014), (Guevara-Rojas et al., 2014), (Rosen et al., 2008), (Sunderland et al., 2015), (Mertens et al., 2013), (Derand et al., 2012), (Singare et al., 2009), (Salmi et al., 2012), (Li et al., 2013b), (Jardini et al., 2014)
E	Consider the CAD / AM / CAM approach to produce implants with a **more accurate fit.**	(Kim et al., 2009), (Goodson et al., 2012), (Guevara-Rojas et al., 2014), (Thien et al., 2015), (Derand et al., 2012), (Singare et al., 2009)

F	Consider the CAD / AM / CAM approach to **overcome the downsides of autologous reconstruction.** *Including: donor site morbidity, longer surgeries, compromised aesthetics, high dependency on surgeon skill, unpredictable resorption, and limited bone graft availability.*	(Camarini et al., 2011), (Watson et al., 2014), (Manrique et al., 2015), (Gerbino et al., 2013), (Alonso-Rodriguez et al., 2015), (Scolozzi, 2012), (Rotaru et al., 2015), (Jalbert et al., 2014), (Guevara-Rojas et al., 2014), (Rosen et al., 2008), (Pritz and Burgett, 2009), (Sunderland et al., 2015), (Lethaus et al., 2014), (Yetiser et al., 2006), (Klammert et al., 2010), (Jardini et al., 2014), (O'Reilly et al., 2015)
G	Consider CAD / AM / CAM methods when a **single-step** excision and reconstruction procedure is required.	(Camarini et al., 2011), (Gerbino et al., 2013), (Alonso-Rodriguez et al., 2015), (Eolchiyan, 2014), (Jalbert et al., 2014), (Rosen et al., 2008)
	Material choice:	
H	Consider PEEK if there is a preference for **standard mini-plate fixation**.	(Marbacher et al., 2011), (Kim et al., 2009), (Camarini et al., 2011), (Gerbino et al., 2013), (Scolozzi, 2012), (Eolchiyan, 2014), (Jalbert et al., 2014)
I	Consider **PEEK** for easy **intra-operative modifications.**	(Kim et al., 2009), (Camarini et al., 2011), (Manrique et al., 2015), (Rudman et al., 2011), (Gerbino et al., 2013), (Alonso-Rodriguez et al., 2015), (Adetayo et al., 2015), (Eolchiyan, 2014), (O'Reilly et al., 2015)
J	Consider **PEEK** for an alloplastic material with mechanical properties (and thickness) which are **similar to cortical bone.**	(Camarini et al., 2011), (Gerbino et al., 2013), (Alonso-Rodriguez et al., 2015), (Lethaus et al., 2011), (Jalbert et al., 2014), (Lethaus et al., 2012b)
K	Consider **PEEK** when there is a need for **radiolucency** (for radiotherapy or post-operative imaging).	(Camarini et al., 2011), (Manrique et al., 2015), (Gerbino et al., 2013), (Scolozzi et al., 2007), (Jalbert et al., 2014), (Thien et al., 2015), (Rudman et al., 2011), (Eolchiyan, 2014)
L	Consider avoiding **titanium** where there might be concerns with **thermal conductivity or sensitivity.**	(Lethaus et al., 2014), (Thien et al., 2015), (Eufinger et al., 2007)
	Strategy:	
M	Consider the use of **surgical guides to accurately translate the digital plan** into theatre. *As a driver for CAD / AM / CAM use.*	(Gerbino et al., 2013), (Alonso-Rodriguez et al., 2015), (Eolchiyan, 2014), (Li et al., 2013b)
N	Consider **navigation** for excision guidance and implant placement in place of guides (where available).	(Jalbert et al., 2014), (Guevara-Rojas et al., 2014), (Rosen et al., 2008), (Mertens et al., 2013)

O	Consider basing implant designs on **mirrored healthy anatomy** wherever possible.	(Watson et al., 2014), (Manrique et al., 2015), (Stoor et al., 2014), (Rudman et al., 2011), (Alonso-Rodriguez et al., 2015), (Scolozzi, 2012), (Jalbert et al., 2014), (Marbacher et al., 2011), (Mertens et al., 2013), (Singare et al., 2009), (Pfaff and Steinbacher, 2016), (Li et al., 2013b), (D'Urso et al., 2000), (Pritz and Burgett, 2009), (Rotaru et al., 2015), (Eolchiyan, 2014)
P	Consider reconstruction-site **soft tissue coverage** to minimise skin tension and risk of implant exposure. *Could be via skin expanders, grafts, reducing implant volume or compromising ideal contours.*	(Marbacher et al., 2011), (Kim et al., 2009), (Manrique et al., 2015), (O'Reilly et al., 2015)
Q	Consider **soft tissue contours** in addition to bone. *Could involve mirroring soft tissues with hard when designing implant contours.*	(Marbacher et al., 2011), (Guevara-Rojas et al., 2014), (Pfaff and Steinbacher, 2016), (Li et al., 2013b)
R	Consider **bone cement** for adjusting contours or margins.	(Kim et al., 2009), (Eolchiyan, 2014), (Rosen et al., 2008)
	Detailed modelling:	
S	Consider adding **holes or a mesh pattern** into the main implant area. *To: provide a foundation for securing the dura and temporalis muscle, preventing epidural hematoma, encouraging better tissue integration and cell growth, reducing weight, and lowering temperature conductivity.*	(Gerbino et al., 2013), (Eolchiyan, 2014), (Eufinger et al., 1998), (Singare et al., 2009), (Salmi et al., 2012), (Rotaru et al., 2015)

6.3.2. Case Study [10] Results: Detailed Design Decisions

An anatomical model was requested from the institute by the surgeon – in addition to images showing the institute design engineer's interpretation of the tumour via manual segmentation. The model, images, and raw scan data were used at an interdisciplinary clinical meeting to determine the surgical plan and excision margins – which were drawn on to the model in pen. At the institute, the engineers transferred the agreed margins to the virtual model using the haptic design software, deleted the anatomy inside this boundary, and protected the resulting virtual model against

further modifications by setting it as a “buck” component. This interpretation was verified by the surgeon via emailed images.

As a basis for accurate implant design, the contralateral healthy anatomy was mirrored to reconstruct the defect in the virtual environment. The resulting shapes were smoothed and blended into the surrounding remaining original anatomy. Material was layered-on to this foundation with a thickness of 0.8mm – indicating the extents of the final titanium implant. As shown in Figure 74, the implant was formed of two components which overlaid the excision margin in order to ensure good support around the edges. Two non-interfacing components were judged to be necessary to permit insertion from two separate directions. The implant replaced the outer bony surface of the defects – not the full bone thickness. Fixation tabs for the orbital component were brought out to the rim – to permit screwdriver access. Fixation tabs for the temporal component were extended – with a view towards permitting successful fixation even in the event of a larger-than-anticipated excision. This would have been necessary if the lesion had grown significantly since the scan was undertaken or if the extent of tissue involvement was difficult to judge pre-operatively. Fixation holes of 1.7mm diameter were added (intended for 1.5mm screws). Fluid transfer holes of 2mm diameter were spaced arbitrarily across the orbital component – but kept away from the implant edge. The implant designs were verified by the prescribing surgeon via emailed images and a 3D PDF - and then sent for fabrication. A satin surface finish was requested – as well as post-fabrication reaming for the screw holes.

Prior to surgery, a medical model of the digitally-planned excision was fabricated, and delivered with the finished implant components for sterilisation at the hospital.

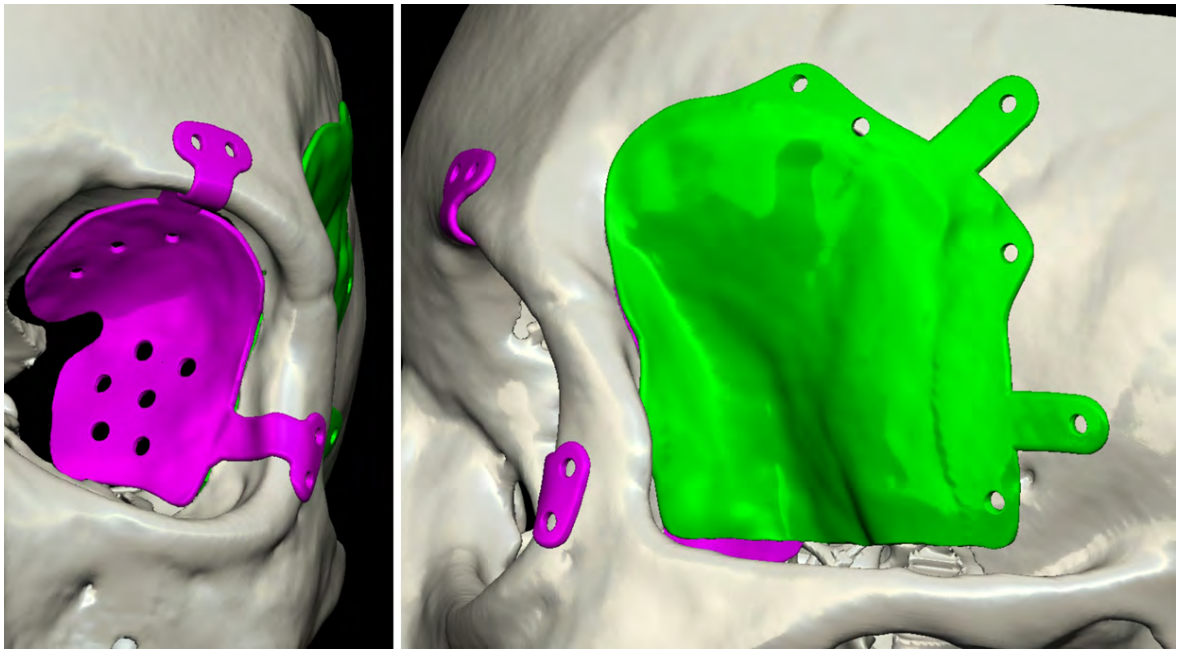


Figure 74 - Implant Designs for Case Study 10

6.3.3. Case Study [10] Results: Clinical Outcomes

The tumour excision was performed, and the implants placed successfully. No significant modifications to the pre-operative digital or clinical surgical plans were required.

This case had a four year follow-up at the time of writing. The patient's exophthalmos was reduced by 4mm – though was not wholly eliminated. Post-operatively there was a black spot in the patient's visual field at the far left of their gaze – this persists. All other pre-operative symptoms were resolved – with a good initial aesthetic result. Three years-on from the procedure, the patient complained of soft tissue hollowing around the temporal implant region – this was corrected by transferring fat grafts into the area.

6.3.4. Case Study [10] Results: Device Cost

The total cost of the digital surgical planning, anatomical models, and patient-specific implants to the NHS was £1988.00 - excluding Value Added Tax (VAT).

6.3.5. Case Study [10] Results: New Design Considerations

Subjective evaluation by the surgeon deemed the single-piece orbital implant design to have resulted in some difficulty with positioning the device intra-orbitally. The surgeon judged a clear and noticeable reduction in surgery duration versus previous cases undertaken with conventional or semi-digital methods. However, quite obviously there remain no direct comparisons for the same patients.

The surgical team highlighted three tentative hypotheses for consideration in subsequent cases: the single-piece design of the orbital component led to the black spot in the visual field (by preventing perfect placement); the on-lay orbital component design caused residual (minimal) post-operative exophthalmos by reducing the orbital volume; and exaggerated fixation tab lengths to permit larger excisions than planned are a worthy inclusion (albeit not required in this case).

6.3.6. Case Study [11] Results: Detailed Design Decisions

An identical method was applied to this case as for patient 1 – up to and including the stage of reconstructing the planned excision by mirroring healthy contralateral anatomy on the virtual model. This time, as shown by Figure 75 a three-component implant design was modelled (0.5mm thickness) – on the basis of being in-laid into the defect margin. The three component design was selected with the aims of addressing the orbital component-placement issue from case 1, and to make the overall implant success less dependent on the success of each individual component. The in-lay design was selected to target the orbital volume hypothesis from case 10. A diamond mesh pattern was embossed into the implant components with a speculative aim of improving any future radiotherapy delivery - in case of disease recurrence. Countersinks were designed-in at the points of fixation. Again, the implant design was verified by the prescribing surgeon – with the same post-fabrication finishing processes requested.

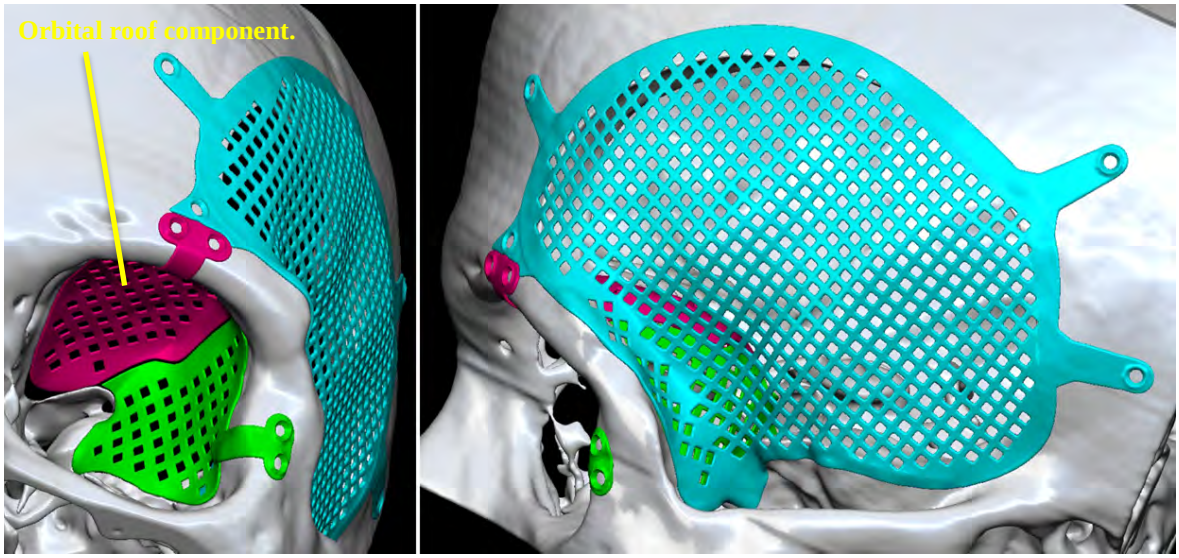


Figure 75 - Implant Designs for Case 11

6.3.7. Case Study [11]: Results: Clinical Outcomes

The tumour excision was performed – mostly according to the pre-operative clinical and digital plan with one key exception. Excision of bone from the posterior orbit was more difficult than expected – as well as being less critical than considered during the plan. The orbital roof component required intra-operative trimming in order to fit the smaller-than-anticipated defect. This slightly reduced the surgery-duration benefit of using the digital approach, and proved to be a difficult task for the available tools because of the hardness of the implant material.

This case had a three year follow-up at the time of writing. The patient's exophthalmos was reduced –again, not wholly eliminated, but demonstrating a better reduction than for patient 10. Post-operatively there was one further issue - seroma of the soft tissues – which resolved spontaneously over eight weeks. All other pre-operative symptoms were resolved – with a good aesthetic result. There has been no disease recurrence and therefore no need for radiotherapy.

6.3.8. Case Study [11] Results: Device Cost

The total cost of the digital surgical planning, anatomical models, and patient-specific implants to the NHS was £2590.00 - excluding VAT.

6.3.9. Case Study [11] Results: New Design Considerations

Subjective evaluation by the surgeon deemed splitting the orbital reconstruction into two components to have improved the manoeuvrability of the lateral component relative to case 10. Aside from having to trim the posterior aspect of the orbital roof component, some difficulty was noted with achieving the butt-joint interface between the two orbital components. Independent fixation for the components was highlighted as being of particular importance to minimise the impact of these unexpected challenges – tiny positioning compensations could be made. Again, the surgeon judged a clear and noticeable reduction in surgery duration versus previous cases undertaken with conventional or semi-digital methods – though not as significant a reduction as would be possible without the noted issues.

The surgical team highlighted three tentative hypotheses for consideration in subsequent cases: a lack of built-in margin flexibility reduced the impact from the digital workflow by forcing time-consuming implant modifications; the missing bony surfaces did not need to be replaced entirely to achieve the desired functional results; and designing an in-lay implant rather than an on-lay implant did not fully solve the patient's exophthalmos – so reconstructing a smaller portion of orbital roof may achieve full orbital volume correction.

6.3.10. Case Study [12] Results: Detailed Design Decisions

An identical method was applied to this case as for patients 10 and 11 – up to and including the stage of reconstructing the planned excision by mirroring healthy contralateral anatomy on the virtual model. This time, as shown by Figure 76, the excision margin included the critical aim of avoiding the frontal sinus. As such, patient specific cutting guides were designed after highlighting the frontal sinus volume in the patient's scan data and overlaying it onto the digital plan. The guides were realised by layering a 2.5mm thickness of material onto the foundation of the patient's original anatomy. Care was taken to model a cutting ledge (around the

outside edge of the guide) which was perpendicular to the sinus border - in case of being used to guide the saw directly. Holes were added to provide the option of screw fixation. A two-part guide design was deemed necessary in order to fit onto the anatomy without being obstructed by the undercuts of the orbit and sphenoid. The two parts were designed to fit together with a notch feature – aiming to provide confidence in achieving correct positioning. Material was removed from the middle of the frontal guide – to accommodate potential further bone growth since the initial scan. A small handle was modelled for this component – with a view towards providing stability during use.

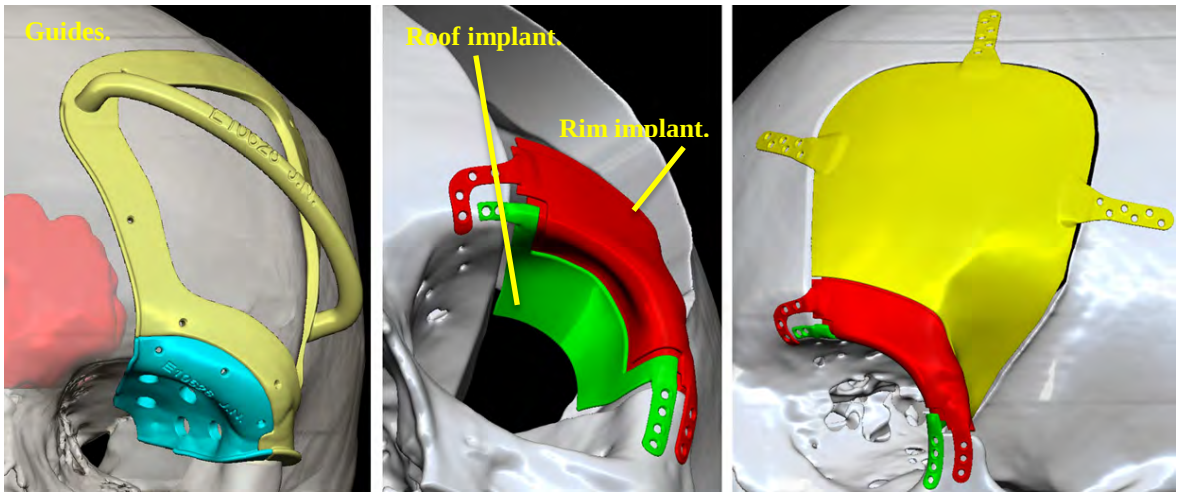


Figure 76 - Guides and Implants Designs for Case 12

The implant design (0.7mm thickness) consisted of three components with functional independence and both margin and fixation flexibility. A 1mm gap was deliberately left between the implant component edges and the defect edge – aiming to build-in scope for sub-optimal excision and implant location relative to the ideal scenario in the plan. Similarly, a 0.5mm gap was inserted between the implant components for the same reason. The orbital rim implant component incorporated recessed ledges running behind the intra-component gaps – targeting support of the other components without compromising flexibility. Long fixation tabs were used as in the previous cases. With the aim of addressing the residual exophthalmos from case 11, the orbital roof component extended only half-way posteriorly.

Identical pre-surgery verification, fabrication, and sterilisation actions were undertaken as for case 10 and 11 – with the exception of requesting a polished finish for the rim and orbital roof implant components.

6.3.11. Case Study [12] Results: Clinical Outcomes

The frontal guide was used as a template for drawing around (Figure 77) – as opposed to being used to guide the saw directly. The orbital guide was used to guide the saw directly – but from the brain-side of the already partially-completed excision. The frontal sinus was successfully avoided. All of the components performed exactly as planned – and the final implants were fixed quickly and easily (Figure 78).

This case had a two year follow-up at the time of writing. All pre-operative symptoms were fully relieved – including exophthalmos. Some post-operative ptosis of the temporalis muscle was noted by the surgeon. Additionally, left upper lid dermatochalasis was present – but no procedures were taken to correct this.

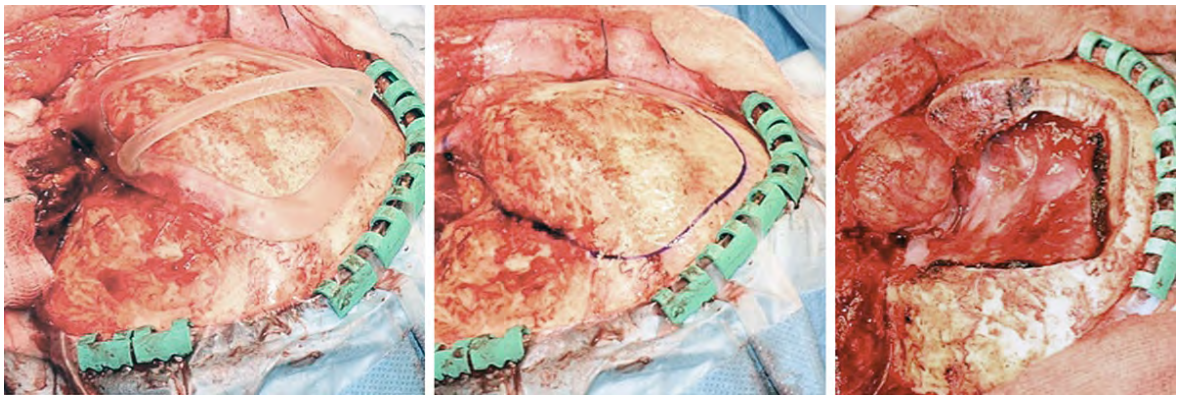


Figure 77 - Guides for Case 12 In-Use

6.3.12. Case Study [12] Results: Device Cost

The total cost of the digital surgical planning, anatomical models, patient-specific guides, and patient-specific implants to the NHS was £2828.00 - excluding VAT.

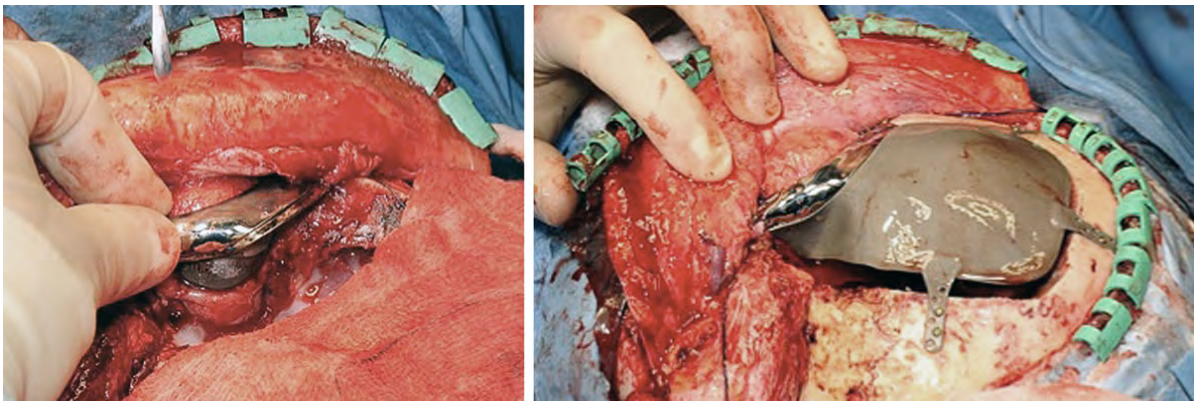


Figure 78 - Implants for Case 12 In-Use

6.3.13. Case Study [12] Results: New Design Considerations

Subjective evaluation by the surgeon centred on the ease of implant insertion – following guided excision. This achieved an accurate translation of the plan into theatre. The interfacing-but-independent implant components anticipated all reasonable plan deviations (though none were tested here). Again, the surgeon judged a clear and noticeable reduction in surgery duration because of this fully-digital method.

The surgical team highlighted four tentative hypotheses for consideration in subsequent cases: a lack of holes in the temporal region of the frontal-cranial implant prevented suturing of the temporalis muscle which led to minor ptosis; good fit (Figure 79) and extremely quick fixation of the implant components was achieved by using guides – which should be used to translate virtually planned cuts wherever possible; implant component functional, fixation, and margin flexibility provided confidence in anticipating possible plan deviations and should be employed wherever possible; an in-lay design and restricting the posterior extension of the orbital roof component to the orbit "equator" contributed to a full resolution of exopthalmos in this case.

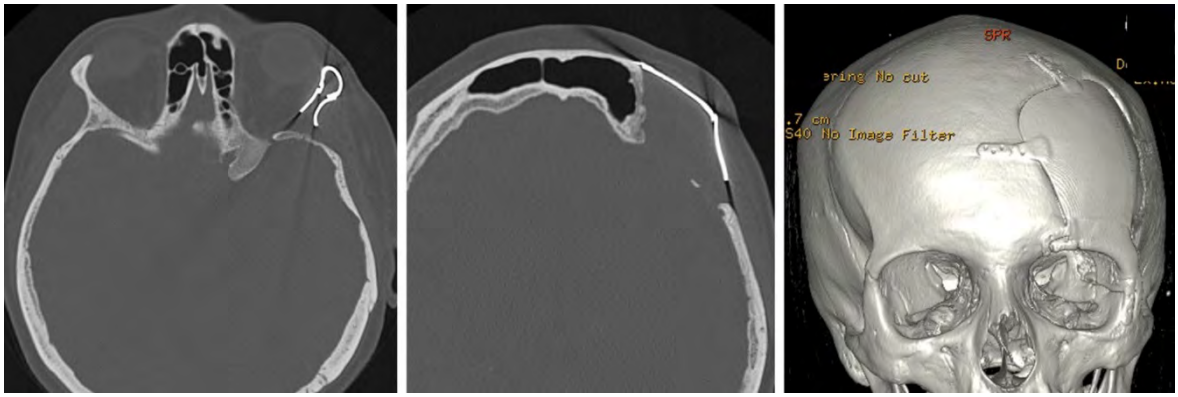


Figure 79 - Post-Operative CT Scan of Case 12

6.3.14. <u>Case Study [13] Results: Detailed Design Decisions</u>

Identical technical procedures were undertaken as in cases 10-12 to design and fabricate devices. As shown in Figure 80, recommendations from those cases were followed: multi-part guides were designed to translate the planned excision margins into theatre; the implants (0.6mm thickness) were designed to leave a 1.5mm gap to the defect edge to address fixation and margin flexibility; the orbital implant components incorporated deliberate gaps so as to remain functionally independent; all components were in-lay designs – with the orbital parts extending only half-way posteriorly; fixation tabs were extended to accommodate larger-than-anticipated excisions; and a mesh pattern was applied to pre-empt potential radiotherapy and provide suture retention options for supporting the temporalis. Uniquely to previous cases, the guides also translated the cutting locations for osteotomising a portion of the lateral orbital rim – which was temporarily removed to improve access. The orbital implant component fixation arms were lengthened to serve a secondary function – fixing the osteotomised bone flap back in its original position. A satin finish was requested by the surgeon for the metal implants – and the same pre-theatre routine undertaken as described for other cases.

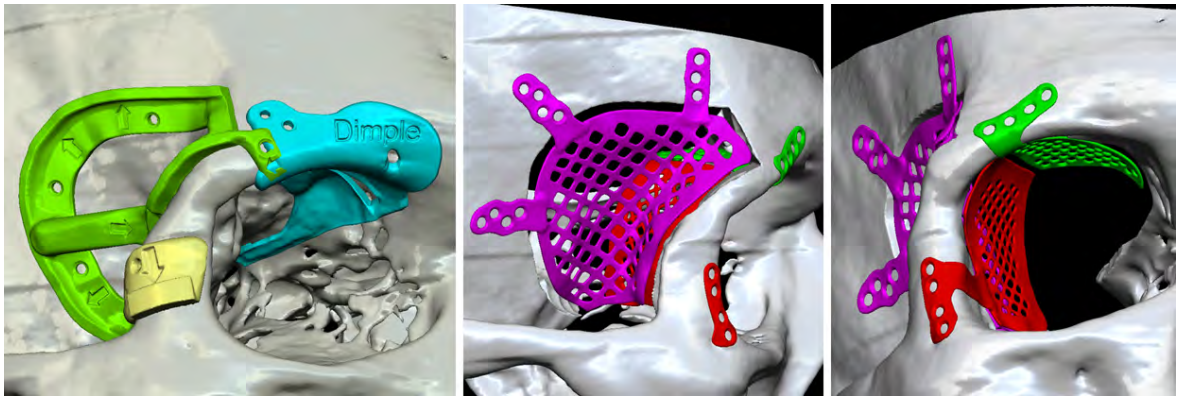


Figure 80 - Guides and Implants Designs for Case 13

6.3.15. Case Study [13] Results: Clinical Outcomes

The lesion was successfully excised – and the lateral rim bone flap replaced. All components fitted and functioned exactly as planned. No intra-operative complications were experienced.

This case had a 22-month follow-up at the time of writing. All pre-operative symptoms were fully relieved. The patient was concerned with palpability of fixation plates used for an extra craniotomy performed for improved access (but not involved in the craniofacial planning). However, no revision procedures were necessary. There has been no disease recurrence – and so no post-operative radiotherapy.

6.3.16. Case Study [13] Results: Device Cost

The total cost of the digital surgical planning, anatomical models, patient-specific guides, and patient-specific implants to the NHS was £2890.00 - excluding VAT.

6.3.17. Case Study [13] Results: New Design Considerations

Subjective evaluation by the surgeon noted the particular importance of the guides in this case because of the morphological complexity of the affected area. The surgical team highlighted how this case offered a validation of the considerations taken forward from previous cases.

6.3.18. Case Study [14] Results: Detailed Design Decisions

As noted previously, this case (Figure 77) was designed for fabrication from PEEK. Otherwise, identical technical procedures were undertaken as in cases 1-4 to design and fabricate guides and implants. As with case 13, a guide was designed to temporarily osteotomise a bone segment in order to improve access – in this case, from the zygoma. A temporal guide component included small tabs to indicate areas of bone planned for burring away. The PEEK implant was split into two components – one reconstructing the lateral orbit and the temporal bone, and the other reconstructing the potential excision of the glenoid fossa. Generally, an in-lay approach was used across both components - though tabs were designed into the temporal device – to brace against the residual cranium in the areas where guided burring was planned. This was surgeon-preference for a bracing tab-style fixation – rather than relying on mini-plates, which caused concern about implant-brain interference in the event of traumatic impact. 2.1mm diameter holes were added into the tabs for fixation with 2mm screws. Unlike the titanium implants, the PEEK was of a 3-7mm varied thickness to take advantage of the material's lower density and contribute to reconstructing the full bone volume. There were no significant modelling or design freedom restrictions to accommodate CAM limitations versus AM. This can be attributed to using five-axis milling, and the geometry of the implant being naturally sympathetic to this process.

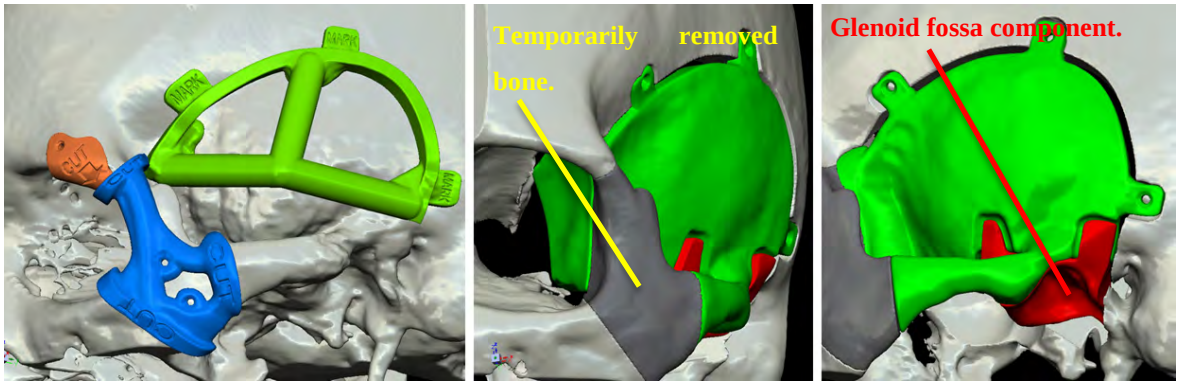


Figure 81 - Guides and Implants Designs for Case 14

6.3.19. Case Study [14] Results: Clinical Outcomes

In theatre, the TMJ was not resected after being judged as too high-risk. The glenoid fossa implant component was left-out without affecting the performance of the temporal component. The bone flap was osteotomised for access and replaced successfully using mini-plates.

This case had a one year follow-up at the time of writing. All pre-operative symptoms were relieved though there were significant post-operative complications. The patient experienced expressive dysphasia for 24 hours post-operatively. The clinical team hypothesised ear and brain involvement as the cause – exacerbated by the ear being exposed to the surrounding environment. Additionally, there was a superficial wound infection for which the patient was taken to theatre for drainage and washing of the wound. The decision was taken to leave the alloplastic reconstruction in place and instigate a long-term antibiotic routine. This was successful and negated secondary reconstruction surgery.

6.3.20. Case Study [14] Results: Device Cost

The total cost of the digital surgical planning, anatomical models, patient-specific guides, and patient-specific implants to the NHS was £5644.00 - excluding VAT.

6.3.21. Case Study [14] Results: New Design Considerations

Subjective evaluation by the surgeon highlighted the further validation of the digital process and evolving design considerations provided by this case. The surgical team highlighted two tentative hypotheses for consideration in future cases: choosing PEEK for this category of cases has no demonstrated downside (in this one example) aside from an increase in cost; and using a PEEK-tab fixation model (with guided bone burring) could offer a more stable fixation than relying exclusively on mini-plates.

6.4. Investigation B3 Results – New Design Considerations – Results Analysis

The case studies corroborated design considerations B, C, D, E, F, G, K, M, O, and S from Table 8 – and introduced nine new considerations as shown in Table 9 below.

Table 9 - Collated and Consolidated New Design Considerations from Case Studies 10-14

New design considerations from case studies:
Consider multi-part implant designs – particularly for the lateral orbital wall and orbital roof. *To enable easy manipulation of the components into the correct (pre-planned) positions.*
Consider robust independent fixation solutions for each implant component. *To build-in functional independence in case one component is omitted from the final reconstruction.*
Consider exaggerated fixation tab lengths. *To provide margin flexibility when excisions are larger than planned.*
Consider designing-in a deliberate gap between the planned margin and the main implant body. *To provide margin flexibility when excisions are smaller than planned.*
Consider designing-in a deliberate gap between interfacing implant components. *To provide positioning flexibility and avoid chain-tolerance errors in the event that one or more components is fixed sub-optimally.*
Consider using in-lay orbital implant designs. *To lower the risk of reducing the orbital volume.*
Consider restricting orbital roof component extents to the anterior half of the globe. *To lower the risk of reducing the orbital volume.*
Consider including fixation tabs in PEEK implant designs – with guided burring of residual bone at the interface points. *To offer a more stable fixation option – or when preferred over mini-plates.*
Consider using AM titanium where specific PEEK properties are not required. *To achieve similar benefits at lower cost.*

Design considerations from the literature in, and from the new primary data in Table 9, together demonstrate a clear progression from macro to micro considerations for successfully designing and using state-of-the-art implants. Generally, considerations from the literature address contextual and materials issues well – and are supported by the new experiences described in this study. Specific design detailing issues are

covered in considerably greater detail by the case studies – though with some key limitations as evaluated in the discussion Chapter.

Investigation B3 has extracted 19 design considerations for complex craniofacial implants from secondary sources, and 9 unique design considerations from new case series data.

6.5. Investigation B4 Results – Constructing a Design Intervention

The requirements and recommendations from results sub-Chapters 6.1, 6.2, 6.3, and 6.4 were collated and formatted into a design intervention document (full-size, populated version in Appendix 7). It was intended for use by in-house hospital designers, or by those located externally. It was specifically targeted towards the design process for devices used in complex craniofacial reconstruction. It aimed to be useful across any software tools used for segmenting CT data and modelling patient-specific devices. Sub-Chapter 6.5.1 presents an annotated summary of the design intervention document - from Figure 83 to Figure 96.

6.5.1. Results: Intervention Prototype

The prototype was a 16 page paper document containing numerous fields for consideration and population by whoever was acting as the project designer. The fields spanned 6 main stages (Figure 82): project set-up; device requirements gathering; specific design considerations for complex craniofacial reconstruction; design review; design verification; and feedback gathering (with a prompt to publish wherever possible).

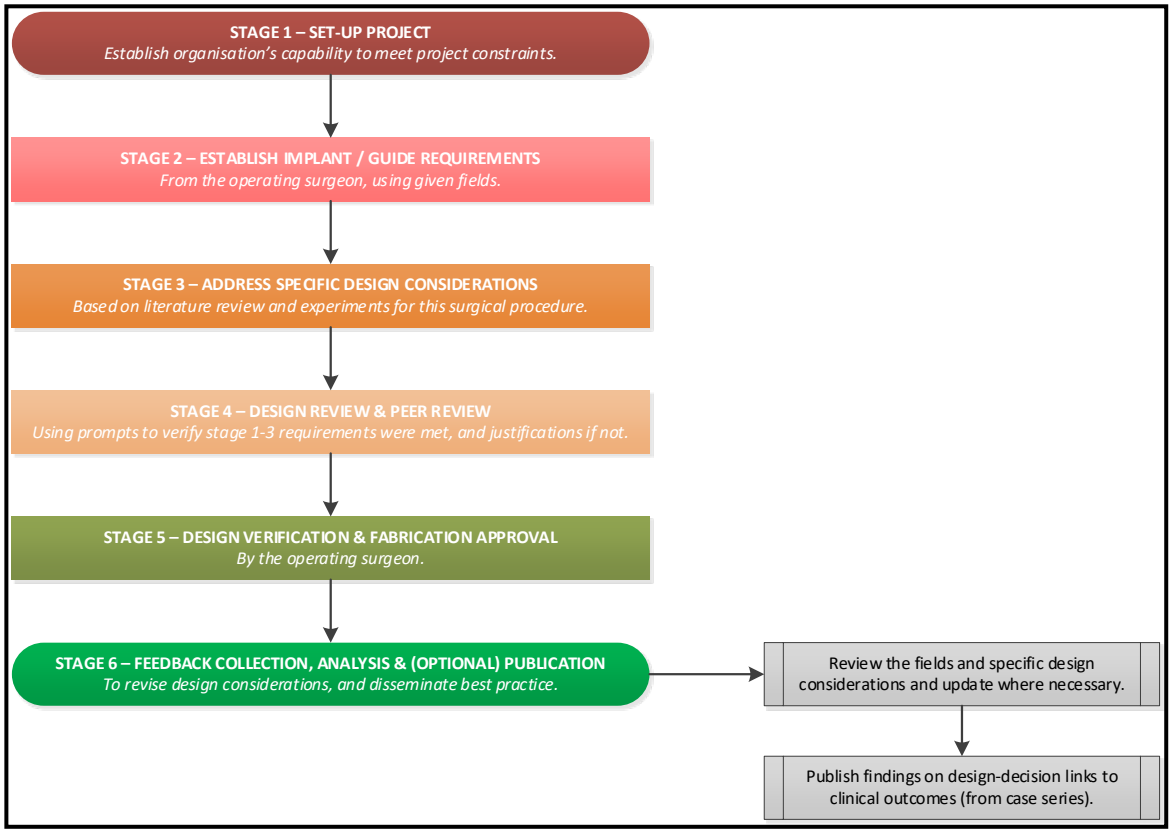
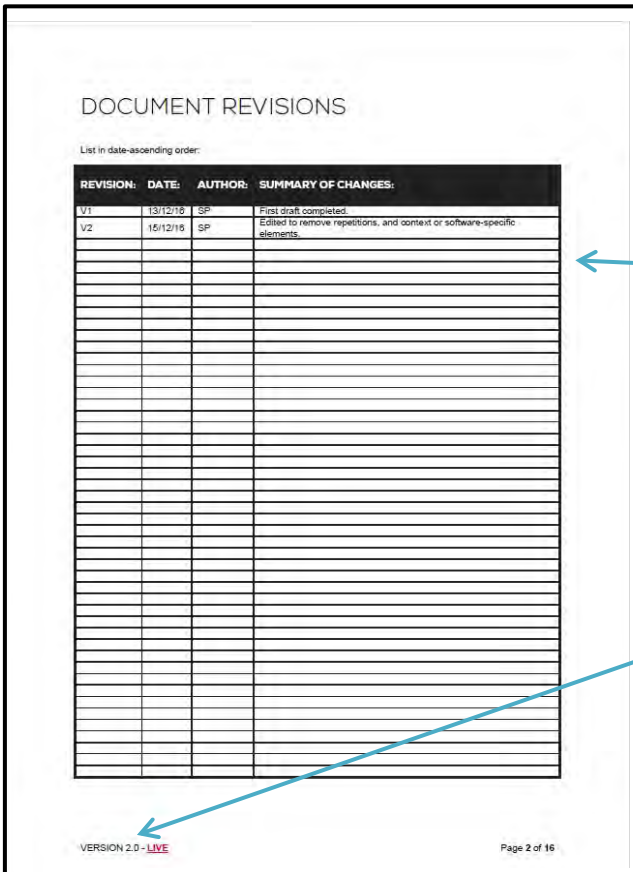


Figure 82 - Design Intervention Workflow (From Document Introduction)

The scope of the document, its intended applications, its limitations, and its conditions for use (such as dealing with the operating surgeon themselves, rather than an intermediary, wherever possible) were described in an introduction which included the overview shown in Figure 82 above. The annotations in Figure 83 to Figure 96 refer to the aims of the highlighted feature. Investigation C (results presented in Chapter 7) sought to evaluate the performance of the intervention.



DOCUMENT REVISIONS

List in date-ascending order:

REVISION:	DATE:	AUTHOR:	SUMMARY OF CHANGES:
V1	13/12/16	SP	First draft completed.
V2	15/12/16	SP	Edited to remove repetitions, and context or software-specific elements.

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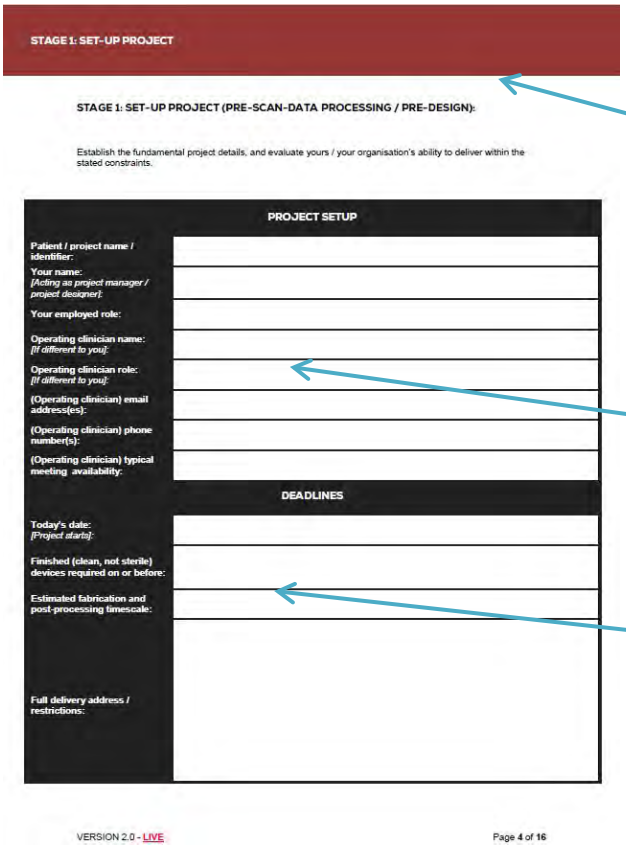
Document revision control table; to prompt, and assist with accommodating document control requirements.

Clear identification of document status in footer; to assist with ensuring that relevant document versions are available at the point of use; and prevent unintended use of obsolete documents.

Figure 83 – Annotated Design Intervention: Revisions History Page



STAGE 1: SET-UP PROJECT

STAGE 1: SET-UP PROJECT (PRE-SCAN-DATA PROCESSING / PRE-DESIGN):

Establish the fundamental project details, and evaluate yours / your organisation's ability to deliver within the stated constraints.

PROJECT SETUP	
Patient / project name / identifier:	
Your name: *[Acting as project manager / project designer]:*	
Your employed role:	
Operating clinician name: *[If different to you]:*	
Operating clinician role: *[If different to you]:*	
(Operating clinician) email address(es):	
(Operating clinician) phone number(s):	
(Operating clinician) typical meeting availability:	

DEADLINES	
Today's date: *[Project starts]:*	
Finished (clean, not sterile) devices required on or before:	
Estimated fabrication and post-processing timescale:	
Full delivery address / restrictions:	

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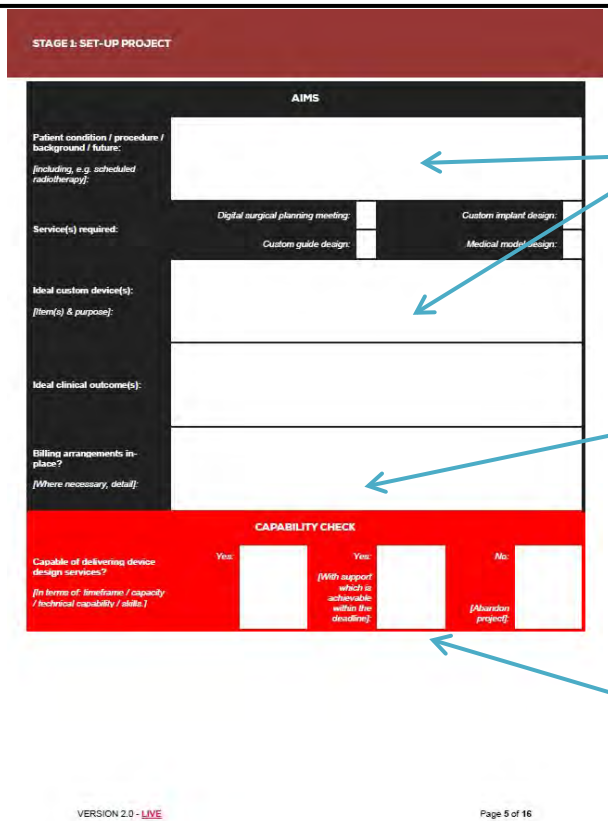
Clear at-a-glance reference to the progress through the prescribed workflow (referencing colours from Figure 82).

Up-front explicit definition of participant roles and contact details to assist with establishing responsibilities, points-of-view, and contact methods.

Immediate clarification of deadlines: from the clinical point of view; the fabrication point of view; and (therefore) most importantly the design point of view.

Figure 84 - Annotated Design Intervention: Project Set-Up and Deadline Fields



STAGE 1: SET-UP PROJECT

AIMS			
Patient condition / procedure / background / future: *[including, e.g. scheduled radiotherapy]:*			
Service(s) required:	*Digital surgical planning meeting:*	*Custom implant design:*	
	Custom guide design:	*Medical model design:*	
Ideal custom device(s): *[Item(s) & purpose]:*			
Ideal clinical outcome(s):			
Billing arrangements in-place? *[Where necessary, detail]:*			

CAPABILITY CHECK			
Capable of delivering device design services? *[In terms of: timeframe / capacity / technical capability / skills]*	Yes:	Yes: *[With support which is achievable within the deadline]:*	No: *[Abandon project]:*

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Prompts to make top-level clinical and service aims explicit. Aimed to draw-out any misconceptions from the surgeon's perspective Re. CAD/AM/service possibilities before addressing requirements in detail.

Early direction to define billing / invoicing approach; with a view towards avoiding delays as a deadline approached.

Explicit capability check; to minimise risk arising from surgeon potentially relying on the CAD/AM/CAM solution; if it were unrealistic for the designer to deliver in line with project constraints / deadlines.

Figure 85 – Annotated Design Intervention: Capability Check Page

STAGE 2: ESTABLISH IMPLANT / GUIDE REQUIREMENTS

STAGE 2: ESTABLISH IMPLANT / GUIDE REQUIREMENTS (PRE-SCAN-DATA PROCESSING / PRE-DESIGN):

Request specific details about the operating clinician's implant and guide requirements – and note them against all of the relevant fields. Where the clinician prompts or agrees to requirements updates through the project (perhaps after design review, further discussion, a design experiment, or a change in project circumstances), note any refined requirements in the third column.

CUSTOMER & IMPLANT / GUIDE REQUIREMENTS		
Requirements:	Design Implications & Requirements Version 1:	(Optional) Version 2: *[If refined / changed]:*
	Context	
Any accommodation required for potential defect alterations between the scan and surgery?		
Any scan-data modifications required before design work? *[E.g. Remove existing devices / grafts?]*		
Any requirements from surgeon experience (and therefore expectations) from using analogous devices?		
Any project requirements from the surgical team having relevant additional needs? *[E.g. accommodating colour blindness?]*		
	Material and Texture	
Device(s) materials:		
Device(s) surface finish(es): *[Including desirability of osseointegration]:*		

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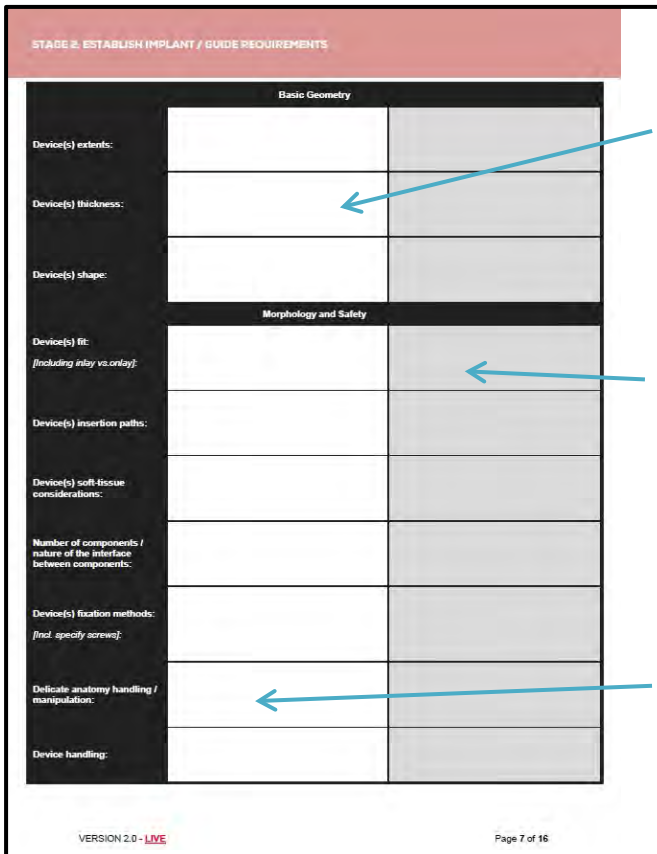
Prompts to establish (where applicable) contextual and material requirements.

Contextual requirements prompt consideration of specific defect-alteration problems from the results in investigation A1 (Chapter 5.1).

Addressed ergonomics and accessibility concerns from case study 7 results.

Second column, to permit updates to requirements, prompted by downstream clarifications during modelling.

Figure 86 – Annotated Design Intervention: Contextual and Material Requirements



STAGE 2: ESTABLISH IMPLANT / GUIDE REQUIREMENTS

Basic Geometry		
Device(s) extents:		
Device(s) thickness:		
Device(s) shape:		
Morphology and Safety		
Device(s) fit: *[Including inlay vs.onlay]:*		
Device(s) insertion paths:		
Device(s) soft-tissue considerations:		
Number of components / nature of the interface between components:		
Device(s) fixation methods: *[Incl. specify screws]:*		
Delicate anatomy handling / manipulation:		
Device handling:		

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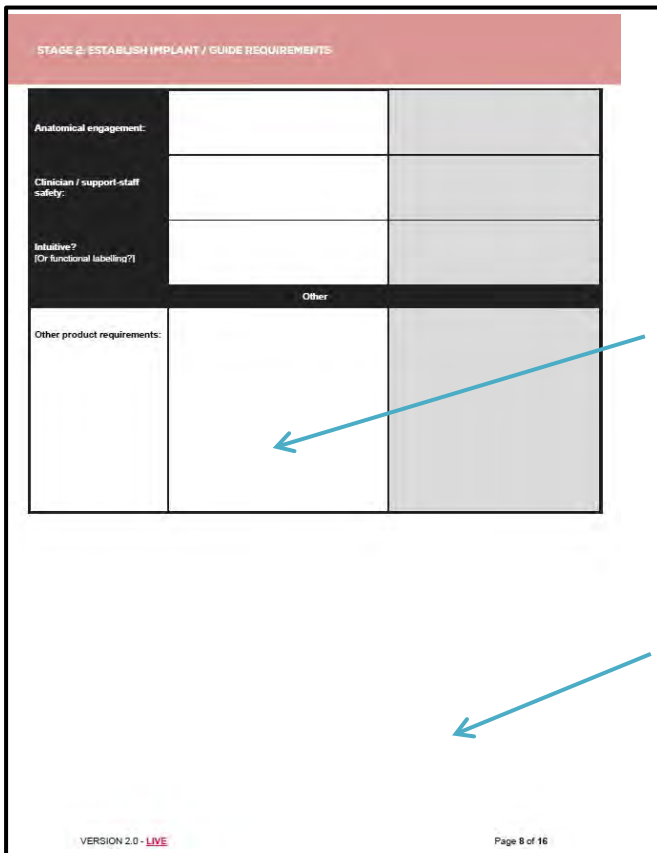
Individual, somewhat basic design details, often overlooked by the literature.

Prompting discussion, for even the most simple or fundamental details; with a view to unearthing any assumptions, misconceptions, or misunderstandings between acting designer and operating surgeon.

Similar aims – but for aspects of the surgical plan (such as determining and acknowledging the chosen insertion path or degree of exposure).

Figure 87 – Annotated Design Intervention: Geometry and Safety Requirements Page



STAGE 2: ESTABLISH IMPLANT / GUIDE REQUIREMENTS

Anatomical engagement:		
Clinician / support-staff safety:		
Intuitive? [Or functional labelling?]		
Other		
Other product requirements:		

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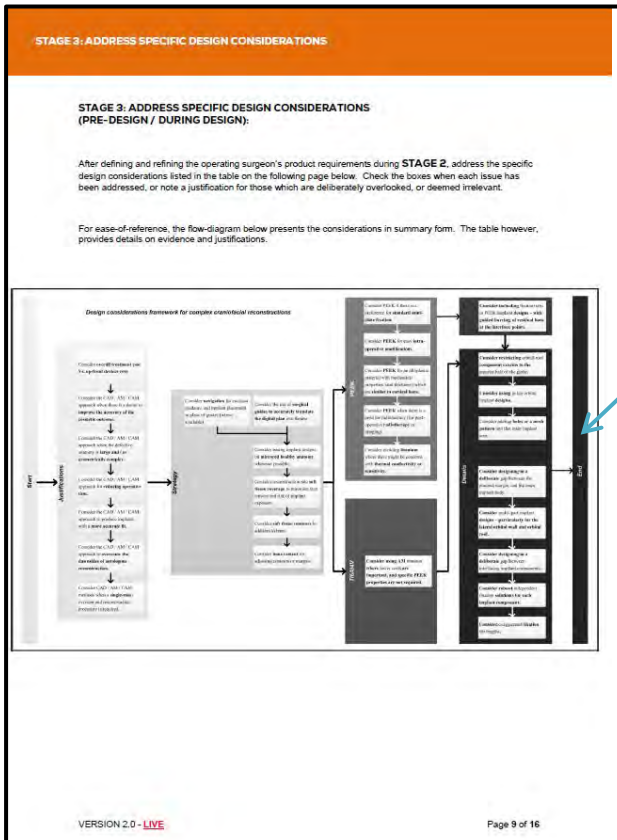
Space to accommodate new requirements, not anticipated by the current version of the design intervention document.

Page break from end of one section to another; to provide clear delineation and orientation in the process as a whole.

Figure 88 – Annotated Design Intervention: Other Requirements Page



STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS

STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS (PRE-DESIGN / DURING DESIGN):

After defining and refining the operating surgeon's product requirements during **STAGE 2**, address the specific design considerations listed in the table on the following page below. Check the boxes when each issue has been addressed, or note a justification for those which are deliberately overlooked, or deemed irrelevant.

For ease-of-reference, the flow-diagram below presents the considerations in summary form. The table however, provides details on evidence and justifications.

Design considerations framework for complex craniofacial reconstructions

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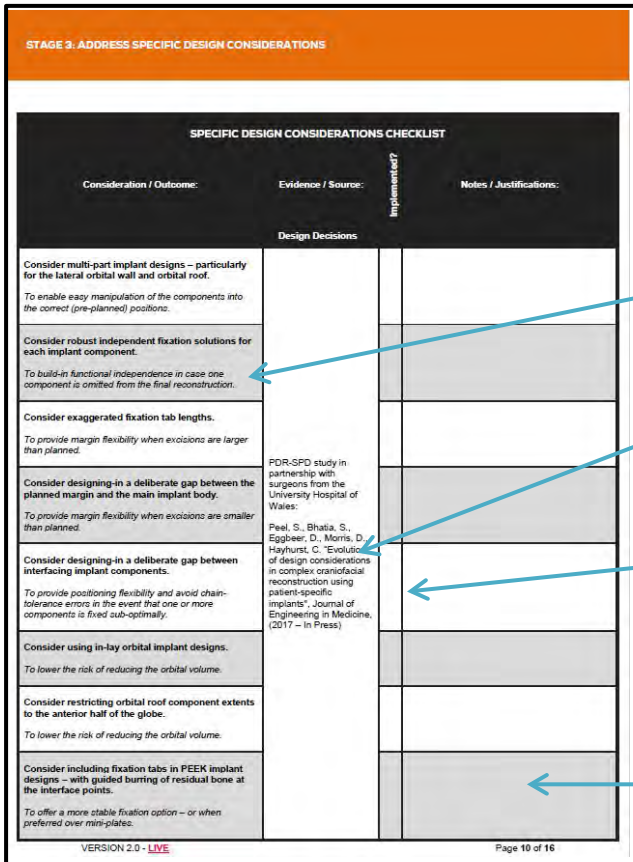
Overview flow diagram of specific complex craniofacial reconstruction design considerations. Aimed to summarise subsequent fields, and prepare the acting designer and surgeon for detailed design decisions by showing how the considerations interact.

Figure 89 – Annotated Design Intervention: Design Considerations Overview Page



STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS

SPECIFIC DESIGN CONSIDERATIONS CHECKLIST

Consideration / Outcome:	Evidence / Source:	Implemented?	Notes / Justifications:
Design Decisions			
Consider multi-part implant designs – particularly for the lateral orbital wall and orbital roof. *To enable easy manipulation of the components into the correct (pre-planned) positions.*	PDR-SPD study in partnership with surgeons from the University Hospital of Wales: Peel, S., Bhatia, S., Eggbeer, D., Morris, D., Hayhurst, C. "Evolution of design considerations in complex craniofacial reconstruction using patient-specific implants", Journal of Engineering in Medicine, (2017 – In Press)		
Consider robust independent fixation solutions for each implant component. *To build-in functional independence in case one component is omitted from the final reconstruction.*			
Consider exaggerated fixation tab lengths. *To provide margin flexibility when excisions are larger than planned.*			
Consider designing-in a deliberate gap between the planned margin and the main implant body. *To provide margin flexibility when excisions are smaller than planned.*			
Consider designing-in a deliberate gap between interfacing implant components. *To provide positioning flexibility and avoid chain-tolerance errors in the event that one or more components is fixed sub-optimally.*			
Consider using in-lay orbital implant designs. *To lower the risk of reducing the orbital volume.*			
Consider restricting orbital roof component extents to the anterior half of the globe. *To lower the risk of reducing the orbital volume.*			
Consider including fixation tabs in PEEK implant designs – with guided burring of residual bone at the interface points. *To offer a more stable fixation option – or when preferred over mini-plates.*			

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Specific design considerations.

Evidence sources to support the decision, or permit further consideration.

Check-box acknowledgement that the consideration has been implemented (i.e. considered and accepted, or considered and rejected).

Space to justify solutions, deviations, or rejections.

Figure 90 - Annotated Design Intervention: Specific Design Considerations Checkbox Page

STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS

Consider using AM titanium where specific PEEK properties are not required. *To achieve similar benefits at lower cost.*			
Consider providing extra holes in the temporal region. *To provide suturing points for the temporalis muscle.*			
Consider slightly flattening the reconstruction contours. *To produce a plate which is not overly bulbous – therefore ensuring good skin flap coverage.*	Literature review – part of a publication which is in development. *"Additively manufactured vs. conventionally precoved cranioplasty implants – an accuracy comparison"*		
Consider removing plate material around areas of potential temporalis muscle-dura fusion. *To maintain implant viability in the event of muscle-dura fusion in the weeks and months following craniotomy.*	Peel S, Eggbeer D. Additively manufactured maxillofacial implants & guides - achieving routine use *Rapid Prototyping Journal*. 2016; 22: 189 - 99.		
Manufacturing (Metal AM)			
Consider adhering to the supplier's minimum part thickness guidelines (Renishaw PLC = 0.4mm). *To prevent the need to redesign areas or components downstream.*	Renishaw PLC correspondence.		
Consider the differences in surface finish achievability for: where a grit blast stream can reach, and where a polishing tool can reach, and where a polishing tool can reach. *To prevent the need to reduce the range of available surface finishes downstream.*			
Consider ensuring the residual material remaining after modelling countersinks in device designs is at least 0.3mm thick. *To adhere to the supplier's guidelines and guarantee the integrity of the fixation solution.*			

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Level of specificity afforded by tangible evidence meant that recommendations could be suggested, rather than just prompting the designer or surgeon to generate own solutions, as in the previous section.

Figure 91 - Annotated Design Intervention: Specific Metal AM Considerations Checkbox Page

STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS

Consider making transitions between part thickness values smooth. *To mitigate issues with distortion and stress during part cooling.*			
Consider chamfering or smoothing sharp corners where possible. *To mitigate issues with support structure modelling.*			
Manufacturing (Machined PEEK)			
Consider adhering to the supplier's minimum part thickness guidelines (DePuy Synthes = 3-4mm except for slight local thinning for onlay implants). *To prevent the need to redesign areas or components downstream.*	DePuy Synthes Correspondence.		
Consider the ability of a machine tool to access undercut areas of a PEEK device design. *To prevent the need to redesign areas or components downstream.*			
Regulatory Requirements			
Consider how to minimise contamination opportunities through the design of the devices. *By, e.g. improving the ease of cleaning, sterilisation, packaging damage prevention.*			
Consider how to minimise risks of leakage from the designed device(s). *By, e.g. ensuring the designed geometry has unintended gaps filled.*			
Consider how to minimise risks of substance ingress into the designed device(s). *By, e.g. ensuring the designed geometry has unintended gaps filled.*			
Consider how to ensure part identification and traceability. *By, e.g. ensuring packaging is labelled if labelling the devices physically is difficult.*			

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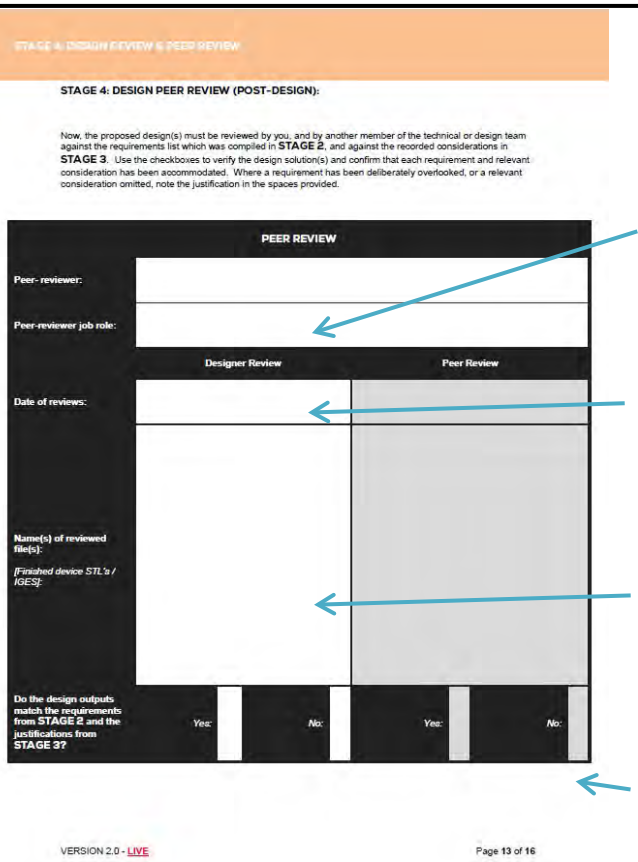
Specific design considerations highlighted by the Medical Device Directive (MDD).

Figure 92 - Annotated Design Intervention: Specific PEEK and MDD Considerations Checkbox Page



STAGE 4: DESIGN PEER REVIEW (POST-DESIGN):

Now, the proposed design(s) must be reviewed by you, and by another member of the technical or design team against the requirements list which was compiled in **STAGE 2**, and against the recorded considerations in **STAGE 3**. Use the checkboxes to verify the design solution(s) and confirm that each requirement and relevant consideration has been accommodated. Where a requirement has been deliberately overlooked, or a relevant consideration omitted, note the justification in the spaces provided.

PEER REVIEW				
Peer- reviewer:				
Peer-reviewer job role:				
	Designer Review		Peer Review	
Date of reviews:				
Name(s) of reviewed file(s): *[Finished device STL's / IGES]:*				
Do the design outputs match the requirements from STAGE 2 and the justifications from STAGE 3?	*Yes:*	*No:*	*Yes:*	*No:*

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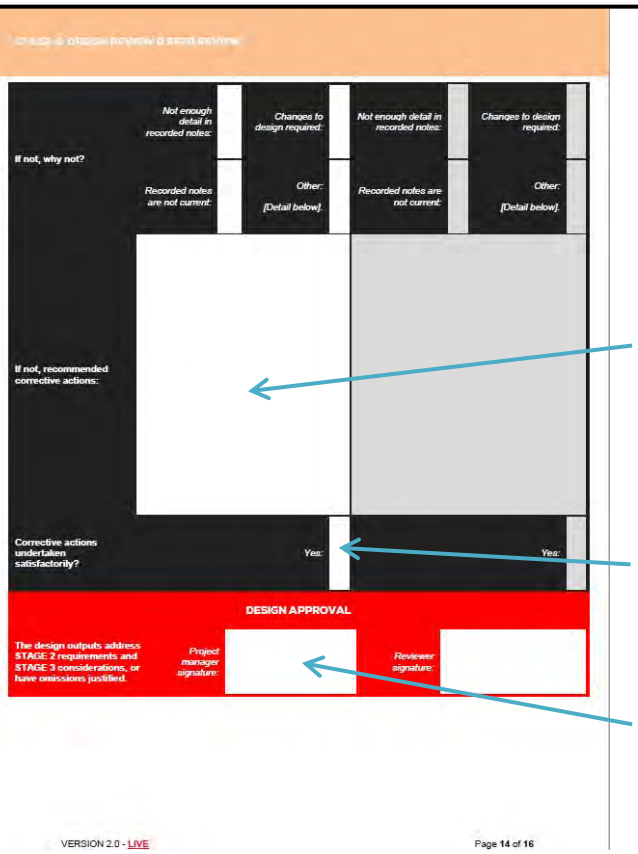
Design reviewer identification.

Prompts for design review by the designer themselves, and by the peer-reviewer.

Explicit ID of reviewed files; to assist with document control, record control, and design transfer.

Check-box approach where possible; aiming for speed.

Figure 93 - Annotated Design Intervention: Peer Review Set-Up Page



If not, why not?	*Not enough detail in recorded notes:*	*Changes to design required:*	*Not enough detail in recorded notes:*	*Changes to design required:*
	Recorded notes are not current:	*Other: [Detail below].*	*Recorded notes are not current:*	*Other: [Detail below].*
If not, recommended corrective actions:				
Corrective actions undertaken satisfactorily?	*Yes:*		*Yes:*	

DESIGN APPROVAL			
The design outputs address STAGE 2 requirements and STAGE 3 considerations, or have omissions justified.	*Project manager signature:*		*Reviewer signature:*

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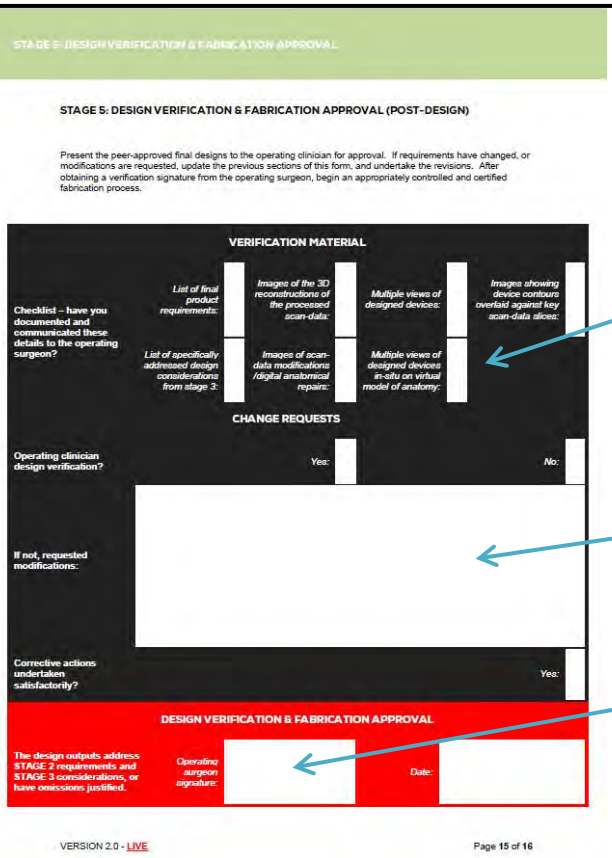
Corrective actions identification, and approval function; aiming to prompt complete design file record keeping, prior to internal design approval and subsequent customer (external) verification.

Only one corrective action response was offered – to mandate compliance prior to design approval.

Two signatures required to proceed with design approval.

Figure 94 - Annotated Design Intervention: Peer Review Approval Page



STAGE 5: DESIGN VERIFICATION & FABRICATION APPROVAL

STAGE 5: DESIGN VERIFICATION & FABRICATION APPROVAL (POST-DESIGN)

Present the peer-approved final designs to the operating clinician for approval. If requirements have changed, or modifications are requested, update the previous sections of this form, and undertake the revisions. After obtaining a verification signature from the operating surgeon, begin an appropriately controlled and certified fabrication process.

VERIFICATION MATERIAL

Checklist – have you documented and communicated these details to the operating surgeon?

List of final product requirements: | Images of the 3D reconstructions of the processed scan-data: | Multiple views of designed devices: | Images showing device contours overlaid against key scan-data slices:

List of specifically addressed design considerations from stage 3: | Images of scan-data modifications /digital anatomical repairs: | Multiple views of designed devices in-situ on virtual model of anatomy:

CHANGE REQUESTS

Operating clinician design verification? Yes: No:

If not, requested modifications:

Corrective actions undertaken satisfactorily? Yes:

DESIGN VERIFICATION & FABRICATION APPROVAL

The design outputs address STAGE 2 requirements and STAGE 3 considerations, or have omissions justified. Operating surgeon signature: Date:

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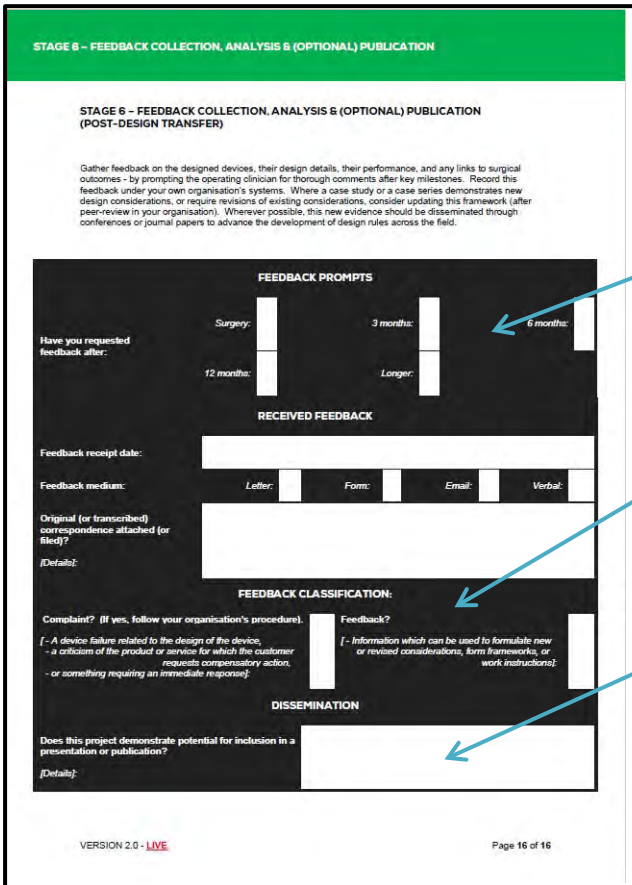
Verification material checklist; sought to ensure that minimum amount of visual information was provided in whatever format or media the acting designer's institution chose to use for verification.

Further "mini Corrective and Preventative Action (CAPA)" functions.

Explicit requirement for operating clinician verification signature.

Figure 95 - Annotated Design Intervention: Design Verification Page



STAGE 6 – FEEDBACK COLLECTION, ANALYSIS & (OPTIONAL) PUBLICATION

STAGE 6 – FEEDBACK COLLECTION, ANALYSIS & (OPTIONAL) PUBLICATION (POST-DESIGN TRANSFER)

Gather feedback on the designed devices, their design details, their performance, and any links to surgical outcomes – by prompting the operating clinician for thorough comments after key milestones. Record this feedback under your own organisation's systems. Where a case study or a case series demonstrates new design considerations, or require revisions of existing considerations, consider updating this framework (after peer-review in your organisation). Wherever possible, this new evidence should be disseminated through conferences or journal papers to advance the development of design rules across the field.

FEEDBACK PROMPTS

Have you requested feedback after: Surgery: | 3 months: | 6 months: | 12 months: | Longer:

RECEIVED FEEDBACK

Feedback receipt date:

Feedback medium: Letter: | Form: | Email: | Verbal:

Original (or transcribed) correspondence attached (or filed)?

[Details]:

FEEDBACK CLASSIFICATION:

Complaint? (If yes, follow your organisation's procedure).

[- A device failure related to the design of the device, - a criticism of the product or service for which the customer requests compensatory action, - or something requiring an immediate response]:

Feedback?

[- Information which can be used to formulate new or revised considerations, form frameworks, or work instructions]:

DISSEMINATION

Does this project demonstrate potential for inclusion in a presentation or publication?

[Details]:

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Feedback checklist; sought to ensure that feedback was prompted at key intervals – whilst leaving the precise format to the discretion of the acting designer or their institution; to minimise barriers to collection.

Prompt to begin (where necessary) the complaints procedure for the specific institution.

Prompt to consider publishing the captured details (if deemed worthy).

Figure 96 - Annotated Design Intervention: Feedback and Publication Prompt Page

6.6. Chapter 6 Summary

In summary, Chapter 6 has:

- identified the most surmountable problems with current patient-specific device design processes (derived from contextual analysis, literature review, and thesis case studies 1-9) (Chapter 6.1);

- identified methods for overcoming those problems – with regards to a paper-based design process intervention (6.1);

- formulated a tangible method of meeting the requirements of BS EN ISO 13485, by creating and verifying a design QMS (6.2.1);

- analysed the documented procedures, forms, and records of that QMS to identify which aspects were highly context-dependent (and less suitable for generalisation) (6.2.2);

- identified which aspects of that QMS were more suitable for generalisation (aiming to provide a framework for satisfying as many of the requirements for a QMS as possible) (6.2.2);

- extracted the specific design considerations for complex craniofacial reconstruction devices from the literature (6.3.1);

- verified those design considerations and identified 9 new ones through the participation in, or observation of, thesis case studies 10-14 (6.3 – 6.4);

- described and justified the choices made in constructing a paper-based design intervention document for controlling and recording the design of complex craniofacial reconstruction devices (6.5);

- And in doing these, has contributed to meeting objective 3 from Chapter 1.9 and to answering research questions 3.1 and 3.2 from Chapter 4.2.4.

7. Investigation C Results – Intervention Verification

This Chapter (Figure 97) presents the results of using the design intervention formulated by Chapter 6. This Chapter therefore contributes to meeting objective 4 from Chapter 1.9 and to answering research question 3.3 from Chapter 4.2.4.

It characterises the behaviours, thoughts, and comments of three expert participants; when following their own standard design workflows, and then when following a workflow prescribed and facilitated by the design intervention. The data extraction fields were designed to permit evaluation of the key factors and key links from the conceptual framework (Figure 29, in Chapter 4). As such notable aspects of: behaviours and workflows, design outputs, identified product requirements, questions or comments, expressed emotions, and QMS compliance are presented across sub-Chapters 7.1-7.6. Discussions of the relevance and validity of these results are presented in the next Chapter (Chapter 8).

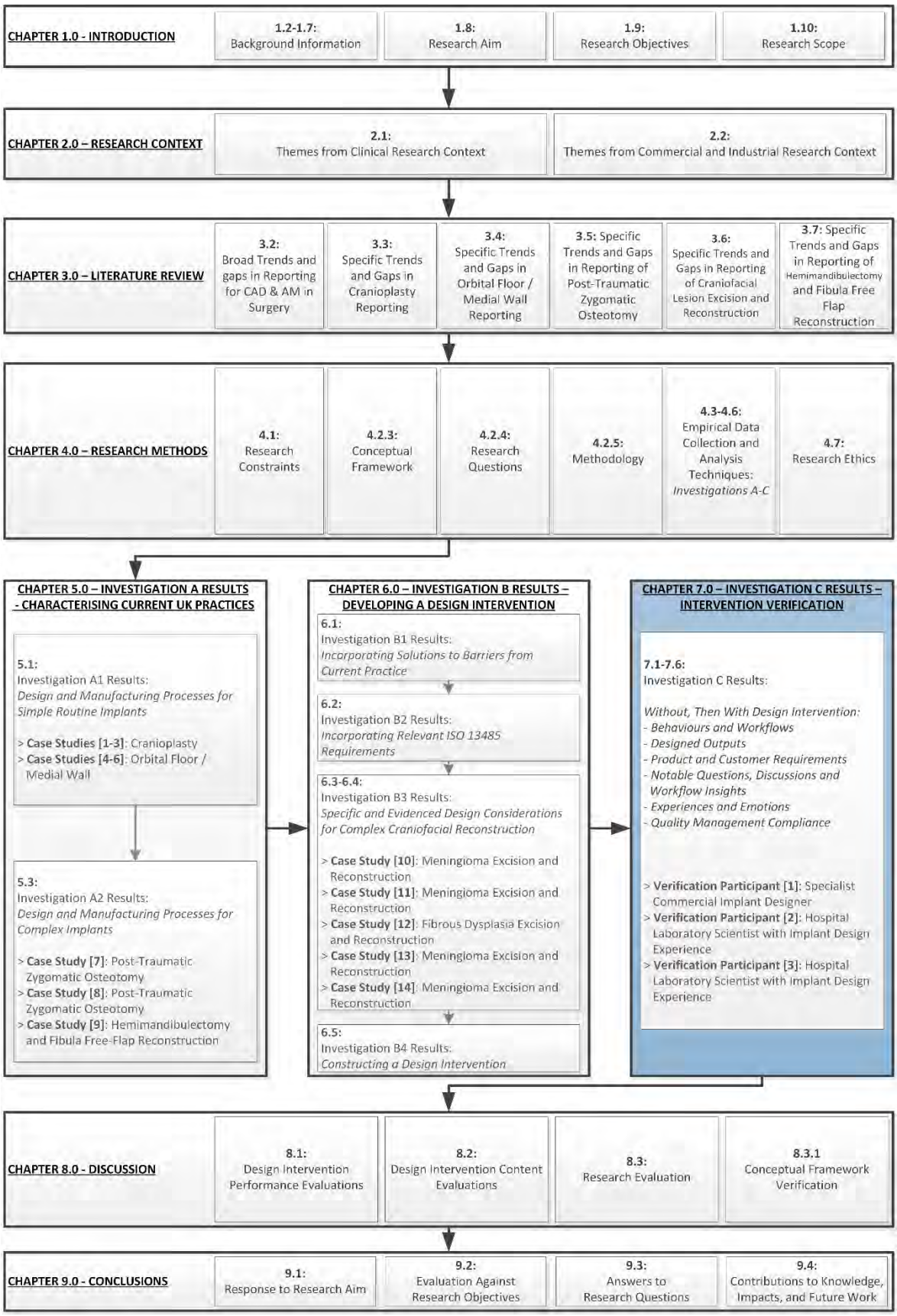


Figure 97 - Thesis Overview, With Current Location Highlighted (Chapter 7)

7.1. Behaviours and Workflows

The observed design and modelling behaviours demonstrated similarities which allowed them to be grouped into 11 clear categories, which are listed and defined below. The order and duration of these behaviours were extracted from notes and video recordings and are presented in graphical overview form for participants 1 (Figure 98), 2 (Figure 99), and 3 (Figure 100).

a) *CAD file / workspace setup*: importing the STL file of patient data, creating planes for mirroring or symmetry judgements, and defining properly aligned views of the 3D form.

b) *Mental / verbal conceptualising*: cognitive thought processes of the participants towards generating solutions to meeting the design requirements.

c) *Anatomical reconstruction*: mirroring, refinement, and blending of the healthy contralateral anatomy to fill the defect.

d) *Sketch modelling*: rough shaping of virtual clay, or marking of that clay with a virtual paintbrush tool; to trial solutions prior to starting modelling proper.

e) *Basic modelling*: of the main implant form and thickness.

f) *Development modelling*: of separated components (where applicable), of their interfaces (with the anatomy and with each other), and of fixation tabs (where used).

g) *Refinement modelling*: of detailed features using virtual clay including countersinks, labels, screw hole positions, screw or venting holes, and of smooth transitions between different implant regions.

h) *Production preparation*: conversion of the virtual clay model to mesh, manipulation of that mesh to e.g. add screw or venting holes with greater edge definition, and clear segregation of the proposed designs from previous iterations in the CAD software.

i) *Self-verification / correction*: against the product requirements list (either physically, digitally, or mentally compiled).

j) *Modelling failures / delays*: including those caused by software malfunction, modelling skill limitations, or hardware issues.

k) *Design questions*: asked by the designer of the consultant surgeon (customer).

l) *Laboratory business interruptions*: caused by unavoidable clinical consultations during the course of the observed design activity.

7.1.1. ***Participant 1***

(Commercial, external designer).

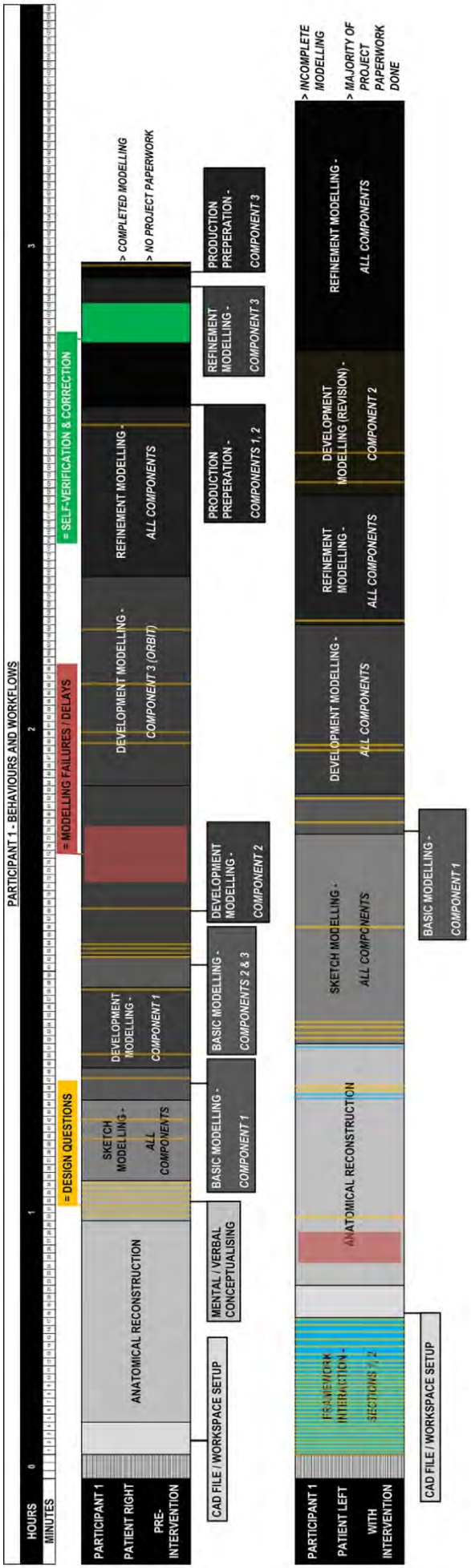


Figure 98 - Categorised Behaviours and Durations for Participant 1

7.1.2. ***Participant 2***

(In-house NHS designer).

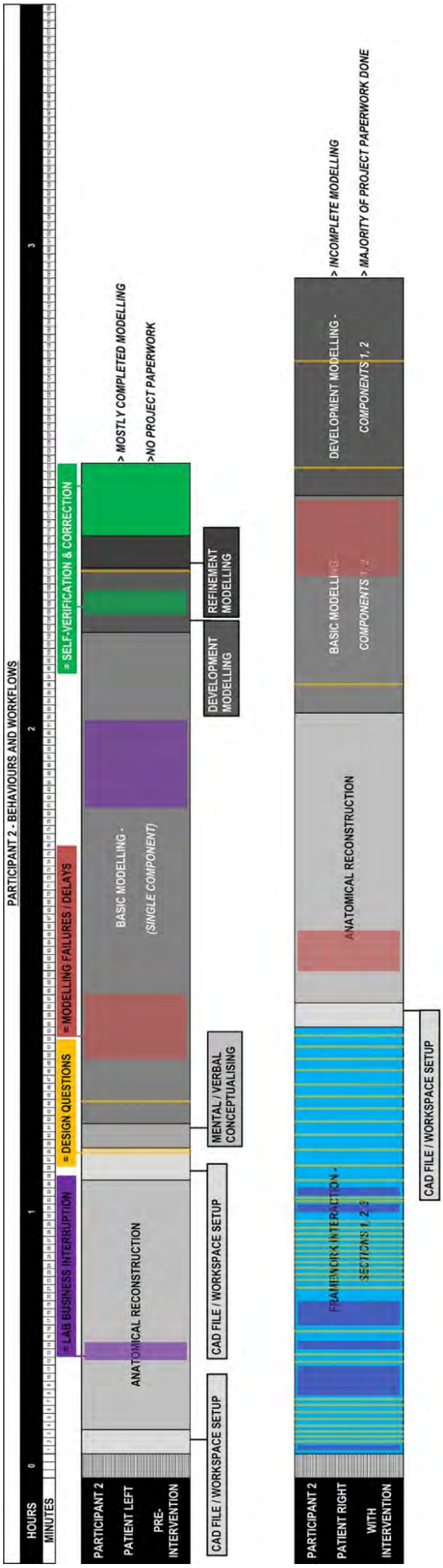


Figure 99 - Categorised Behaviours and Durations for Participant 2

7.1.3. ***Participant 3***

(In-house NHS designer).

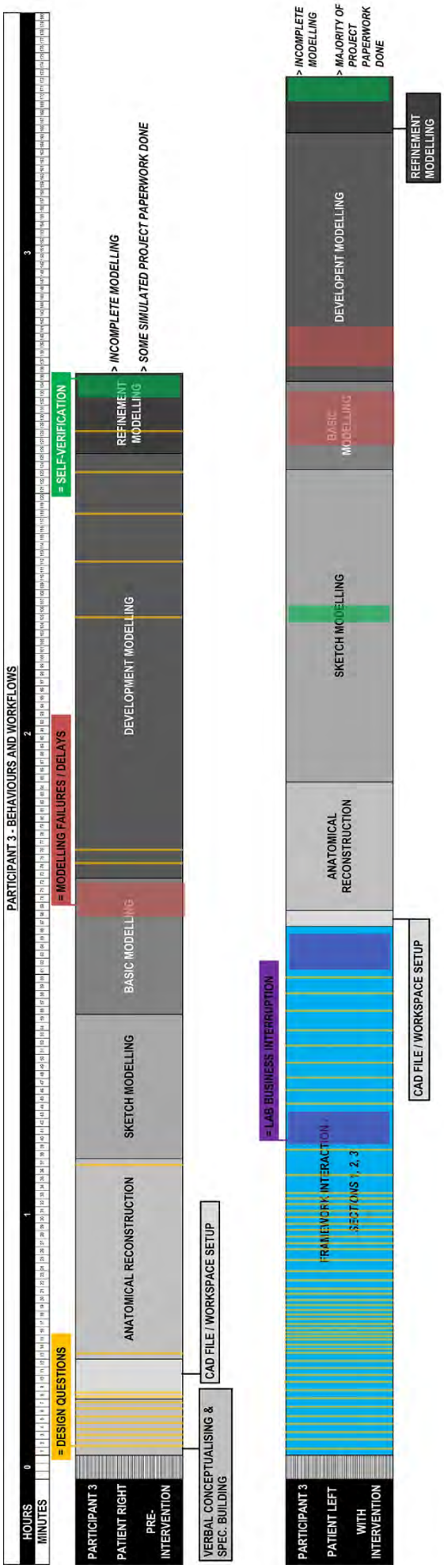


Figure 100 - Categorised Behaviours and Durations for Participant 3

7.2. Designed Outputs

Design process outputs varied across sessions – in terms of design details and the degree-of-completeness within the allotted timeframes. As such, images of the outputs from the sessions are presented alongside the participants stated intentions for completing the modelling process for their finalised outcomes. For some participants, painted intended details are visible in the screen-grabs from the CAD software.

7.2.1. Pre-Intervention

Table 10, Table 11, and Table 12 show images of the designed outputs from the design sessions without using the intervention. They also describes the main (stated) characteristics of the outputs, upon completion of modelling activities.

Table 10 - Participant 1 Design Outputs (Without Intervention)

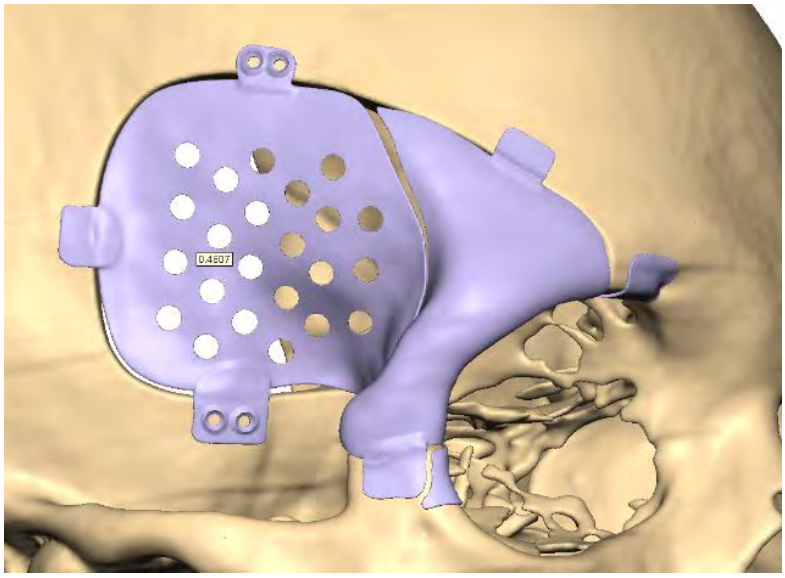
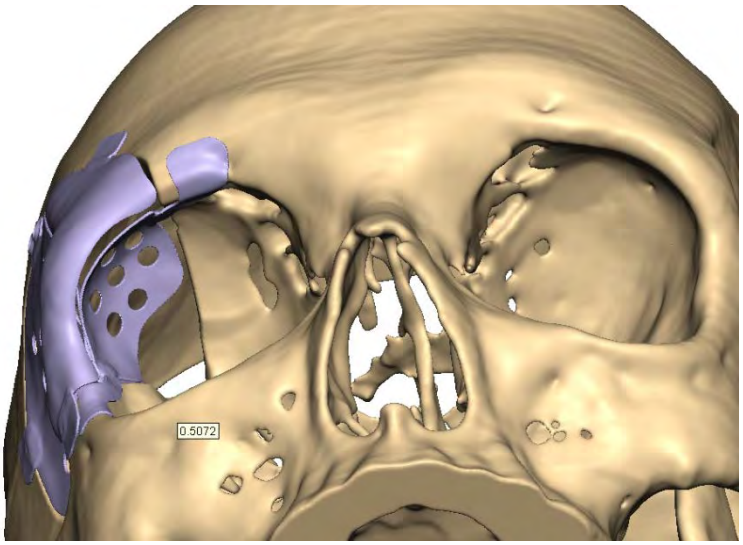
Designed Output(s) from Time-Limited Session	Description of Modelled or Intended Outputs (Upon Modelling Completion)
	1x inlay temporal component. 1x inlay orbital rim component. 1x inlay orbital roof component. 0.5mm uniform thicknesses (all components). 7x onlay fixation tabs. Inferior rim and orbit tabs mirror each other at the interfacing edge.
	3.5mm tab thickness on top of the 0.5mm implant thickness. 2.0mm diameter venting holes (temporal / orbital components). Countersunk screw holes of 1.6mm diameter. 2x per tab – next to each other. 1.4mm gap between components. 1.0mm gap between defect edge and devices. Maximum 14.0mm gap at posterior aspect of orbital component.

Table 11 - Participant 2 Design Outputs (Without Intervention)

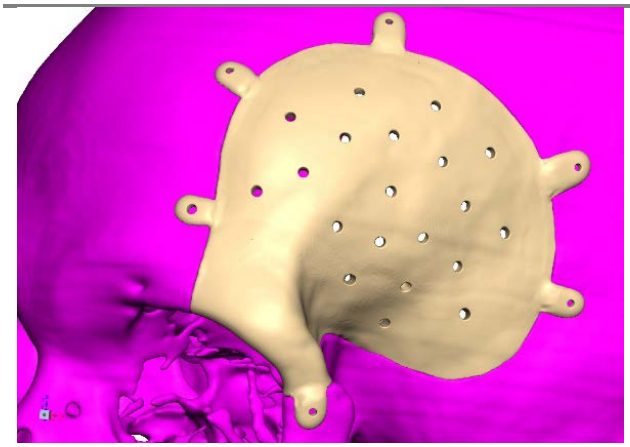
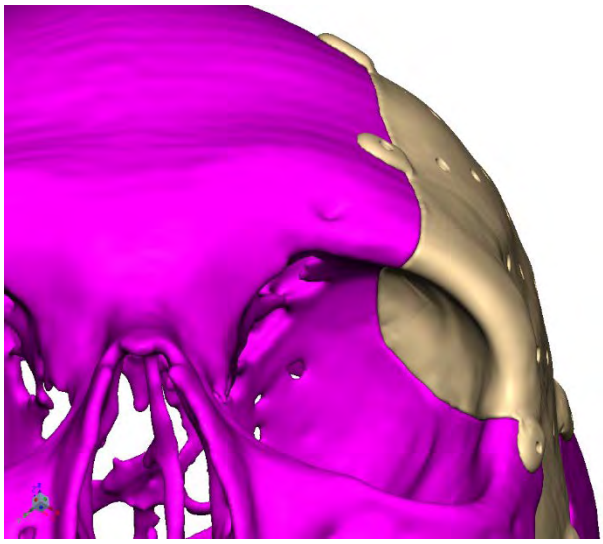
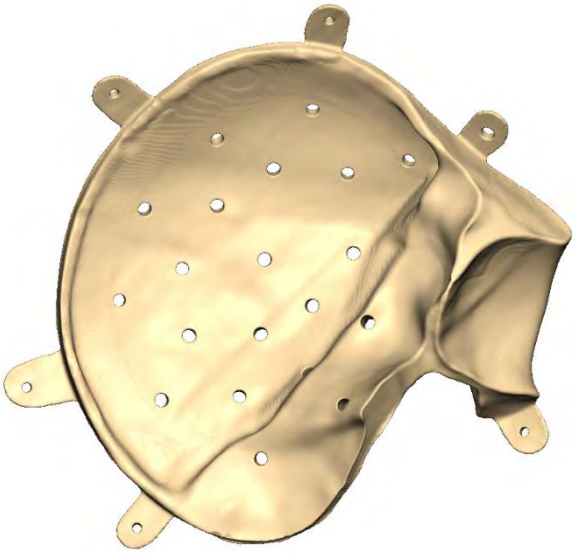
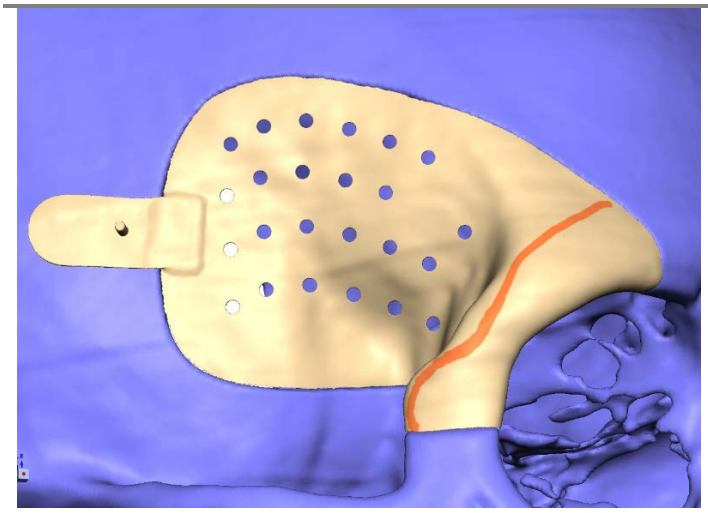
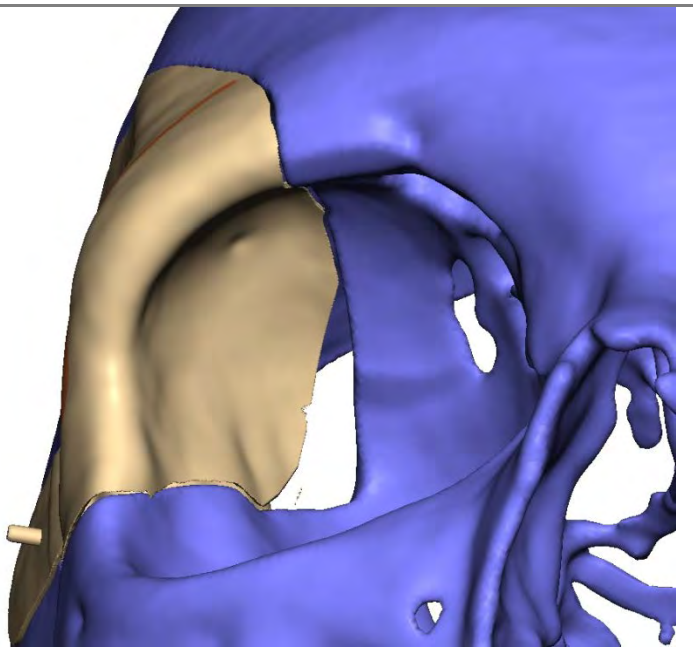
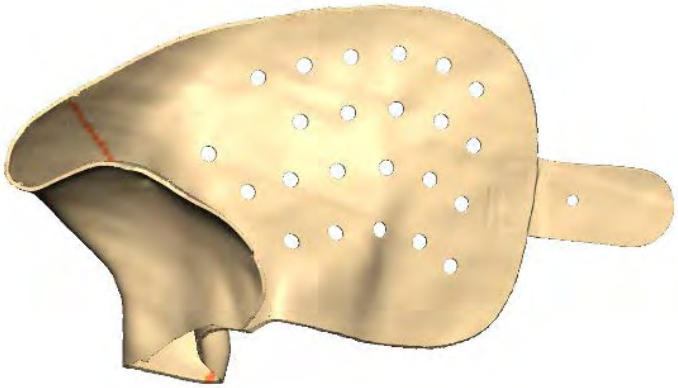
Designed Output(s) from Time-Limited Session	Description of Modelled or Intended Outputs (Upon Modelling Completion)
	1x inlay single temporal-rim-orbital component. Non-uniform thickness ranging from 2.0mm-6.0mm across the main temporal area > 23.0mm at the thickest point of the rim. 6x onlay fixation tabs. Tabs of 1.0mm thickness on top of the implant thickness. Thickness reduces to a minimum at the implant edges (0.7mm). 2.0mm diameter venting holes (temporal region). Non-countersunk screw holes of 1.5mm diameter. 1x per tab. No gap between defect edge and devices. No gap at posterior aspect of orbital component.
	
	

Table 12 - Participant 3 Design Outputs (Without Intervention)

Designed Output(s) from Time-Limited Session	Description of Modelled or Intended Outputs (Upon Modelling Completion)
	1x temporal component. 1x rim-orbital component (see painted split line). 0.5mm uniform thicknesses (both components). 5 onlay fixation tabs. 0.5mm tab thickness on top of the 0.5mm implant thickness. 2.0mm diameter venting holes (temporal component). Non-countersunk screw holes of 1.5mm diameter. 2x per tab (behind one another). 2.0mm gap between components. 0.5mm gap between defect edge and components. Maximum 7.0mm gap at posterior aspect of orbital component.
	
	

7.2.2. With Intervention

Table 13, Table 14, and Table 15 show images of the designed outputs from the design sessions without using the intervention. They also describes the main (stated) characteristics of the outputs, upon completion of modelling activities.

Table 13 - Participant 1 Design Outputs (With Intervention)

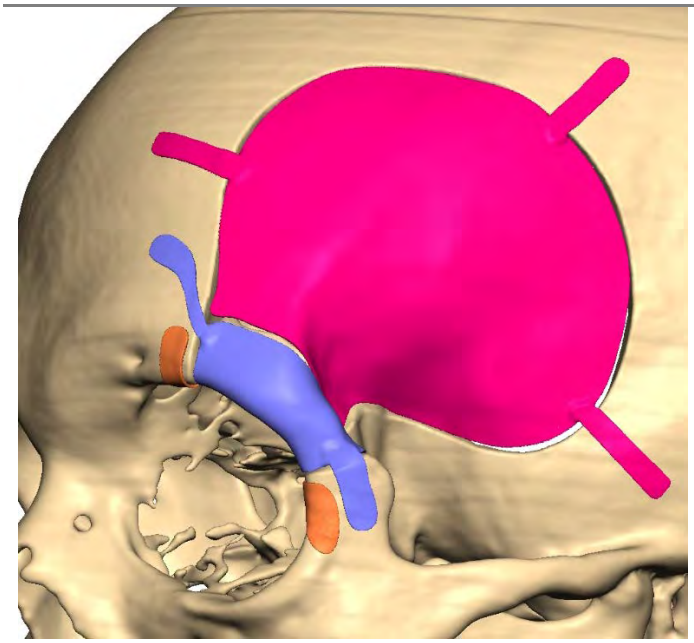
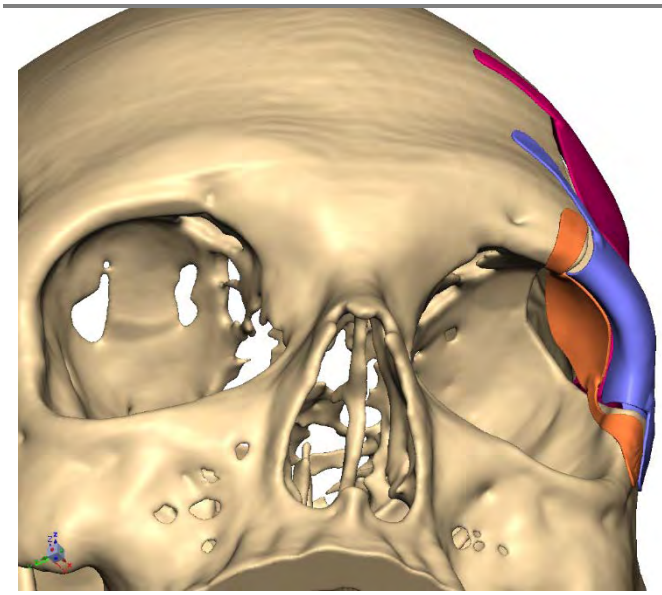
Designed Output(s) from Time-Limited Session	Description of Intended Outputs (Upon Modelling Completion)
	1x inlay temporal component. 1x inlay orbital rim component. 1x inlay orbital roof component. 0.5mm uniform thicknesses (all components). 7x onlay fixation tabs. 0.5mm tab thickness on top of the 0.5mm implant thickness.
	3.0 diameter venting holes (temporal / orbital components). Countersunk screw holes of 1.6mm diameter. 2x per tab – behind one another). 1.0mm gap between components. 1.4mm gap between defect edge and devices. Maximum 4.0mm gap at posterior aspect of orbital component.

Table 14 - Participant 2 Design Outputs (With Intervention)

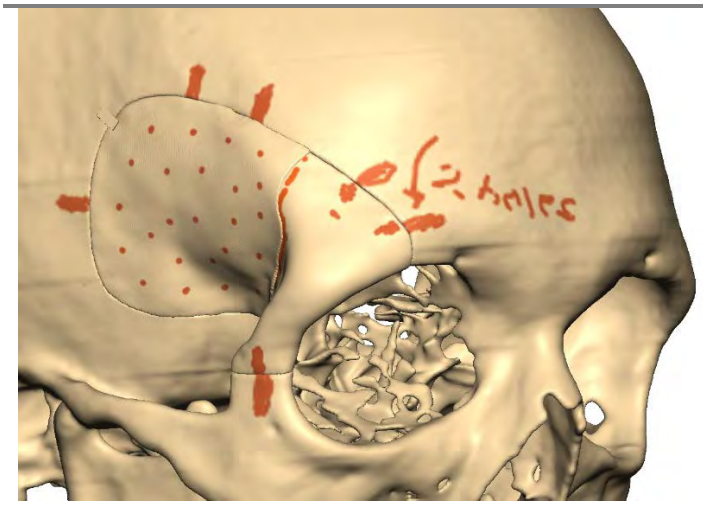
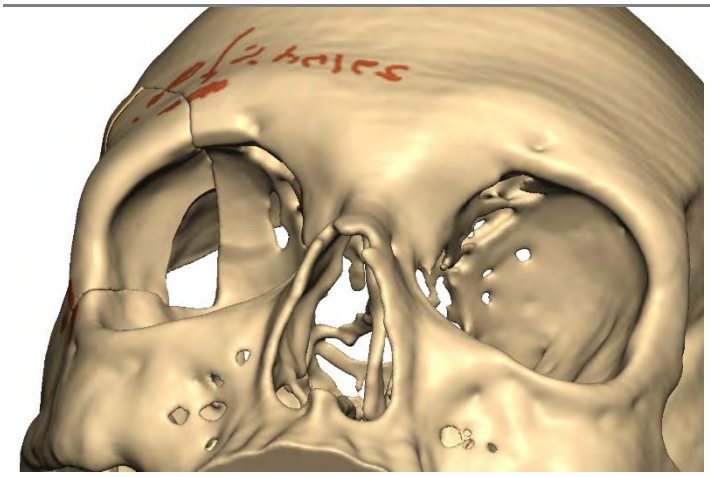
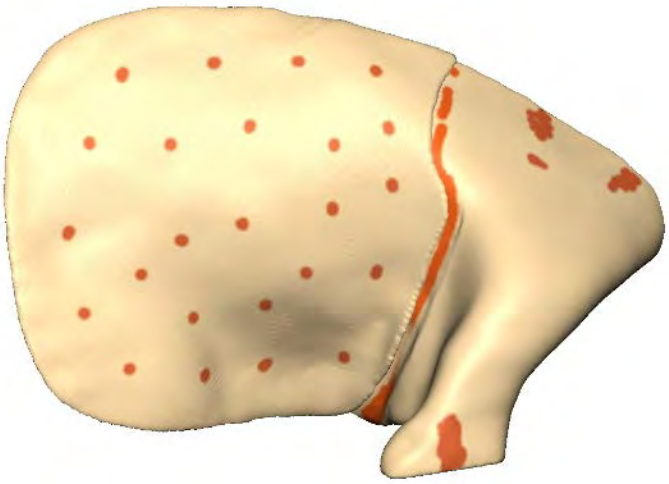
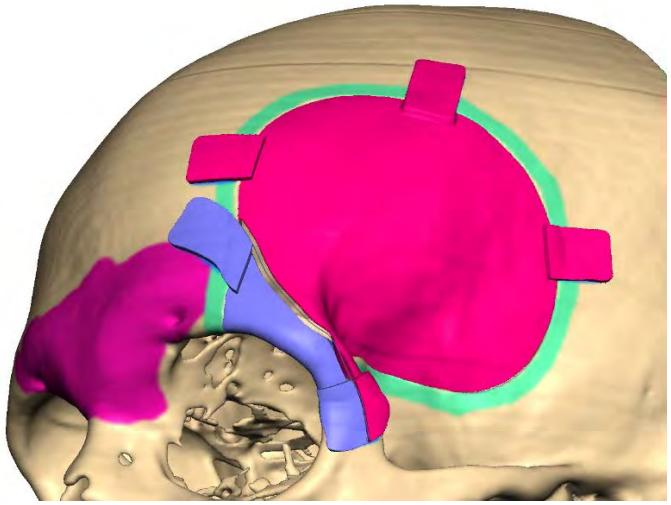
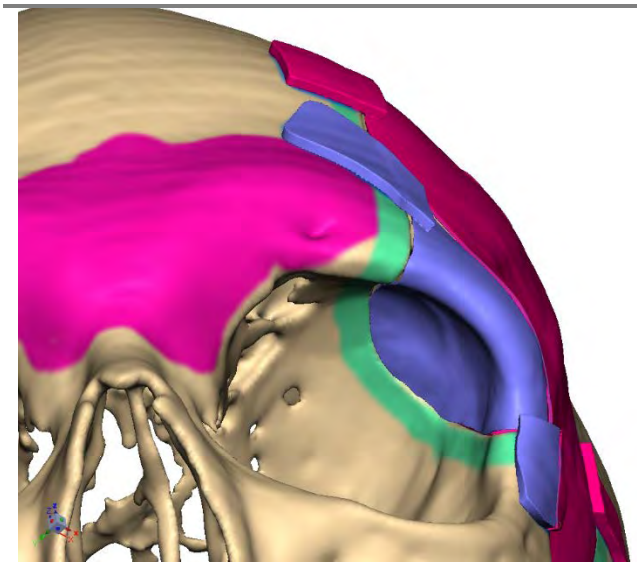
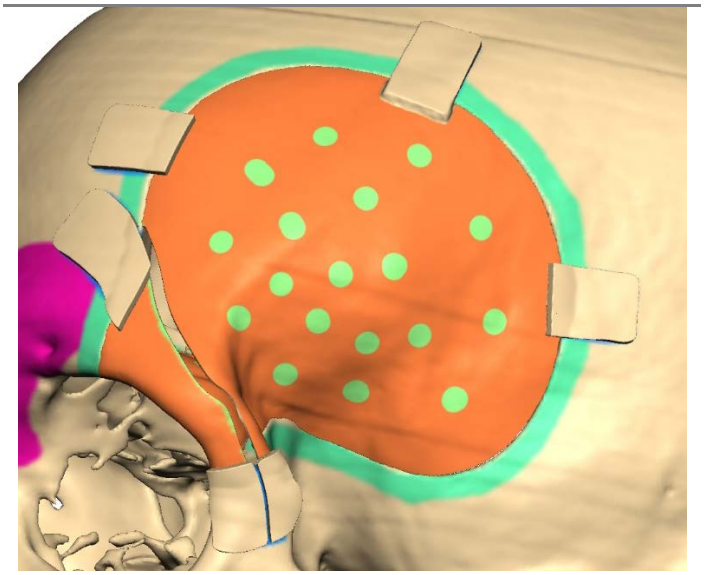
Designed Output(s) from Time-Limited Session	Description of Intended Outputs (Upon Modelling Completion)
	1x inlay temporal component. 1x inlay rim-orbital roof component. 0.5mm uniform thicknesses (both components).
	7x onlay fixation tabs (see painted areas). 0.5mm tab thickness on top of the 0.5mm implant thickness. 2.0mm diameter venting holes (temporal component – see painted detail). Non-countersunk screw holes of 1.5mm diameter. 2x per tab.
	1.5mm gap between components. 0.5mm gap between defect edge and devices. Maximum 15mm gap at posterior aspect of orbital component.

Table 15 - Participant 3 Design Outputs (With Intervention)

Designed Output(s) from Time-Limited Session	Description of Intended Outputs (Upon Modelling Completion)
	1x inlay temporal component. 1x inlay rim-orbital roof component. 0.5mm uniform thicknesses (both components). 6x onlay fixation tabs. 1.5mm tab thickness on top of the 0.5mm implant thickness. 4.0mm diameter venting holes (temporal component). Non-countersunk screw holes of 1.5mm diameter. 2x per tab. 2.0mm gap between components. 0.5mm gap between defect edge and devices. Unspecified gap at posterior aspect of orbital component.
	
	

7.3. Product and Customer Requirements Assessment

This sub-Chapter identifies which of the customer and product requirements were identified and met by participants (either by verbalising their thoughts, by asking questions or engaging in discussions with the customer, or in writing). Table 16 below, shows which customer and product requirements were identified and met by the participants (P) when using their standard workflows (A) and their standard workflows enhanced by the design intervention (B).

Participants were judged against a requirements master list. The master list was derived from the fully-populated fields of the design intervention from Chapter 6.5. Results included: ON (an overlooked or not-explicitly-identified requirement, which was therefore not met in the design); IM (an explicitly identified requirement, which was therefore deliberately met in the design); and OM (an overlooked or not explicitly identified requirement, which was then coincidentally, routinely, or accidentally met by design). Where there has been a change in a requirement's assessment from a standard workflow to the intervention workflow, the cell is highlighted. Orange cells indicate an improvement of one aspect (from the 'identifying/overlooking' and 'meeting/not-meeting'). Green cells indicate an improvement of both aspects.

Table 16 - Requirements Identified and / or Met by Participants 1-3

(A – Without Intervention; B – With Intervention)

Customer / Product Requirements	P1A	P1B	P2A	P2B	P3A	P3B
	Identified (I) // Overlooked (O) Met (M) // Not Met (N)					
Colour blind member of surgical team. Make images highly contrasting.	ON	IM	ON	IM	ON	IM
Titanium.	IM	IM	IM	IM	IM	IM
Outermost bone contours only (as opposed to full bone thickness).	IM	IM	IN*	IM	IM	IM
Polished outer surfaces.	IM	IM	IM	IM	IM	IM
Satin inner surfaces.	IM	IM	IM	IM	IM	IM
Reconstruct entire defect, except for posterior orbit (where a partial reconstruction is desired, only).	IM	IM	ON	IM	IM	IM
0.5mm thickness.	IM	IM	IN*	IM	IM	IM
Mirror contours from healthy contralateral anatomy.	IM	IM	IM	IM	IM	IM
Inlay design across main implant area(s).	IM	IM	IM	IM	IM	IM
Slight over-correction in temporal region, slight under-correction in the remaining areas.	ON	IM	ON	IM	ON	IM
Temporalis muscle suturing and temporal venting holes.	OM	IM	IM	IM	OM	IM
Divide into 2 or 3 components.	IM	IM	ON	IM	IM	IM
1.5mm diameter screws.	IM	IM	IM	IM	IM	IM
Screws should avoid frontal sinus.	IM	IM	IM	IM	IM	IM
Ensure implant components are not so small as to be difficult to handle.	OM	IM	OM	IM	OM	IM
Implant should engage anatomy securely.	OM	IM	OM	IM	OM	IM
Avoid sharp corners (chamfer or smooth).	OM	IM	IM	IM	OM	IM
Implant components should be independently fixed.	IM	IM	N/A**	IM	OM	IM
Exaggerate fixation tab lengths and arrange multiple screw holes behind each other.	ON	IM	ON	IM	OM	IM
Create a gap between the implant edge and the defect edge.	IM	IM	ON	IM	IM	IM
(Where multiple components are used): create a gap between components.	IM	IM	N/A**	IM	OM	IM
Screws should be countersunk.	IM	IM	ON	IM	IM	IM
Countersinks should retain at least 0.3mm material at their base.	OM	IM	ON	IM	IM	IM
Smooth transitions between part thicknesses.	OM	IM	OM	IM	IM	IM

**This requirement was identified, and not met at the conscious recommendation of the designer-clinician.*

*** Single-component design used by this participant.*

7.4. Notable Questions, Discussions, and Workflow Insights

This sub-Chapter transcribes key questions, discussions, and comments about the workflows used in the design sessions (both pre-intervention, and with intervention). The extracts presented in sub-Chapters 7.4.1 and 7.4.2 were selected on the basis of: typifying a recurring characteristic of a given design workflow; being unusual in the context of the individual workflow; or providing an insight into a particular aspect of a workflow. The majority of transcribed quotations came, from the design sessions themselves (as opposed to the post-session interviews). This reflects the considerably longer duration of the design sessions, relative to the interviews, and the emotional user-experience focus of the interviews.

7.4.1. Pre-Intervention

Table 17, Table 18, and Table 19 below present transcriptions of key quotes from the pre-intervention design sessions for participants (P) 1-3 respectively. As described in Chapter 4, the timestamps for notable quotes were recorded in real-time in the contemporaneous field notes. Quotes were deemed as being potentially notable on the basis of providing a demonstration or an explanation of: the given participant's design process structure; their motivations; their design decisions; their emotional and cognitive responses to the design activity; insights into their standard practice and its context; and justifications for any of the above.

After reviewing and transcribing the recordings of the highlighted key sections, the quotes were grouped with those which had been included for similar reasons, on a per-participant basis. Descriptive labels were applied to these groups and are shown in the middle column of the tables below. This rationalised and consolidated the presentation of the data tables and improved the ease with which overarching themes could then be identified and explored in the discussion. Those emerging themes are identified and their implications explored in the final columns.

Table 17 - Key Quotes for Participant 1 Workflow Insights (Pre-Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"Sorry for being pedantic, but this is kind of the most important bit isn't it – to make sure it matches up?" "To get an exact mirror image – so I put some reference planes in to use as a guide – I'll use this model as a basis to design the implants on."	Workflow insights.	Refers to anatomical reconstruction and correct mirroring; the foundation of the modelling strategy used, and therefore the most sensitive.
"Do you want to reconstruct this rim as well?" "So I can crop off somewhere along here." "Did you say two screws in each?"	Examples of informal design verification questions.	Double-checking previous assumptions, and previously unrecorded requirements.
"Because of the access and things like that, would you want a two part implant?" "Would you prefer them to like, butt-up against each other as opposed to say, overlap?" "In terms of access, would you make the cuts just wherever you feel fit for the implant, or would you want the implant designed around where you'll make the excision, if that makes sense? So for example, if you were making a cut here to insert this implant, you don't want it coming too far out this way – does that make sense?" "Do you need fluid transfer holes, or something to reduce the weight of the material?"	Examples of formal requirements-gathering questions.	Requirements intermittently gathered – but after significant amounts of modelling have already been completed. Not open-ended questions. Suggesting solutions (which the designer may have used before). This could be negative – in restricting innovation or restricting thinking. This could be positive
"I'm just working out the basic shapes of the implants – and just trying to work out how they will fit together".	Workflow insight.	Working on-the-fly. Designing through modelling. Didn't establish clear design intent before starting the modelling activity.
"First, I'm gonna make a copy and decrease the clay coarseness – to get the sharper edge to the implant, I'll be able to edit a thinner piece more easily".	Workflow insight.	Software-specific technical modelling detail. Important for a successful outcome from this software, but not specifically generalisable across other software. However, there may be generalisable ways to frame this and add to the framework (if needed).

Table 18 - Key Quotes for Participant 2 Workflow Insights (Pre-Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"It seems fairly symmetrical, so I think that anything we do, we can rely on the symmetry from the other side for the most extent". "It's got to be an insert, so we probably wouldn't do it the full depth of the defect, but we will probably around the orbit".	Workflow insights.	Commentary on workflow, without requirements gathering first. Reliance on own knowledge, at least for the beginning.
"I'm not very process oriented – so I just think, like, oh how did I do it last time?" "I still think the most important thing is going to theatre, and, just every time we'll make slight changes to the design – just tweaking it so that there's improvements on there".	Workflow insights.	Clear evidence of a feedback loop, but seemed to be informal and subjective. Inconsistent documentation of findings and no evident verification or validation with literature or experiments.
"Well, I mean you could put screws in, but then really because it's used by cortical bone, you're not really going to engage the cortices – so I would probably be tempted to do tabs I think." "I would probably avoid anything here, because you've got the masseter muscle coming up here, and the temporalis, so you've got a huge muscle bulk here – so I would expect the surgeon to not want to dissect all that muscle out to put a plate in or fix the plate".	Examples of formal requirements-statements.	Working on-the-fly. Designing through modelling. Didn't establish clear design intent before starting the modelling activity. Better clinical insight, more specific, drawing on anatomical knowledge more than P1. Statements, rather than questions.
"When we're doing these, we're lucky in that we have a surgeon 'on tap'- so for every decision we would either sit down with them and do it, or send them a PDF and say 'what do you want doing here?'" "You've got to advise them about what are the material problems, like if you've got a larger bulk of metal etcetera – but we very much try and put the ball in their court as far as the design is concerned, so that we don't – get the blame".	Workflow insights.	Continuous design verification – possibly unique to the in-hospital context of this participant. Despite driving the design more from previous personal experience (over asking design questions) in this instance, they demonstrated a clear awareness of liability. Defensive attitude towards design decisions.

Table 19 - Key Quotes for Participant 3 Workflow Insights (Pre-Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"What we usually do is take screenshots in FreeForm, and then print them out, and then they draw on it – from my point of view I don't really come up with the design as such – they tell me what they want, and when it comes to the design in FreeForm, I'll adapt to what they want". "I usually agree *everything* – so that if it comes back you can say 'well you agreed it'". "If it's in an email, that's fine. I have a 3D planning spreadsheet that's rather – 'anal' … I'll keep everything, I'll keep when the CT was done and for example this one says 'waiting on consultant to decide on leg". "So I write it down, there's nothing to stop the consultant saying 'you've written it down wrong' – but it's my way of just keeping record, and also reminding me".	Workflow insights.	Surprisingly defensive – suggestive of prior unjust blame for design decisions – possibly a combative undertone to relationship with surgeon colleagues. Although not consciously or formally undertaken for that reason, these comments showed good record keeping towards documenting design review, design verification, and process validation. Demonstrates that even basic project management (undertaken through personal preference, not institutional protocol) can achieve some aspects of compliance.
"How much of it do you want reconstructing?" "Have you got an incision?" "Keeping the eye? Does the eye see?" "What about fixation?" … "Is that the thread?" "What happens if one piece of a two-part goes in and another one doesn't?"	Examples of formal requirements-gathering questions.	Clear, more comprehensive questions than P1 and P2 before beginning modelling activities; including many more examples than featured here. Although lacking a formal documented procedure, this participant drew on day-to-day collaborative device design experience.

"That's difficult – because you can tell one person to create folders – but, erm, they don't". "You can't really tell people how to work fully, because then it will just stop design completely". "If you need to do it quickly, you could argue there's no time".	Workflow insights.	Appreciation of the tension between protocols, encouraging compliance, and ensuring design freedoms. Suggested difficulty in encouraging intra-department compliance with own basic system. On the one hand, negative indicator for adopting an external structure. On the other hand, an external structure may assist with *compelling* compliance.
I don't know if they've fully worked out that the more time you spend with me on the computer, the better the outcome you will get – I find [consultant name] very good like that – he'll say 'this is urgent' and when you ask when, it's for November next year (!)". You can do a bit of research to see what's out there, rather than just worrying about getting it done – you can do a bit of research and design something you're actually happy with, rather than something that you'll think 'for now, that'll be ok'". "I don't think, with any of this, that I've ever designed anything where you'd say as a designer – 'that is absolutely spot-on' because – here anyway – we don't have the time".	Workflow insights.	Even when based in a hospital surgery department / clinic, the designer experiences difficulty in always securing enough of a surgeon's time or scheduling enough design time for urgent patient cases. Whilst this is a significant practical limitation, further investigation would be required to understand how a mandatory structured process (as a result of the Medical Device Regulations) might impact on scheduling and surgeon co-operation.

7.4.2. <u>With Intervention</u>

Table 20, Table 21, and Table 22 below present key quote transcriptions from the pre-intervention design sessions for participants (P) 1-3 respectively. Identical processes were followed regarding data extraction, presentation, and analysis as were described in Chapter 7.4.1.

Table 20 - Key Quotes for Participant 1 Workflow Insights (With Intervention)

Transcribed Quotes	Category	Relevance?
"Have you got a contact email address?" "And a contact number?" "Are you happy with the scan data you've sent us? So, is there any existing metalwork that needs removing?" "Surface finish of the implants – do you have any requirements or are you happy for us to choose it?" "We would usually print titanium at 0.4mm thick – is that what you would like?" "And the number of implants? – Usually for these types of cases we would do three parts…"	Examples of formal, requirements-gathering questions, asked prior to modelling.	Asking questions from sections 1 and 2 of the design intervention. Questions asked prior to any modelling work taking place. Framework section 3 was read at the beginning, but the associated questions and discussion prompts were left until modelling had commenced. Still often used closed ended questions – by suggesting answers and prompting agreement or discussion. Made the framework fields more specific and constrained than they were when provided; by bringing experience-specific details and manufacturers recommendations to bear.
"Are you happy with how this reconstruction is looking?" "Would you like a three-part implant? I think that might be better than two."	Examples of informal design verification questions – asked during modelling.	On-the-fly verification; seeking to reassure themselves that they are proceeding 'correctly'.
"Would you like the reconstruction to be slightly relieved, erm, to allow for the thickness of the implant…though I guess because we're having inlay, that's not necessarily an issue – the skin-flap coverage?" And for attaching the orbital implant – are you happy with tabs running from inside the orbit?" "In terms of the screw angle, would you like to go up into the rim – as in from this angle?" "What length screws are you actually using?"	Examples of formal requirements-gathering questions, asked during modelling and design.	Details not explicitly listed in the intervention framework – though their general themes were. Potentially too-specific for framework inclusion in light of the lack of evidence for even basic design details form the literature. However, this level of detail may offer an ultimate target fidelity once the requisite evidence is gathered.

Table 21 - Key Quotes for Participant 2 Workflow Insights (With Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"Patient name…?" "Required on or before…?" "Device material…?" "Device surface finish…?" "Device fit morphology and safety… … device fit?"	Examples of formal, requirements-gathering questions, asked prior to modelling.	Asked quite robotically – not rephrased conversationally. Suggestive of a lower level of enthusiasm. Asking questions from sections 1-2, and prompting discussion about factors from section 3 of the design intervention. Questions asked and discussions prompted prior to any modelling work taking place.
"Estimated fabrication and post-processing timescale…what's that then?" "Patient condition, procedure background-future…ooh gosh". "With support which is achievable within the deadline … Yes? … I don't understand what that means! (laughs)".	Examples of clarifying design intervention fields.	Suggested that some design intervention fields may need to be re-worded – with a better balance achieved between brevity and explanation.
"(Turns page of framework)… cor blimey – this isn't as much fun as last week".	Workflow insights.	Frustration demonstrated towards the front-loaded requirements gathering and record-keeping process.
"(After a request for at least two implant components)…I'm not sure you really need it in two pieces…anyway…"	Workflow insights.	Some slight discomfort at not driving the design details themselves.
"I'm just taking away what we don't need now – then I'll work out a way to get down to the thickness we need"	Workflow insights.	Seemed to have a clear idea of where to go with the modelling, but not necessarily how to get there. Many more modelling difficulties than in P2's first session. Might reflect the effort to match a design intent established early; rather than just doing what their modelling skills will most easily permit.

Table 22 - Key Quotes for Participant 3 Workflow Insights (With Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"…and your email?" "…number?" "Meeting availability?" "Finished, clean sterile devices required on or before?" "Patient-condition-procedure-background-future, including e.g. scheduled radiotherapy". "Device materials?" "Device surface finish?"	Examples of formal, requirements-gathering questions, asked prior to modelling.	Asking questions relating to framework sections 1-3. Questions asked and discussions prompted prior to any modelling work taking place. Again, asked quite stiffly – like in the case of P2. This, when combined with the requests for clarification of some fields (see below) may indicate that P3 was being careful to apply the framework properly at this, their first viewing and experience of it.
"(After colour-blind surgeon reply)…red-green colour blind?" "What is the distance that you would like to stay away from that defect edge for a screw?"	Formal requirements-gathering questions prior to modelling.	Details not explicitly listed in the intervention framework – though their general themes were.
"Your name…? Is that me?" "Operating clinician name – that's just me isn't it?" "Any requirements from surgeon experience, and therefore expectation, from using analogous devices? ----- ... (then in response to question about the field making sense) … no". "Erm…delicate anatomy handling-manipulation…what does that mean?" "Device handling…I don't know what that means either".	Examples of clarifying design intervention fields.	Like P2, this suggested that some design intervention fields may need to be re-worded – with a better balance achieved between brevity and explanation.

"Do you have a specific time frame you'd want – so you'd say 'if the scan is done more than a month away, then we wouldn't use it, or something?" "Do you have a requirement for what scan slice thickness you've got?"	Workflow insights.	Details not explicitly listed in the intervention framework, not their general themes. Future developments should consider evidence-based inclusion.

7.5. Experiences and Emotions

This sub-Chapter transcribes key quotes about the participants experiences of, and emotions expressed towards the design challenge and procedures associated with it (both pre-intervention, and with intervention). The quotes were extracted from the post-session interviews.

7.5.1. Pre-Intervention

Table 23, Table 24, and Table 25 below present key quote transcriptions from the pre-intervention design sessions for participants (P) 1-3 respectively. Notes on the thematic relevance of quotes are provided. As described in Chapter 4, inclusion criteria were based on a quote's ability (alone or in a group) to clearly represent a recurring emotion or theme, or based on a quote's ability to represent a unique emotion or theme.

Table 23 - Key Quotes for Participant 1 Experience and Emotion Insights (Pre-Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"While I'm mirroring something, I don't really know about the access, or what screws, or about how many implants or things like that – 'cos obviously that's a final outcome that you want. It is as I go along really…"	Spontaneity.	Not conducive to a properly compliant and planned process – but illustrative of the reality of the barrier which needs to be overcome.
"When I initially saw it, I had to like, take a bit of time to think about it". "I would say it's one of the more complicated cases that I've, personally, done."	Caution.	Suggestive of the design task being outside of the participant's comfort zone, or routine.
"I initially was a bit worried and a bit concerned, but when the surgeon had specified quite a few things, it becomes easier and you've got your head 'round it, and you have like a vision in your head of what you want the outcome to be". "I think it's about getting that vision and that outcome to aim towards, you can then go about thinking 'how am I going to achieve this aim?'"	Visualisation.	Demonstrates an appreciation of the value of design intent.
"I think it's still quite a scary concept having the surgeon sitting next to you – it feels like you're working under pressure"	Pressure.	Suggestive of a desire to be perceived as competent – perhaps preferring to make mistakes in private.
"When you initially get the data, it's like 'how am I going to fix this?' – but then you ask yourself smaller questions, and it gets easier".	Overwhelmed.	Suggests methodical problem solving - should be well suited to QMS approach.
"We can advise, and tell them why we're designing it in such a way, and like, tell them it's based on previous outcomes or previous problems – but at the end of the day, if they want a certain implant to locate at a certain point we disagree with, I'd say you have to go with it." "At the end of the day, they're the ones doing the operation." "We can advise, and give them all of the evidence, but it's down to them I would say."	Deference.	Clear deference to customer and experts. Understandable and justified under the MDD, but scheduled to be unacceptable under the MDR.

Table 24 - Key Quotes for Participant 2 Experience and Emotion Insights (Pre-Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"It varies depending on their (surgeon) availability – we like to see them with the initial scans" … "then with design changes through the process we try to email them back and make sure they're happy with the design changes and record the design changes". "We've had instances where they've said you know – 'design this for the left leg' … and we've gone and made it for the left leg, and then it was the right they wanted". "Getting the consultants here is by far the biggest problem – because a lot of the time we know there are deadlines to meet, we feel we can't progress until we've shown them". "I don't think when they look at something on their phone or their computer, I don't think they necessarily give it the time and value that it needs".	Frustration / caution / defensiveness.	Participant based in a hospital – perhaps exaggerating the deference exemplified by P1 because of the seniority of the surgeons and their location in the same hierarchy. The design intervention alone would be unlikely to be able to solve these issues of surgeon engagement, but it represents an important wider barrier to successful (compliant) in-house design.
"It's not easy – certainly the mirroring because it's a relatively sort of symmetrical … so that you're not working against the symmetry, but again, thinning the plate could be challenging". "My thinking against prescriptions is – they do work, and I understand that, but they can just – stifle your creativity and your ability to work quickly". (About fibula flap workflows) "Knowing where everything is going, it's a bit nerve-wracking because wherever they make those cuts is where you're telling them to make the cuts."	Responsibility / freedom.	Clear appreciation of the freedom they enjoy – and with that, the responsibility for the device design and surgical performance.
"It is quite stressful – because we don't follow a particularly prescriptive path, (and I've not done one for a while), so I'm not following a checkbox down – so that makes it more stressful". "You are thinking – what do other people think of your design, you know?"	Self-consciousness / pressure.	Contradicting the desire for design freedoms from the row above. Suggestive of a desire to be seen as competent and skilled – especially in the face of a new challenge.

Table 25 - Key Quotes for Participant 3 Experience and Emotion Insights (Pre-Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"It was slightly challenging because I'd not done it before – had someone like (lab manager) or a consultant been here, they could maybe have offered some ideas on how to develop it – however doing it just then, I've picked up on how I'd do things differently." "If I was to do it again, I'd find it quite simple." "I think it's the method – it's the way in which you do things – the stages that for me, because I hadn't done it before, I didn't know what to do at what point".	Quiet confidence.	Methodical problem solving in evidence. Confidence in own ability to improve the process in future instances – by establishing a mental product design workflow.
"Because you're in a hospital, you can't put a do not disturb sign on the door". "You're never allowed to sort of shut off from everything else and get on with things". "Contact with the consultant – they're not on call for you – they might pop in when they have five minutes in between clinics – and you have to down tools and go back to an old case". "You're constantly flitting in between designs". "That means you can't refine or finesse a design as much as you'd want to". "I don't know whether it will change (lack of consistent record-keeping across lab staff) – I don't know how you're going to get over that really, because everyone works differently, and people have other things – I mean if you take (staff names) they've got patients to see, which is probably more important than naming a file at the end of the day".	Flexibility, acceptance of limitations.	In-hospital context dependent. Suggestive of a lack of managerial commitment to quality – accepting of barriers to basic requirements gathering and design verification. Understandable, given resourced pressures on NHS – but incompatible with future regulatory requirements.
"Had you told me it was for a real case, there might have been more frustration – because you're under a time constraint – and you know that you need to provide a good outcome".	Pressure.	Caveat on realism of the observed design session.

*7.5.2. **With Intervention***

Table 26, Table 27, and Table 28 below present key quote transcriptions from the pre-intervention design sessions for participants (P) 1-3 respectively. Notes on the thematic relevance of quotes are provided. As described in Chapter 4, inclusion criteria were based on a quote's ability (alone or in a group) to clearly represent a recurring emotion or theme, or based on a quote's ability to represent a unique emotion or theme.

Table 26 - Key Quotes for Participant 1 Experience and Emotion Insights (With Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"I found it easier than the first time – not easy, but easier…just because I knew what to expect a bit more. I had a method in my mind already".	Familiarity.	Caveat on realism of the observed design session.
"The first time I did this, I asked you questions as I went along – saying 'oh, by the way, what's this or that?' – in this case I took time beforehand and the form prompts things I wouldn't necessarily have thought of." "So this time round, I filled out all these forms, I knew in my head what I needed to achieve, whereas the time before that I started designing and – not made things up as I went along – but kind of, changed things as I went along". "I spent more time initially, but then I could just get on with it. I feel like I asked you less questions this time - during." "Maybe they (the surgeon) can sit down next to you, and once they've given you an overall idea, they can go away…the first time I kept thinking of questions I hadn't thought of initially."	Confidence, order, satisfaction.	Confidence arising from establishing the specification early could perhaps be related to the desire to be seen as competent from the previous section (after further research).
"There was a lot of text initially so – I feel overwhelming is a bit of a strong word to use"… "Quite a lot to take in, but like I said earlier, you're then prepared". "During the design you're a bit more relaxed because you're not constantly thinking – 'oh what other considerations do I need to be thinking about?' – if you've got them written down in front of you". "When you've got it written down in front of you, it's less stressful"… "rather than trying to remember". "It would give a better outcome, definitely – using this, because it's more structured"…"It's better to have direction and know your outcomes, rather than design it as you go along – which is what I did".	Calmness, order.	Suggestive of appreciation for a structure, even a generic one, where personal experience is lacking. Should consider the impact on implant types with which the participants are personally familiar in future work – with potentially more entrenched routines.

Table 27 - Key Quotes for Participant 2 Experience and Emotion Insights (With Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"I found it a lot harder because I was trying to take in more parameters"… "There was a lot more going on in my head." "I think I would probably have had (preferred) a final crib sheet to refer to, throughout the design process so that I wasn't looking back". I was trying to make a lot more design decisions, I suppose to a certain extent I feel like the goalposts have moved a bit in some respects – uh I suppose in the first one I didn't ask the questions so I just carried on designing as I saw fit". (Normally) "I would tend to go with my gut to be honest – although, to be fair, when I'm say designing tabs or whatever I might ring (experts) and consider".	Complexity, specificity, high fidelity.	Increased difficulty would seem at first glance to be a negative outcome of using the framework. However, where it simply reflects the correct identification of mandatory product requirements, it might be excused.
"Panic! Yes – no, I think it was good actually, I sort of felt a bit happier because sometimes when you sit with surgeons, they drift through – they might say 'ooh we've got this case and we want to do this'". I think it is useful to use a prescription that you go through because I think you think about the things you wouldn't normally think about". "It makes them think about what they want, so I think it's a good idea" … "But you have to record that because we have had cases when they've said 'left fibula' – then they say 'did we say right fibula' and you have to say look, no you said left fibula".	Confidence, order, protected / insured.	In-hospital hierarchy might be levelled, at least for questions of design – where comprehensive record keeping permits the designer to point to evidence of past decisions.
"It wasn't that obvious, what you wanted really – but yeah, they are all important things really".	Frustration (with framework).	Confusion stemming from poor wording in aspects of the framework.
"It did help crystallize what you're trying to achieve by having a prescription there, or a checklist" "Prior to having something like this, things were a little more amorphous, and you would rely a lot more on luck – and you'd make a lot more mistakes".	Calmness, order.	Establishes design intent, and a generic design workflow – increasing comfort, confidence, and certainty of designer.

Table 28 - Key Quotes for Participant 3 Experience and Emotion Insights (With Intervention)

Transcribed Quotes	Category	Relevance / Theme?
"It made me more confident at the end of my own design because you're double checking everything is right – it didn't get angry or frustrating or anything". "It might get frustrating when I'm trying to fill it in when they're (consultant) not there". "If it says 'patient number' or whatever and you don't have it – I can't stand that empty box – it has to be filled in". "You're more confident in it – it's a lot of money, and it's quite easy to send the file off overlooking a tiny element of it – so having that workflow really does make you double check and achieve what you wanted to and what the consultant wanted to". "Good for future papers and things – to keep a record of it" … "because consultants are definitely going to forget because they're doing it every day".	Confidence / satisfaction.	Positive review – despite this participant already having an established (personal) system recording some of the aspects of the design process and its correspondence.
"I think it's handy to have those sources (of evidence) next to it (design intervention fields), just to back you up".	Confidence, order, protected / insured.	Confidence in subverting the hospital job role hierarchy would be an essential aspect of proper adherence to the MDR.
"If they (consultants) ask for things we'll always try, because we know if we do say no, they won't come back – so we try and say yes to everything – the things we do say no to is the timing of things".	Defensiveness.	Surprising market forces at play even within a hospital department. Worthy of consideration through future research.
"Getting consultants to give a precise, definite answer is quite difficult".	Frustration.	The framework can only be as effective as the relationship between the designer and the surgeon.

7.6. Quality Management Compliance Assessment

This sub-Chapter presents assessments of the degrees (if any) to which the stated or observed participant workflows met the requirements for a ISO 13485 compliant QMS. Data was extracted from notes about the observed procedures, and from interview answers about routine procedures undertaken by each participant. Table 29 permits direct comparisons of workflow capabilities with regards to what is, as explained in Chapter 1.6, soon to be a mandatory standard for all design contexts.

Table 29 below, shows which requirements of the quality standard were met by the participants (P) when using their standard workflows (A) and their standard workflows enhanced by the design intervention (B). The QMS requirements in **bold** are those which were targeted, at least in part, by the design intervention. The QMS requirements in *italics* are those which were unable to be targeted by the design intervention. The latter are displayed to permit gap-analysis between current practice and future mandatory compliance. Where there has been a change in a requirement's assessment from a standard workflow to the intervention workflow, the cell is highlighted.

Table 29 - Assessment of Participant Workflows (A – Without Intervention; B – After Intervention) against Requirements of BS EN ISO 13485:2016

Section of Standard	(Summarised) QMS Requirements	P1 A	**P1 B**	P2 A	**P2 B**	P3 A	**P3 B**
		(Y) Requirement Met // (N) Not Met // (P) Partially Met //					
4 – QMS	*Document: a quality policy and quality manual.*	*Y*	*Y*	*N*	*N*	*N*	*N*
	Document: determined procedures; determined forms, and determined records.	**Y**	**Y**	**N**	**P**	**N**	**P**
	Establish and maintain a medical device file.	**P**	**P**	**N**	**P**	**P**	**P**
	Control all documents.	**Y**	**Y**	**N**	**P**	**P**	**P**
	Control and maintain records.	**Y**	**Y**	**P**	**P**	**P**	**P**
5 – Management Responsibility	*Evidence top management's commitment.*	*Y*	*Y*	*N*	*N*	*N*	*N*
	Provide a framework for reviewing quality objectives.	*Y*	*Y*	*N*	*N*	*N*	*N*
	Define responsibilities and authorities.	*Y*	*Y*	*N*	*P*	*N*	*P*
	Appoint a management representative.	*Y*	*Y*	*N*	*N*	*N*	*N*
	Implement management review.	*Y*	*Y*	*N*	*N*	*N*	*N*
6 – Resource Management	*Document process(es) for staff competence and training.*	*Y*	*Y*	*N*	*N*	*N*	*N*
	Document infrastructure requirements.	*Y*	*Y*	*N*	*N*	*N*	*N*
	Document work environment requirements.	*Y*	*Y*	*N*	*N*	*N*	*N*
7 – Product Realisation	*Document process(es) for, and record risk management.*	*Y*	*Y*	*N*	*N*	*N*	*N*
	Determine and review requirements specified by the customer.	**Y**	**Y**	**P**	**Y**	**P**	**Y**
	Determine product requirements not stated by the customer.	**Y**	**Y**	**P**	**Y**	**P**	**Y**
	Document plans for customer and regulatory authority communications.	*P*	*P*	*N*	*N*	*N*	*N*
	Document stages including: reviews; verification; validation; and responsibilities assignments.	**Y**	**Y**	**N**	**P**	**N**	**P**
	Produce outputs which are verifiable and approved prior to release.	**Y**	**Y**	**Y**	**Y**	**Y**	**Y**
	Document systematic design and development review.	**Y**	**Y**	**N**	**Y**	**P**	**Y**

	Document appropriate design verification plans.	**Y**	**Y**	**N**	**Y**	**P**	**Y**
	Document procedures for design transfer.	*Y*	*Y*	*N*	*N*	*P*	*P*
	Document procedures to control design and development changes.	**Y**	**Y**	**N**	**P**	**P**	**P**
	Maintain a design and development file for each medical device.	**P**	**P**	**N**	**P**	**P**	**P**
	Document procedures to ensure purchased product conformity.	*Y*	*Y*	*N*	*N*	*N*	*N*
	Create purchasing information template.	*P*	*P*	*N*	*N*	*N*	*N*
	Document procedures for production.	**Y**	**Y**	**N**	**Y**	**P**	**Y**
	Document procedures for validating processes.	*Y*	*Y*	*P*	*P*	*P*	*P*
	Document procedures for product identification and segregation.	*Y*	*Y*	*P*	*P*	*P*	*P*
	Document processes for product traceability.	**Y**	**Y**	**P**	**Y**	**P**	**Y**
8 – Measurement, Analysis & Improvement	**Document procedures for feedback.**	**Y**	**Y**	**P**	**Y**	**P**	**Y**
	Document procedures for timely complaints handling.	*Y*	*Y*	*N*	*P*	*N*	*P*
	Document procedures for notifying regulatory authorities of complaints.	*P*	*P*	*N*	*N*	*N*	*N*
	Document a procedure for internal audits.	*Y*	*Y*	*N*	*N*	*N*	*N*
	Monitor the QMS processes for effectiveness.	*Y*	*Y*	*N*	*N*	*N*	*N*
	Monitor and measure product characteristics.	**Y**	**Y**	**P**	**Y**	**P**	**Y**
	Document a procedure for issuing advisory notices.	*N*	*N*	*N*	*N*	*N*	*N*
	Document procedures for rework.	**Y**	**Y**	**N**	**P**	**P**	**P**
	Document procedures to determine QMS effectiveness.	*Y*	*Y*	*N*	*P*	*N*	*P*
	Document procedures for reviewing and correcting nonconformities.	**Y**	**Y**	**N**	**P**	**P**	**P**
	Document a procedure for determining and preventing potential nonconformities.	*Y*	*Y*	*N*	*N*	*P*	*P*

7.7. Chapter 7 Summary

In summary, Chapter 7 has:

- categorised the behaviours of each participant from each design session and presented them in diagrams reflecting the structure of their workflows (Chapter 7.1);

- highlighted the distribution of design questions throughout those workflows (7.1.1 – 7.1.3);

- presented images and key specification details of the design outputs produced by the participants using their pre-intervention workflows and with-intervention workflows (7.2);

- assessed which of the product and customer requirements from a master list were identified and then met (or not) by each participant, both with and without the design intervention (7.3);

- transcribed and justified the relevance of key participant quotations from the design sessions about the particular workflows which were undertaken (7.4);

- transcribed and justified the relevance of key participant quotations from the design sessions about their feelings towards their standard workflows and their workflows after intervention (7.5);

- assessed the size of the gap between standard workflows, intervention workflows, and ISO 13485 compliance (7.6);

- and in doing these, has therefore contributed to meeting objective 4 from Chapter 1.9 and to answering research question 3.3 from Chapter 4.2.4.

8. Discussion

This Chapter (Figure 101) evaluates and discusses the performance of the design intervention, using the results from Investigation C. Additionally, it relates those findings to the rest of the evidence generated by this research, which was used to justify the content and format of that design intervention. Furthermore, it comments on the success of the research as a whole. Finally, it discusses the research in relation to the objectives in Chapter 1.9 and the research questions in Chapter 4.2.4 in anticipation of solidifying the answers in the conclusion (Chapter 9).

At a general level, Investigation C demonstrated that the design framework was capable of driving a more consistent and rational product realisation workflow across three different operators and contexts. It showed that the actual or intended design outputs resulting from intervention-use succeeded in identifying and meeting more of the customer and product requirements than without intervention use. Indeed, it showed that the intervention could not only prompt the generation of a higher fidelity list of requirements at the outset, but could encourage those requirements to be made explicit, and consciously acknowledged. Participants generally displayed a positive reaction to their modified workflows; citing increased confidence, decreased stress, and a sense of comfort from having a clear structure and peer-reviewed evidence to-hand. Furthermore, the results indicated that the framework could assist with meeting a majority of pre-requisites for product realisation in ISO 13485 design certification.

On the other hand, the data suggested that the benefits from using the design intervention came at the cost of some discomfort on the part of the participants; who experienced a reduction in their process-flexibility and an increase in administrative demands. It also slowed the development process – at least during those first experiences of the new approach, and could not mitigate broader institutional weaknesses in demonstrating commitment to Quality Control (in the NHS). Given the mandatory nature of design controls in the medium term, thanks to an evolving regulatory landscape; the evidence from Investigation C pointed to the importance of future work, on expanding the intervention with extra and more robust evidence, and on facilitating efficient compliance with international standards by the inexperienced NHS institutions. After all, those institutions are predominantly set-up for delivering patient care, not design consultancy and design control.

The following sub-Chapters explore these general claims in more detail; beginning with those related to the performance of the design intervention (sub-Chapter 8.1), then those about the content of the intervention (sub-Chapter 8.2), before addressing those associated with the quality and success of the research itself (sub-Chapter 8.3).

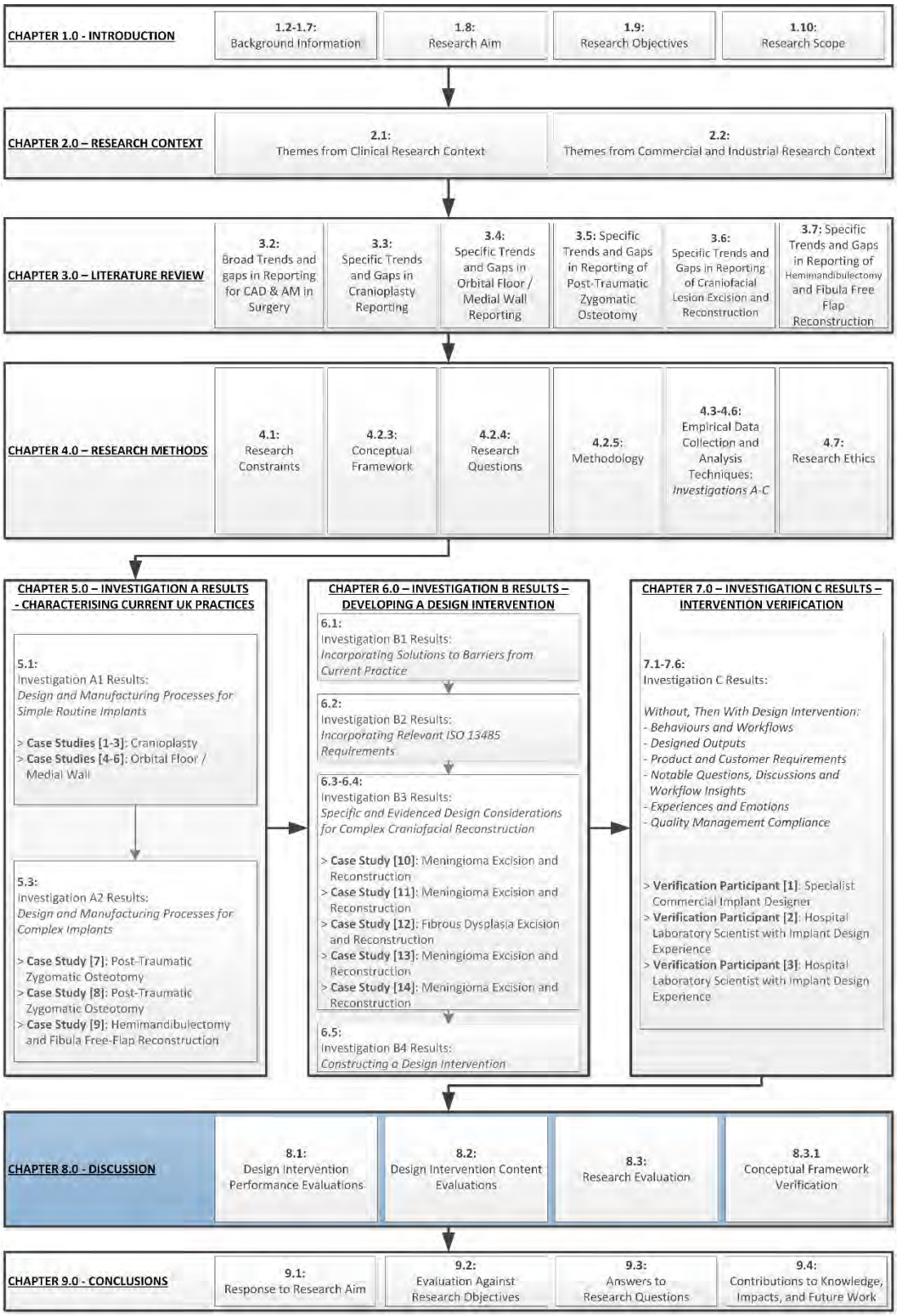


Figure 101 - Thesis Overview, With Current Location Highlighted (Chapter 8)

8.1. Design Intervention Performance

'Performance' was taken to be the ability of the design intervention to directly (or indirectly) help lower the barriers to efficient, safe, and routine adoption of CAD and AM or CNC patient-specific devices. It relied on deep insights from rich data, across a purposive selection of three participants.

8.1.1. Workflow Evaluation

Sub-Chapter 7.1 evidenced a significant realignment of the observed design workflows after deploying the design intervention. In every case, the intervention workflow was shown to take up the full duration allowed for the design task, and resulted in less-thoroughly progressed CAD models than when participants worked as normal. However this apparent cost came with the benefit, at the end of the design sessions, of having the majority of the product realisation documentation already prepared – which was not the case with standard processes. That documentation was a tangible measure of progress towards one appropriate method of quality management for medical device design. This is vitally important in the context of a compulsory-compliance future, and in the context of a present which is on the evidence of this research, and the wider experience of the institute, fundamentally lacking in commitment to formal design controls on the part of the studied NHS institutions.

For Participant 1, the workflow driven by the design intervention was more linear – with the behaviour categories appearing once, and in their natural sequence – with the minor exception of a single correction during development modelling of the second implant component. This contrasted with the standard workflow which was more back-and-forth. For example, Participant 1 said:

> *"So this time round, I filled out all these forms, I knew in my head what I needed to achieve, whereas the time before that I started designing and – not made things up as I went along – but kind of, changed things as I went along".*

This was reflected by the fact that behaviours were observed for longer periods in the intervention sequence, with this participant constructing their intervention workflow from the perspective of discrete modelling stages, as opposed to fluctuating between stages on a component-by-component basis. This change cannot be said to have an intrinsically positive value, at least based on the evidence from this research. However, it did perhaps *represent* a greater sense of patience and a more methodical approach. It also acknowledges the importance of design intent – before starting to design. Incidentally, the use of 'design' to refer in actuality to 'modelling', is indicative of the misunderstanding of design – even amongst its professional practitioners. This theme ran through the sessions.

The gratification (or, indeed relief) of seeing a completed component was offset to the end of the process, where development and refinement 'finishing' activities could be grouped together. Future work should investigate the value of this 'functional rhythm' in which similar modelling functions are deployed consecutively across separate components. Similar trends in workflow realignment were more difficult to discern for Participants 2 and 3. Participant 2 produced a single-component design using their standard workflow which tempered the strength of the comparison with their intervention workflow. That said, when using the intervention, they too adopted a structure based on undertaking similar modelling activities across multiple components, rather than discretely completing each component in sequence.

Participant 3 had already deployed a discrete modelling-stage-driven approach in their standard workflow. In their intervention workflow however, they more than doubled the time spent on a "Sketch Modelling" phase. This involved using virtual painting tools to draw their design solution onto the anatomy before committing to modelling proper. While this does not suggest a significant realignment of the behaviours and activities as for Participants 1 and 2, it hints at a more considered, methodical, and stage-gated approach. When using the intervention, Participant 3 spent longer clarifying their design intent before investing time and energy in realising the implant geometry.

Most strikingly on the issue of design intent, was the very significant up-front time spent by all participants on populating the design intervention form – in their second sessions. There were no direct equivalents of this activity in any of their standard

workflows. Instead, bursts of verbal conceptualising (speaking out loud, both to the researcher and to themselves) were the limited extent of planning design, reviewing design considerations, and project management. This behaviour also appeared at different points of the workflow in each case: immediately prior to beginning CAD software setup (Participant 3); prior to basic modelling (Participant 2); and prior to sketch modelling (Participant 1). To some degree, the workflow variation from Investigation C echoes the multitude of different service models and procurement methods offered by commercial design services (Chapter 2). Theoretically, so long as the product requirements are identified and met, and the quality standard compliance requirements are fulfilled, the variation in workflow structures should not affect product quality. This was not the case for the participants in Investigation C. The consistent structure of the design intervention workflows (at least for the front-end) ensured that the product requirement and QMS pre-requisites were met. They were met whilst presenting a regular, reliable front (or touchpoint) to the customer, via the designer.

The success of this new approach, at least amongst the small sample of participants in this research, should not be too surprising, given the nature of the design process across other contexts. Traditional depictions of the design process place an emphasis on defining the design brief in the first instance; ahead of defining a high-fidelity product design specification after technical and user research (Pugh, 1991, Norman, 1998, Shove et al., 2007). The only surprising aspect is that these characteristics were absent from the observed standard workflows, as well from any kind of commentary in the published literature (Chapter 3). Perhaps this is related to the relatively modern focus on the importance of design (as well as the difficulty in communicating its value to surgeons). Despite descriptions of best practice always featuring collaboration as a central theme (Sugar et al., 2004, Thomas et al., 2013, Huotilainen et al., 2013, Martelli et al., 2016, Bibb et al., 2015), true cross-disciplinary research outlets are limited. For instance, conferences and publications tend towards divergence; with clinical specialties (British Association of Oral and Maxillofacial Surgeons, 2018, Journal of CranioMaxilloFacial Surgery, 2018) mostly separated from technical or engineering expertise (Rapid Prototyping Journal, 2018, Additive Manufacturing, 2018). This is not to say that they do not have anything to say about their competing fields; but it does heavily favour their own perspectives. The Advanced Technologies in Head and Neck Reconstruction

Triennial Congresses (ADT Foundation, 2018) are an outlier; in specifically aiming to attract dissimilar researchers and practitioners in order to seek a new cross-disciplinary perspective. Furthermore, the defensive approach of some UK NHS institutions towards CAD and AM professionals (as discussed in Chapter 2) is an indication that the trend could continue to be one of specialism divergence unless innovative ways of transferring knowledge can be implemented.

Aside from encouraging the participants towards a more traditional and more consistent workflow structure, the design intervention concentrated the occurrence of questions to the very front-end of the design process. This was to be expected – because of the expansive range of data fields which had to be considered when properly populating the form. Asking more questions up-front improved the identification of product requirements, which therefore improved the degree of ISO 13485 compliance. This also improved the collective anticipation and clarity of the participants design intent – as will be explored in detail in sub-Chapter 8.1.3. Exploring the theme of pragmatism and practicality further, the concentration of questions into a more systematic workflow, also served to rationalise and streamline the need for communication with the surgeon. Communication and discussion was focused on approximately 60 minutes at the outset of the projects. For the standard workflows, questions about design features or the surgical plan were spread throughout the session and across the discrete-yet-cyclical observed behaviours. Furthermore, there were significantly fewer questions asked during the standard workflows.

A word of caution was sounded by Participant 3 when discussing major difficulties during their standard working days. They often failed to obtain sufficient surgeon contact-time for design feature discussions or virtual surgical planning. This effect was more pronounced for Participant 3 than for Participant 1, partly because of the staff hierarchy from being based in the same NHS institution as the surgeons. Participant 3 demonstrated, via interview quotes, a significant awareness of their perceived junior standing and sub-ordinate position in relation to their consultant surgeon colleagues. In the experience of Participant 3, those surgeons would spontaneously call-in to discuss patient cases in short bursts when they could find time:

"they might pop in when they have five minutes in between clinics – and you have to down tools and go back to an old case".

It was also a frustration of Participant 2:

"getting the consultants here is by far the biggest problem – because a lot of the time we know there are deadlines to meet, we feel we can't progress until we've shown them".

Clearly then, the design intervention workflows observed during Investigation C would be incompatible with these realities if implemented in their current form. However, a mandatory compliance future suggests that there would be a power bias towards the designer in this new scenario – in terms of being able to demand compliance or (preferably) encourage co-operation through justifying design control activities. After all, non-co-operation risks missing out on a CAD and AM or CNC macined device altogether. Persson and Warell (2003) noted the importance of a mutual understanding between industrial and engineering designers, in terms of the respective purposes and consequences of each stakeholders' actions. Although different competencies to that previous work, a similar requirement was evident, by its absence, for Participants 2 and 3. The understanding was not necessarily mutual between surgeons and designers (or acting designers). Installing quality management systems into NHS institutions (or more specifically, individual departments involved in device design and fabrication) will therefore need to involve more than technical compliance. Even based on this limited evidence, it seems that it would represent a step-change in terms of interpersonal power structures and perhaps, the workplace culture; through this suggestion should be explored through future work.

As verifiable patient safety, and the basic legal capacity to deploy these cutting edge techniques, hinges on more thorough surgeon commitment to the front-end of the design process, future research will be required to determine effective ways of communicating the value of this disruption to them. To this end, as raised in Chapter 2.1.2, the training programs for trainee doctors, NHS managers, and support staff should find ways to accommodate modules or other insights to the key aspects of design control and product safety. This is particularly important in a health service which shows little sign of retreating from an increasingly market-driven philosophy. Ideology aside, a successful free-market requires informed customers (Darby and

Karni, 1973), and this would be the case whether procuring a custom device from an internal hospital department, or from an external commercial supplier.

Contact or collaboration time between clinical and design knowledge-bearers in the literature, was often overlooked and had to be inferred. One example of a clear statement was about the size of the fundamental knowledge-gap between the disciplines – which Mazzoli et al. (2009) described as making teamwork more difficult. This was corroborated by Case Study 3 from Investigation A in this research. It showed how that knowledge-gap led to an insufficient clarity of problem definition. This in turn, failed to build all of the necessary constraints into the device specification. There was an inconsistent comprehension of the surgical plan across customer and designer. To this end, the design intervention was wholly successful in reducing the working knowledge-gap, at least to the reasonable degree it was measured in the simulated design exercises.

8.1.2. Requirements Evaluation

Sub-chapter 7.3 showed that participants identified, and then met, more of the customer and product requirements when using the design intervention than when not. In fact, all three participants met *all* of the requirements when using the intervention; having identified them clearly beforehand. This indicated that meeting the requirements was entirely deliberate when using the intervention. Instances of a requirement being accidentally met, coincidentally met, or assumed and then met, were reduced to zero. A quotation from Participant 2 highlighted the element of chance in the standard approach, relative to the intervention:

> *"Prior to having something like this, things were a little more amorphous, and you would rely a lot more on luck – and you'd make a lot more mistakes".*

Quite apart from being logically sound and a requirement for compliance, the aim to have a high-fidelity design brief and product specification (requirements list), was validated by case studies 3, 8, 9, and 13 – across Chapters 5 and 6. In each instance a design failure was (or could) have been avoided, or a successful design output was produced; on account of deploying lessons from experience with similar cases, and

a familiarity with their unique, specific, evidenced design considerations. While the design intervention cannot ever manufacture true first-hand experience, it appeared to successfully transfer the knowledge from others' experiences to the designers who were unfamiliar with the given pathology. Additionally, as noted by Participant 3, the intervention form prompted the maintenance of comprehensive records on details which would be necessary for proper presentation or later publication. It is reasonable to suggest that this aspect may offer a subtle route to improving the quality of the description and analysis in surgical, design, and additive manufacturing journals.

The intervention form prompted the designer to ask questions and engage in focused short discussions about each field. It (however artificially) created the framework for a methodical, systematic, and importantly a repeatable approach to defining requirements and ensuring a shared comprehension of the surgical plan. At times, the questions were asked in a fairly bland, monotonous, robotic manner (possibly suggestive of boredom) such as by Participant 2:

> *"Required on or before…?"*
> *"Device material…?"*
> *"Device surface finish…?"*

Still, repetition of this project front-end structure may be an avenue for future investigation and development. The utility of this repetitious approach, for educating surgeons about the importance and breadth of design parameters, is likely to depend on finding a careful balance between demonstrating the mechanics of the design process, and doing so in a manner which is sympathetic to busy schedules. There were expressions of concern about standard operating procedures from Participant 3:

> *"You can't really tell people how to work fully, because then it will just stop design completely"*

and from Participant 2:

> *"they can just – stifle your creativity and your ability to work quickly"*

during their first design sessions. However, these statements were contradicted by their statements during the intervention-led sessions. That fact would suggest that the framework achieved a reasonable balance between freedom and structure.

8.1.3. Experiences, Emotions, and Interactions Evaluation

The main emotional themes (see sub-Chapter 7.5.1) arising from the standard workflows were confusion, frustration, and separately - a degree of enthusiasm (about being able to try, and overcome, a new type of implant design problem). To take one example in detail, on the issue of confusion, participant 1 said:

> *"I initially was a bit worried and a bit concerned, but when the surgeon had specified quite a few things, it becomes easier and you've got your head 'round it, and you have like a vision in your head of what you want the outcome to be"*

and:

> *"When you initially get the data, it's like 'how am I going to fix this?' – but then you ask yourself smaller questions, and it gets easier".*

This is relevant not only for its demonstration of an initial confusion, but also because it demonstrates the means by which the participant solved their confusion. They broke the problem down into smaller individual questions in order to establish a manageable design direction. By referencing the mental vision of the desired outcome, the participant seems to be establishing a basic design intent – knowing what they wanted to achieve before starting the modelling stages. This was an aspect which was multiplied by the addition of the design intervention. Crucially, the participant ascribed their lack of initial mental vision, as a reason behind their concern. This may reinforce the technical and logical assertions that recommend establishing design intent before modelling. Moreover, the primacy of material visualisation (sketches) during conventional new product development (Pei et al., 2010) was not replicated to any degree by the participants in Investigation C. Perhaps then, future work could explore the value (or lack thereof) of tools to enable visualisation at the earliest requirements-gathering stage to explore their implications. However, any such tools should make the provisional, limited nature

of those visual representations clear, so as to avoid narrowing the perceived scope for downstream modelling activity (Stacey and Eckert, 2003).

A caveat to this analysis was provided by Participant 3 during their standard workflow session:

> *"I think it's the method – it's the way in which you do things – the stages that for me, because I hadn't done it before, I didn't know what to do at what point"*

and by Participant 2 during theirs:

> *"It is quite stressful – because we don't follow a particularly prescriptive path, (and I've not done one for a while), so I'm not following a checkbox down – so that makes it more stressful".*

It was difficult in isolation to ascertain whether the up-front confusion and trepidation had been caused by the workflow, by the fact that visualisation was difficult because the design exercise was based on a brand new surgical procedure (to the participants), or caused by something else entirely. However, as will be noted in the next sub-Chapter, the total absence of *design* confusion emotions from the intervention workflow results, did suggest that the issue of process had a significant causal role. That is not to say there was a complete absence of confusion; for example there were significant problems with the wording of a range of design intervention field headings.

Utterances from Participants 2 and 3 illustrated a surprisingly defensive activity in their standard workflows; not associated with design control or compliance per se, but with accidentally achieving limited record-keeping to fend-off potentially misplaced future blame for mistakes. For example, Participant 2 said:

> *"but we very much try and put the ball in their court as far as the design is concerned, so that we don't – get the blame"*

and Participant 3 said:

> "*So that if it comes back you can say 'well you agreed it'".*

Again, this refers to the power imbalance between the design project collaborators. Here, the designer feels the need to have hard evidence for use in disproving a more senior staff member's claims. The intervention did not, and could not directly overcome interpersonal issues such as these. Nor the lack of appreciation surgeons have for the difficulty of making last minute or large scale changes to a design file.

On the other hand, the main emotional themes arising from the intervention-driven workflows were confidence, calmness, and a small amount of irritation (about the extent of the new considerations). Overall, the degree of confidence and calmness created by the intervention was surprisingly high. The intervention excelled in this aspect. This was demonstrated specifically by Participant 1:

> *"during the design you're a bit more relaxed because you're not constantly thinking – 'oh what other considerations do I need to be thinking about?' – if you've got them written down in front of you"*
>
> *"when you've got it written down in front of you, it's less stressful"*

and Participant 2:

> *"it did help crystallize what you're trying to achieve by having a prescription there, or a checklist"*

and Participant 3:

> *"it made me more confident at the end of my own design because you're double checking everything is right – it didn't get angry or frustrating or anything".*

Of course, the emotional improvements were observed only across a small sample of specialist participants. But, given the uniformity of their reactions, it demonstrated real promise for experiential improvement – at least for the designers, in parallel to the more tangible benefits about product requirements, quality and regulatory compliance, and workflow structuring. It appeared that these benefits were sufficient to overcome the scepticism and irritation demonstrated by Participants 2:

> *"(turns page of framework)… cor blimey – this isn't as much fun as last week".*

"I found it a lot harder because I was trying to take in more parameters"… "there was a lot more going on in my head."

and 1:

"there was a lot of text initially so – I feel overwhelming is a bit of a strong word to use"… "Quite a lot to take in, but like I said earlier, you're then prepared".

8.1.4. Compliance Evaluation

It is vital to be aware of the participants QMS contexts before evaluating the value of the intervention - towards ISO 13485 design compliance. Only Participant 1 was from an organisation which was aiming to comply with the ISO 13485 requirements at the time of Investigation C. The results in sub-Chapter 7.6 mirror this; where Participant 1 demonstrated no change in compliance-rate from their standard workflow to their intervention-led workflow. The comprehensive existing system left little room for greater compliance. The improvements for Participant 1 were restricted to the workflow re-structuring (which grouped the majority of the questions, surgeon interactions and a significant amount of paperwork to the front-end).

Where participant 2 or 3 met the requirements, it was for basic internal project management reasons, or it was coincidentally – through personal style or preference. Participants 2 and 3 naturally, demonstrated more numerous changes, all of which were improvements of some kind. Judgements were conservative – because a 13485-compliant QMS must be by definition, extensively documented by, and specifically tailored to an individual organisation. As a result of this, the most frequently occurring changes were from 'Not Met' to 'Partially Met'. The intervention was able to introduce some key procedures and record-keeping practices as a push towards proper quality management, but could not be expected to introduce full compliance.

There are two technical barriers to implementing an ISO 13485-compliant QMS in a hospital laboratory (or equivalent unit). Firstly, a system must demonstrate management commitment to quality and proper resourcing to achieve that aim. With increasing financial pressures on the NHS, even under the current lighter regulatory burden, the likely difficulty is clear. Secondly, a system must be uniquely tailored to the unit's size, skills, scope, and purpose. A catch-all QMS template, dropped into hospital units, would be the most immediately satisfying solution to the lack of Quality Management Systems in the NHS. However, such a move would be unlikely to succeed in demonstrating system appropriateness, tailoring, and full integration, to visiting auditors. This leaves space for important future research. It would be focused on finding effective and cost-efficient methods to introduce *adaptable* template-style systems, and the training required for NHS staff to adapt and implement said procedures, forms, and records.

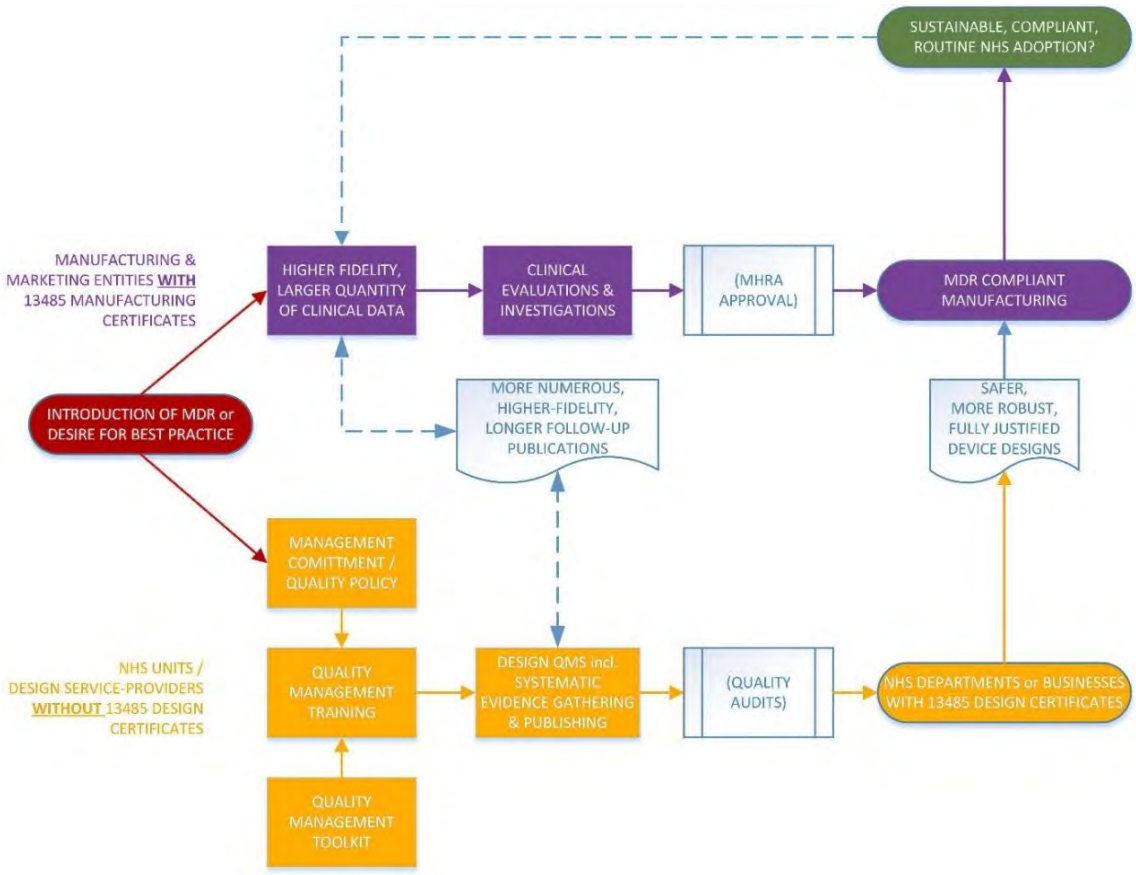


Figure 102 - Potential Aim of Future Work

Given the infrastructure costs, the financial pressures on the NHS, and the manufacturing regulatory burden, a system as depicted by Figure 102 above may

offer a viable future route to routine CAD and AM or CNC device use. In it, AM or CNC remain the domains of external manufacturing entities (at least for the medium term); until costs and ease-of-use improve. Device design services, be they in-hospital or externally-supplied, would be prepared for audit to ISO 13485 by an expanded array of transferrable, and generalisable QMS template documents – building on the design intervention form evaluated here. Parallel training courses would be required for both design staff and management. This would be vital for a context in which there is very little experience with international quality standards. Even in the design and engineering context of the institute, understanding the lexicon, accepted norms, and assumed knowledge around QMS development, was a particularly high barrier to development of the QMS aspects of the design intervention. Management commitment through tangible resource allocation and ethos buy-in would be required, external to any generalised support which might be developed from the initial findings in this research.

In this predicted system, better published data (in fidelity and quantity), which is enabled by the QMS record-keeping requirements, is the fulcrum around which the design and manufacturing quality and regulatory compliance hangs. Figure 102 is a reasonable extrapolation of this research context. The MDR emphasises the manufacturer's responsibility for verifying the efficacy and safety of design considerations through clinical evaluation and investigation (European Council, 2017); it will no longer be acceptable to cater solely to surgeon requests for a specific approach or feature. Therefore, only design solutions proven to be safe by the manufacturing entities' own evidence may be used. The pre-eminence of better data in the diagram is then, appropriate.

Compliance, by meeting the product and customer requirements to the letter, does not necessarily indicate a good modelling technique or a highly refined geometry. This was a weakness of the framework, but was a necessary to facilitate use across different design software tools. Indeed the flexibility of the framework across contexts and users, can offer a perspective on how benefits and drawbacks may differ across those ranges. Benefits for users who are already operating under a QMS, or who are otherwise structured in their standard workflows, might be limited to evidence provision and record keeping. Benefits for unstructured designers might be more noticeable in an improved ability to identify requirements, even if support

is required to meet them through modelling. Intriguingly, a further power-balance development might be catalysed – in addition to that between designer and surgeon, which was discussed already. Participant 3 said:

> *"that's difficult – because you can tell one person to create folders – but, erm, they don't"*

Which indicated that frustration about intra-institution compliance was an issue. Perhaps with an external template and an internal mandate, the issue of power to compel internal compliance will be at least partially solved. This would be a more minor avenue for future investigation – in the area of change management.

8.2. Design Intervention Content

This sub-chapter will reflect on, and evaluate the data collected and analysed in Investigations A and B. It was these data and these conclusions which served to justify the content, structure, and medium of the design intervention – as presented in Investigation B4.

8.2.1. Project Management and QMS Compliance Content Evaluation

The fundamental need for a robust and repeatable design process for patient-specific devices, was identified predominantly through the results from Investigation A. Within the constraints of the research scope, and the limitations of the research methods, the new evidence and analysis generated through Case Studies 1-9 led to clear and relatively conservative inferences. For example: the AM cranioplasty design failure in Case Study 3 resulted in the stipulation for dealing with the operating clinician in the design intervention. Furthermore, the dramatic improvements in design time (and therefore design costs) from having limited design intent and no set workflow in Case Study 7, to having standard operating procedures and increasingly evidenced design considerations in Case Studies 8 and 9; resulted in the same recommendations for the intervention. This analysis in turn, had been framed by the poor consistency and fidelity of reporting by authors in the published literature.

Simple inferences like those referenced above, might on reflection be seen as pragmatic, logical, and natural reactions to current practice failures. Even so, they meshed easily with, and were significantly bolstered by the requirements arising from the regulatory and quality management landscape. Though less directly linked to the observed processes, and certainly with a more opaque path to implementation, the steps taken in Investigation B to systematically adhere to the requirements of ISO 13485 (and so the MDR) were ultimately complimentary to the solutions to issues from Investigation A. Eventually, the nature of individual components of the design intervention were not surprising, nor dramatic departures from standard product design documentation. What was distinctive, was the systematic synthesis of experienced barriers to routine adoption, observed barriers, existing clinical evidence, solutions to clinical evidence gaps, a need for design context flexibility, and a looming legal requirement to meet the ISO 13485 standard for design.

At a granular level, the verification activities in Investigation C suggested some improvements for future iterations of the design intervention. A delay was caused by a CAD software crash for Participant 2. The intervention form should provide a simple reminder to save the CAD file at regular intervals. Furthermore, it could recommend a modelling strategy which permits reversion to previous stages where required (because some software has limited 'undo' functionality); in those instances where the software does not possess this ability already through employing a parametric modelling method. In similarly quick-win fashion, generalised recommendations to name, store, backup, and correctly maintain CAD files in accordance with the institution's procedures could be included.

8.2.2. Design Considerations Content Evaluation

As detailed in Chapter 6.3, the specific design intervention content for considerations in orbital-temporal reconstruction were derived from Case Studies 10-14. Again, within the resource and time constraints of this research, the limitations stemming from a relatively small patient cohort were reasonable residual methodological weaknesses. This was particularly the case in light of their standardised and more detailed reporting compared with much of the existing literature. The risk of falling

prey to rushed conclusions from the small series was tempered by comparing the primary findings with those stated or inferred from the secondary literature.

All five implants presented in Case Studies 10-14 were evaluated, by the surgical team, as clinical improvements over conventional methods in terms of: cosmetic accuracy; replicating complex geometries; reducing surgery durations; avoiding the downsides of autologous reconstructions; basing reconstructions on mirrored healthy anatomy; and helping to enable successful single-step procedures. After iterative improvements between cases, outcomes corroborated the literature in four other areas: using guides to accurately translate plans into theatre; achieving a more accurate implant fit; using PEEK for cases requiring radiolucency for post-operative radiotherapy and imaging; and applying holes or a mesh pattern across the main implant surfaces.

Post-operative soft-tissue (including muscle) concerns in cases 10 and 12, echoed similar issues from other studies (Scolozzi et al., 2007, Rotaru et al., 2015, Jalbert et al., 2014). Currently, virtual soft-tissue predictions are difficult (Pfaff and Steinbacher, 2016) and were not available in any of the cases 10-14. There was a reliance on clinical judgement instead – with no explicit design changes made beyond aiming for good symmetry. Recommendations (where available) were split between: anticipating soft-tissue atrophy by over-correcting contours (Pfaff and Steinbacher, 2016); mirroring soft tissues as well as hard tissues when planning implant forms (Marbacher et al., 2011); and noting that soft tissue asymmetry cannot always be dealt with using implants alone (Alonso-Rodriguez et al., 2015). The palpability issue in case 13 was not directly related to digitally designed and fabricated devices, but supports a general aim of making implants as small as possible – to avoid this, and to lower the risk of exposure (Mertens et al., 2013).

The detailed design issues raised by the case studies have flexibility as the major theme – of fit, of function, and of margins. Alternative margin solutions from the literature appeared muddled; including the notion of deliberately designing over-sized implants, before adjusting them in-theatre once the margins were finalised (Pfaff and Steinbacher, 2016). Whilst this offered an answer to intra-operatively modified margins, it introduced extra time into the procedure as a matter of routine. The solutions from cases 10-13 of using long tabs, and deliberate gaps between the

residual anatomy and the main implant components, at least created the probability of instant insertion without sacrificing fit and margin flexibility. The opposite solution has also been proposed; with deliberately-undersized implants, having large gaps to the bone subsequently filled with cement (Rosen et al., 2008). This still under-exploits the time advantages created by using digital surgical planning and custom implants.

Smaller margins than anticipated are difficult to foresee in similar cases – especially with using slice-by-slice analysis of the CT scan data to delineate the lesion at the point of planning (Jalbert et al., 2014). Planning generous excisions (Gerbino et al., 2013) was supported, as was the use of guides to translate them into theatre. However, guides were not reported as often as expected (given the previously described benefits) which may indicate why PEEK's intraoperative modifiability was often cited as a significant positive. On the question of modifications versus plans, seven reports cited standard mini-plate fixation for PEEK devices. The solution from Case Study 14 was unique in incorporating titanium-device-style tab fixation. The concern about the implant sinking into the skull was shared by Jalbert et al. (2014) who chamfered the bone edge and contacting implant edge to achieve a robust brace. Before judging effectiveness, a comparison would be needed between the time-taken to burr-away tab-acceptance grooves as in case 14, and the time taken to chamfer the bone and implant edges. Simpler edge-overlap approaches were demonstrated by Guevara-Rojas et al. (Guevara-Rojas et al., 2014) who also added fixation holes to the implant edge. For implant fitting flexibility, experience from Case Studies 10-14 which recommended multiple part devices, was supported by Goodson et al. (Goodson et al., 2012) – for aesthetic and insertion-path independence reasons.

Accurate cost assessments across techniques and materials were difficult because of variations between service provision, currencies, and the previously-identified bias towards PEEK devices in the literature – compared to AM titanium. Furthermore, titanium was sometimes identified as the chosen material – without full clarity on the fabrication method. Manrique et al. (2015) provided an average cost for PEEK devices of $8493 from six cases. This was at least somewhat similar to the cost of the PEEK implant in case 14. The AM titanium devices were of a lower cost in cases 10-13. This again requires more evidence from future studies, but on the basis of the

primary data available to the researcher, the consideration was justified for using AM titanium where specific PEEK properties are less relevant.

On the whole, the design considerations content of the intervention form was unique in drawing together these different strands from what was an inconsistent body of existing work. Its contributions, through identifying new clinical design considerations need to be strengthened by long-term follow-up of Case Study patients, but also from other clinicians and researchers contributing to consistent data fields.

Finally, and more tangentially, there was little evidence of overt, detailed consideration of ergonomics factors in the patient-specific AM device literature. A useful framework for rationalising what can otherwise be abstract concepts was offered by Jordan (2000) which centred around product-related pleasures. These could (and on the evidence of Investigation A, should) play a larger role in device specification development. For example, physiological pleasures from comfortable implant handling, psychological pleasures from easy verification of correct guide seating, and sociological pleasures from peer perceptions as being state-of-the-art, could all be additional factors for exploitation towards routine adoption.

8.2.3. Format Evaluation

In this research, the design intervention was presented as a paper based form to accommodate research constraints and to ensure generalisability. Conceivably, future work on new iterations either on an individual implant-category level, or on an institutional level, could be presented as mobile applications, or web pages for browsing and using across a range of platforms. Even when considered briefly, the potential is evident for helping to alleviate the difficulties in capturing sufficient surgeon time. If, for example there were a mobile app containing: the data entry fields; the referenced evidence for design considerations from the published literature; the patient's scan data; and (or) images of design detailing options; the designer or acting designer could accommodate the surgeon's ever-changing schedules and locations. This may also have scope for solving a minor complaint about presentation from Participant 2:

"I think I would probably have had (preferred) a final crib sheet to refer to, throughout the design process so that I wasn't looking back".

Here, Participant 2 was referring to a desire for a verification summary – to make it easier to hold the sometimes competing design considerations in their mind; whilst solving the design problem and modelling the devices. With tight control of the content of a mobile application (especially where crucial stages like verification are concerned); personalisation of the presentation or recall functions might help lessen the burden of adapting to the new workflows. However, as so often when considering the NHS context, resources and infrastructure are the potential barriers. Data security in the NHS is critical, which results in significant restrictions on access to web services and devices. Combined with ageing hardware, this is a barrier to overcome in future investigations.

8.3. Research Evaluation

Within the scope and resources of this research (Chapter 1.10 and Chapter 4.1), and having mitigated the acknowledged weaknesses to the degree permitted (throughout Chapter 4), the realisation of this research is most effectively evaluated by revisiting and updating the refined conceptual framework (from Figure 29 in Chapter 4.2.3).

8.3.1. Conceptual Framework Verification

Figure 103 shows a final version of the conceptual framework constructed for, and verified by this research. It includes minor clarifications in phrasing. Most importantly, it adds factors and links (both indicated by dashed lines) which have emerged from investigations B and C. Although the majority of the links in the framework will benefit from a larger quantity of, and higher fidelity of clinical and economic evidence, the newly added factors represent promising avenues for future work which did not feature in the existing literature. Each link from the framework is, once again, evaluated (in Table 30) in the context of the totality of data from this work.

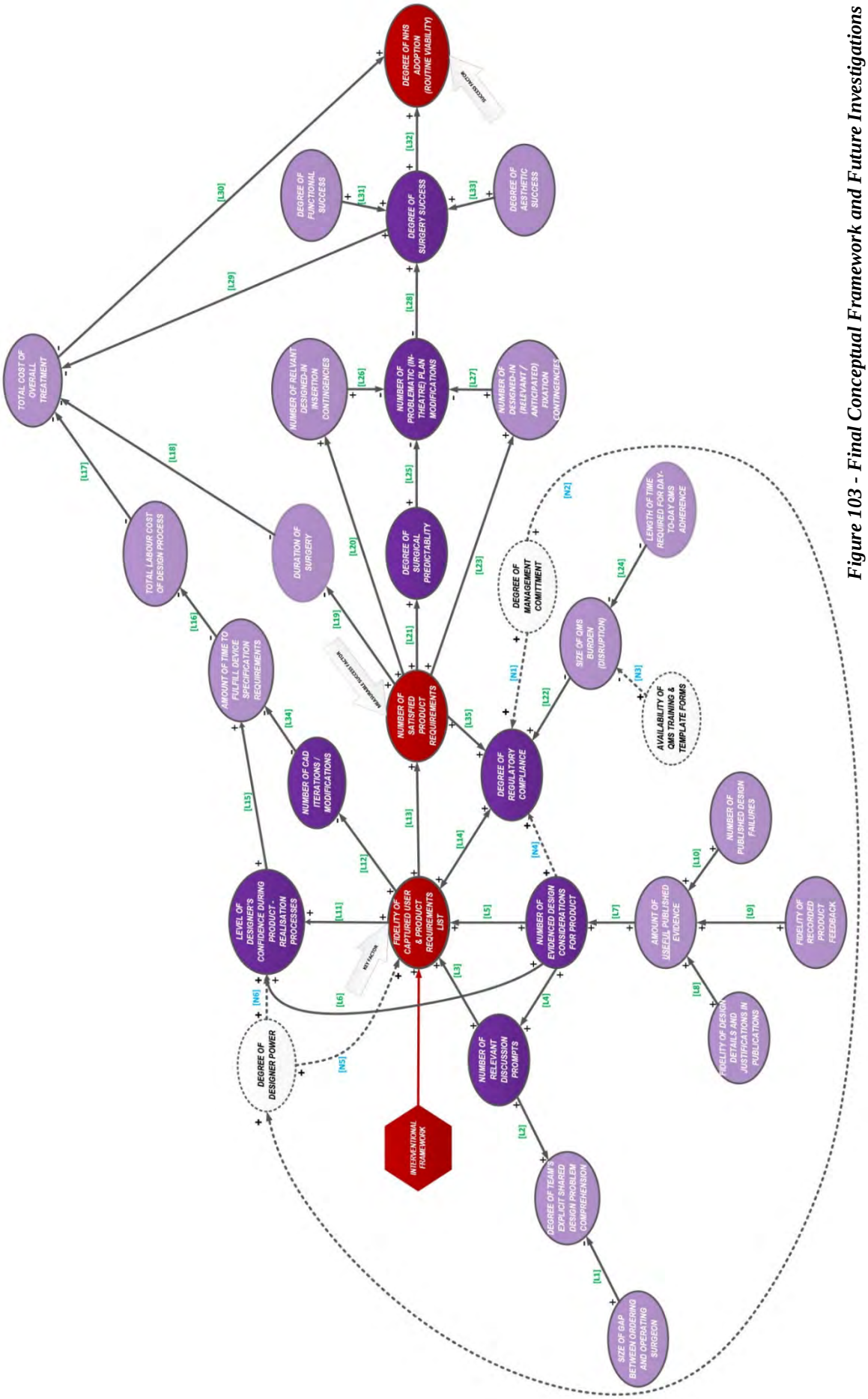


Figure 103 - Final Conceptual Framework and Future Investigations

Table 30 - Individual Links from the Final Conceptual Framework

Individual Links	Original / Proposed Evidence Source(s)	Evidence from Investigations B / C & Future Work
[L1]	Investigation A1. / (Peel and Eggbeer, 2016)	Not targeted for support from Investigations B and C. However, this deserves consideration by authors when publishing higher fidelity papers in the future – such was its significance in Investigation A.
[L2]	Chapter 2 – Research Context. *Targeted by Investigation C.*	Supported by all three participant datasets from Investigation C. Designers shared the surgeon's problem comprehension more thoroughly when using the intervention form.
[L3]	Investigation A1. / (Peel and Eggbeer, 2016) *Targeted by Investigations B and C.*	Very strongly supported by all three participant datasets in Investigation C.
[L5]	Investigation A1, Investigation A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016). *Targeted by Investigations B3 and C.*	Very strongly supported by the general design considerations from Investigation B1 and the specific considerations from B3; which led to improvements when using the framework in C.
[L7]	Chapter 3 – Literature Review. Investigations A1 and A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016) *Targeted by Investigation B3.*	Very strongly supported for the single implant type (temporal-orbital) by Investigation B3. Considerable further work required from the field as a whole; via better reporting in publications.
[L8]	Chapter 3 – Literature Review. *Targeted by Investigation B3.*	
[L9]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. Chapter 3 – Literature Review. *Targeted by Investigation B3.*	
[L10]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)	Not directly targeted for support from Investigations B and C. However, the in-depth criticism and hypotheses-for-improvement in Investigation B3, represented the type of detailed evaluations required in future - from a design perspective rather than a clinical point-of-view alone.
[L6]	Chapter 2 – Research Context. *Targeted by Investigations B3 and C.*	Very strongly supported by all three participant datasets in Investigation C.

[L11]	Chapter 2 – Research Context. *Targeted by Investigations B3 and C.*	Very strongly supported by all three participant datasets in Investigation C.
[L12]	Investigation A2. / (Peel et al., 2016) *Targeted by Investigations B3 and C.*	Supported by the rationalisation of the participant workflows in Investigation C. However, no participants in Investigation C undertook discrete wholesale design iterations.
[L34]	Chapter 2 – Research Context. Investigation A2. / (Peel et al., 2016),	Not targeted for support from Investigations B and C (because of session time limits). However, when using the intervention, participants demonstrated significant modelling progress *whilst also* completing the majority of product realisation QMS paperwork.
[L15]	*Targeted by Investigation C.*	Weak support – for similar reasons to [L34] in the row above. Reasonable to suggest that with practice and familiarity, this link could be supported. However, future work is required to verify this fully.
[L16]	Investigation A1. / (Peel and Eggbeer, 2016), (Peel et al., 2016)	Not targeted for support from Investigations B and C. Largely evident from Investigation A – but economics evidence is significantly lacking across the field as a whole. Major area for future work.
[L17]	Investigation A1. / (Peel and Eggbeer, 2016)	
[L13]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. Investigation A1. / (Peel and Eggbeer, 2016)	Not targeted for support from Investigations B and C. However, good support offered by each participant dataset in Investigation C – by capturing a higher fidelity requirements lists with the intervention; and describing more appropriate design solutions having done so.
[L14]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. *Targeted by Investigations B4 and C.*	Very strongly supported by all three participant datasets in Investigation C.
[L35]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards.	
[L22]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. *Targeted by Investigations B4 and C.*	Supported by participants 2 and 3 in Investigation C; via concerns about achieving compliance given time constraints and personal style differences. Future work required to define the ideal balance between compliance and usability.
[L24]	Chapter 1.6 – Relevant Bodies, Regulations, and Standards. *Targeted by Investigations B4 and C.*	

[L21]	Chapter 3 – Literature Review. Investigation A2.	Not targeted for support from Investigations B and C. However, these demand consideration by authors when publishing higher fidelity papers in the future – such was their significance in Investigation A.
[L25]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)	
[L20]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)	
[L26]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)	
[L23]	Chapter 3 – Literature Review. Investigations A1 and A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016)	
[L27]	Chapter 3 – Literature Review. Investigations A1 and A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016)	
[L28]	Chapter 3 – Literature Review. Investigations A1 and A2. / (Peel and Eggbeer, 2016), (Peel et al., 2016)	
[L29]	Chapter 3 – Literature Review.	Not specifically targeted for support from Investigations B and C. However, good support offered by continued Participant emphasis on cost as a critical factor for adoption.
[L30]	Chapter 3 – Literature Review. Investigation A1. / (Peel and Eggbeer, 2016)	
[L31]	Chapter 3 – Literature Review.	Not specifically targeted for support from Investigations B and C. Descriptive.
[L33]	Chapter 3 – Literature Review.	
[L32]	Chapter 3 – Literature Review.	
[N1]	N/A	Future work will be required to determine the nature of certification – when dealing with the NHS context. The scope and management level of that QMS may be difficult to define.
[N2]	N/A	Suggested by the discussion about giving designers (or pseudo/acting designers) the tools to educate and persuade clinicians about the significance and necessity of design, and quality / regulatory compliance. The question of power balance (both intra and inter teams) represents a highly promising avenue for future work.
[N5]		
[N6]		

[N3]	N/A	Future work is required to ease the transition from design contexts with no experience of quality management systems, to full (mandatory) compliance.
[N4]	N/A	A significantly higher volume and quality of clinical (and design) evaluation data is required across the field as a whole.

8.4. Chapter 8 Summary

In summary, Chapter 8 has:

- evaluated the performance, content, and format of the design intervention when tested with three participants (Chapter 8.1);
- related these findings to the research context, existing literature, and characterisations of current practice from Investigation A (throughout);
- verified factors and links in this research's conceptual model, and where links are weaker or out of immediate scope, used it to prescribe future work (8.3.1);
- and has discussed the responses to research questions about: current practice, drivers and barriers to routine use, the extent to which quality management can structure a design intervention, the fidelity and generalisability required in product and customer requirements lists, and about how an effective design intervention could be formulated to address these key factors.

9. Conclusions and Future Work

This Chapter (Figure 104) collates, summarises, and reflects upon the main findings from this research, to evaluate its performance against the stated aim, objectives, and ability to answer the research questions. Where limitations or gaps remain, the need for future work is described.

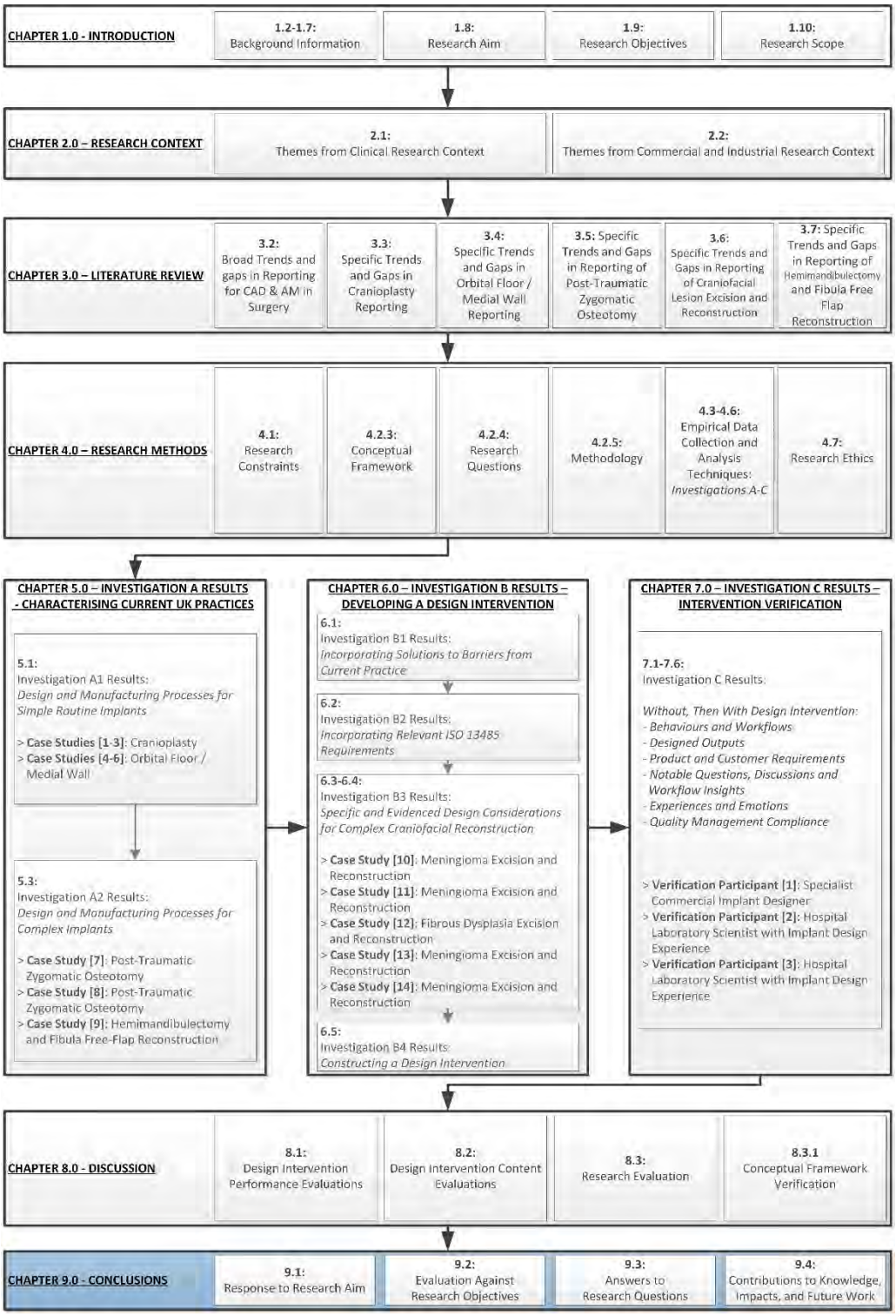


Figure 104 - Thesis Overview, With Current Location Highlighted (Chapter 9)

9.1. Response to Research Aim

This research aimed:

> *"to **identify limitations** in patient-specific device design processes, and to **evaluate effective routes** to overcoming them, **towards enabling routine adoption** of digitally designed devices."*

It achieved this aim by formulating a research plan which was well-suited to the context, resources, and timeframe. It adopted an inductive, theory-generative research structure in which the lack of existing theories or hypotheses in this field were overcome by describing current design and fabrication practice in unique detail. These descriptions were combined with prevailing assumptions, contextual and industrial factors, and previously published evidence, to construct a novel conceptual framework. In doing this, three general research questions, derived from the themes evident in the research aim, were split and refined into five more specific, focused questions which were addressed by answered by the data in chapters 5-7 and the analyses in Chapter 8.

Limitations in achieving the research aim were related to the number of different routes which could be evaluated. Only the most promising route for the given research duration and resources was explored. This used a paper form to prescribe a structure for the design and development process; where one did not previously exist in this field. With access to specialist training or expertise in software development, the paper-based medium of the featured solution could have been tested against more interactive methods of presenting the design stages, their possibilities, and their constraints, in a reactive wizard-like format to the user. Instead, exploration of the media by which the product requirements are gathered and verified should be explored in future work.

9.2. Evaluation against Research Objectives

9.2.1. Objective 1

> *"To establish an overview of the UK NHS maxillofacial surgery context specifically, and the existing literature more broadly, regarding the clinical, regulatory, technical, social, economic,*

and political drivers and barriers related to the design and use of patient-specific guides and implants."

Objective 1 was achieved to as full a degree as possible, given the research constraints (Chapter 4.1) and stated research scope (Chapter 1.10). A descriptive contextual review was combined with a critical narrative literature review to establish both the explicit and inferred drivers and barriers to the use of maxillofacial patient-specific implants and guides in the UK NHS.

Limitations in meeting this objective centre around the tradeoffs which are required between detail and duration. Without the time and scope constraints typical of any Ph.D. research project, the literature and context could potentially have been reviewed in a systematic fashion across a broader range of surgical applications and in greater technical detail. However, given the uniquely valuable insights to reporting fidelity offered by this work, as demonstrated via peer review (Peel et al., 2017), the selected approach can be seen to have been proprtionate and suitable.

9.2.2. Objective 2

"To identify the predominant methods of maxillofacial patient-specific device design and fabrication in the UK NHS. To characterise them in terms of their practical, economical, and clinical strengths and weaknesses; using observation, reflection on professional industrial practice, and conceptualisation."

Objective 2 was achieved to as full a degree as possible within the given research constraints, and to a degree which was original in the published literature (Peel and Eggbeer, 2016, Peel et al., 2016, Eggbeer and Peel, 2018). Observations of current hospital practice, and reflecting on participation in current industrial practice, provided a thorough understanding of discrete categories of practice in the collaborating UK NHS hospitals and laboratories.

Limitations in meeting this objective relate to the small variations in practice which exist between hospital units and between hospital laboratories within the UK. A full national survey was outside of the scope of this work, but would be at least in part, an important aspect of future work. This would especially be the case when the

characterisation of commercial service procurement is explored further. Internationally, where in-hospital laboratories are not necessarily as common, the economic comparisons may tilt more favourably towards CAD and AM or CAM devices even for simple geometries and procedures. Again, this was beyond the scope of a Ph.D. thesis, but would be relevant to future studies.

9.2.3. Objective 3

> *"To specify and prototype a new design process intervention which overcomes the key barriers identified in objectives (1) and (2); towards promoting routine and safe deployment of digitally designed implants and guides."*

Objective 3 was achieved fully by designing a paper based design intervention, comprising instructions and references, which explicitly addressed the barriers identified by the data generated to meet objectives 1 and 2. The intervention prescribed a structure for the maxillofacial implant and guide design process, encouraged the collection of high fidelity design requirements lists, prompted important quality management and regulatory compliance related activities like design verification, and provided evidence to support design decisions at-a-glance.

Limitations in meeting this objective were associated with the large amount of work involved in gathering and developing evidence for just one type of cranio-maxillofacial procedure (complex craniofacial excision and reconstruction). Future work should develop pragmatic evidence to support detailed design decision making for a wide range of other patient-specific surgical device applications. A further limitation involved the degree to which a Quality Management System, required for regulatory compliance and best practice, can be parachuted into a new context. The relevant medical device standard (ISO., 2016) mandates a system which is tailored to the specific needs and size of the given organisation. A promising avenue for future work involves more detailed investigation of QMS training requirements, and the extent to which template procedures can be used, in addition to template forms.

9.2.4. Objective 4

> *"To test and verify the effectiveness of that intervention against current design processes through empirical testing and appropriate research methods. To analyse the extent to which the new or enhanced intervention has been successful and to make recommendations for its future development."*

Objective 4 was achieved to as full a degree as possible within the time and resource constraints relating to a piece of Ph.D. research. Significant time comittments were obtained from one industrial and two clinical device designers. Their responses to complex implant design challenges were characterised and, where relevant, quantitatively measured to verify the intended performance of the design intervention against their standard design practices.

Limitations in achieving this objective centred around the significant time comittment asked of the participants and required of the researcher for analysis. Given the absence of similar data in the published literature, the richness of collected data across a relatively large number of categories suited the context well. However, with some of the insights being about the subjective emotional responses of the individual participants, opinions and reactions should be collected from a wider range of designers in future work; across locations, experience levels, specialisms, and using a range of CAD tools. This would serve to even better support the factors and links in the final conceptual model.

9.3. Answers to Research Questions

The final refined research questions (Chapter 4.2.4) were the result of a conceptualisation process, designed to generate hypotheses and theories on a topic where none existed, and to improve the generalisability of case study data.

9.3.1. Refined Research Question 1

> *"What are the tasks, processes, materials, resources, expertise, tools, and costs involved in current patient-specific device production techniques?"*

This question was answered primarily using data from Investigation A1 and A2. This was supplemented by additional information from the existing literature. Existing patient-specific implant and guide practices lent themselves to being classified as either: conventional; semi-digital; or fully digital.

Current conventional and semi-digital practices presented in Investigation A1 required highly skilled and experienced manual practitioners. They achieved good clinical outcomes at reasonably low cost at least for simpler devices; though they demonstrated little consciousness of design intent or of standard product design process stages.

Current digital practices were shown to be lacking evidence and a standardised process. They were economically and time inefficient for simpler devices. However, they demonstrated increases in surgical predictability and accuracy, and reductions in (subjectively reported) surgery durations. Albeit at the expense of increased planning time. Complex digital projects were shown to benefit significantly from designer and surgeon experience of similar projects, and from detailed standard operating procedures.

9.3.2. Refined Research Question 2

> *"What are the clinical, technical, and structural drivers and barriers experienced by medical professionals when adopting digital surgical planning and digital design techniques?"*

This question was primarily answered using secondary data from the contextual review and from the review of existing academic and clinical literature. These were supplemented by a review of the major commercial patient-specific device services available in the UK.

Contextual barriers to routine adoption, even for complex devices, were identified as: downward NHS funding pressures; poor infrastructure; trends towards in-hospital 3D printing as a protectionist measure; commercial service model fragmentation; touchpoint inconsistencies; secrecy; a limited (though understandable) appreciation of the value and extent of necessary design work; and deficiencies in clinical or technical training, despite the increasingly fashionable appeal of AM in medicine.

A more fundamental threat to approximately twenty years of progress in applying CAD and AM or CAM to surgery, was the medium-term requirement for NHS units to adopt quality management systems in order to comply with a new regulatory landscape. This drove the QMS-centric approach to developing a design intervention which could contribute to overcoming regulatory, user experience, and design practice barriers. This approach has not been demonstrated in the academic literature previously.

In the academic context, significant barriers were identified in transferring knowledge across disciplines. Previous work in technical and clinical publications was shown to be limited by: adopting discrete perspectives; being restricted to short or medium-term follow-up; a near-universal refusal or oversight in describing and justifying design details; a conservative consensus about what constitutes gold-standard treatments; an inconsistent and low-fidelity treatment of health economics issues; and an unwillingness to publish negative results.

9.3.3. Refined Research Question 3.1

> *"To what extent can quality management system and regulatory compliance functions be incorporated into, and satisfied by, a prototype design process intervention for complex patient-specific devices?"*

This question was answered primarily using data from Investigations B2 (Chapter 6.2) and C (Chapter 7.6). This was supplemented, logically, by the review of quality management system requirements (Chapter1.6).

The design intervention was verified to, at least amongst the participants in Investigation C, successfully implement key design aspects of ISO 13485: design requirements gathering, requirements verification, design review, and design verification. This was particularly relevant for the hospital laboratory context, where no QMS or top-management-driven review procedures were in place.

Of particular note was the ability of the intervention to transform design requirements from being overlooked or met accidentally, to being identified explicitly and met deliberately. In addition to these functions, others were partially implemented or indicated, if not directly used by participants during the design exercises: prompting structured feedback collection; controlling production (of the final digital file); controlling documents; and controlling records.

9.3.4. Refined Research Question 3.2

> *"What level of fidelity is required in a device specification or requirements list for successful design outcomes in complex craniofacial reconstruction?"*

This question was answered using results and analysis from Investigations A1 (Chapter 5.2), A2 (Chapter 5.3), and from Investigation B3 (Chapter 6.3). This was supplemented by contextual data about ISO 13485 requirements (Chapter 1.6) and the level of fidelity of reports in the literature (Chapter 3.2.9-3.2.10).

This work showed that, by investigating the causes of and then learning from design failures, and from reflecting on both routine and exploratory projects to compile a list of key design requirements fields, a sufficiently high fidelity specification can be structured if the intervention is deployed in full. Broadly, the requirements list fields which were related to the process workflow were driven by risk mitigation pre-requisites for service delivery; in terms of dealing with appropriate stakeholders (the operating surgeon) and appropriate resources (realistic timeframes and design expectations). The research demonstrated that the published literature overlooked such fundamental issues – hence the importance of describing failures and improvements in this work.

Most significantly, the near total absence of published analyses from a design or biomedical engineering point of view was mitigated by the generation of very high fidelity, very granular design requirements for consideration in complex craniofacial reconstructions. Investigation B3 (Chapter B3) linked design features with clinical and usability outcomes. Their validity and the appropriateness of their fidelity can only be said to apply to Case Studies 10-14, or similar cases to them. However, even within these limitations, the new specific considerations for design requirements presented in the design intervention were a step-change. The latter point applies especially when compared to the disparate tranches of clinical and technical perspectives which are often presented in the literature, and which require inference and assumption to translate into tangible design (including modelling) specifications.

9.3.5. Refined Research Question 3.3

> *"Can a practical and effective design intervention be formulated, that contributes to meeting regulatory, clinical, technical, and user requirements for the routine design of complex patient-specific devices?"*

This question was answered using results and analyses from Investigation C (Chapters 7 and 8).

Within the research constraints and the scope of this work, and within the degree to which QMS solutions and design considerations can be generalised, a practical and effective design intervention was successfully formulated. The effectiveness was shown to apply to improving the degree to which Participants adhered to QMS and so regulatory requirements (Chapters 7.3 and 7.6); and the degree to which their confidence improved and stress decreased (Chapters 7.4 and 7.5). The intervention successfully complied with the most generalisable procedural and record-keeping aspects of ISO 13485 for design; a pre-requisite under the forthcoming MDR. It did not, and by definition in the standard could never, wholly implement a full certifiable QMS. The design and modelling workflow were shown to be more structured and defined when using the intervention, including a consolidation of clinician contact time and engagement.

The practicality of the intervention was demonstrated by its use across the hospital and industrial contexts, in a paper based format. Some indications suggested participants were surprised by the extent of information gathering and project-setup. However, this was significantly less of a factor than the overall positive reactions they expressed towards the intervention-driven workflow.

9.4. Contributions, Research Impact, and Future Work

This research made eight key original contributions to the literature. They are summarised below:

- It characterised typical patient-specific cranioplasty implant production methods in the UK NHS, and compared their costs and resource requirements for the first time.

- It characterised typical patient-specific orbital floor and medial wall implant production methods in the UK NHS, and compared their costs and resource requirements for the first time.

- It described a world first application of CAD and AM to every stage of the post-traumatic zygomatic osteotomy and orbital floor reconstruction treatment process.

- It specified and justified a repeatable and flexible workflow for the design of patient-specific maxillofacial implants, including acceptance criteria and validation techniques, where none existed previously.

- It formulated and verified the performance of a translatable and expandable design intervention for use across contexts and tools.

- It synthesised key design considerations from the literature and generated new insights from five case studies about complex craniofacial reconstructions.

- Additionally, it made key methodological contributions. The development and refinement of the conceptual model provides a framework for future investigations and improves the generalisability of work in a field which predominantly relies on case study reports. Of particular note are the promising avenues for immediate investigation: the efficacy of a template QMS; and of standardised case study reporting templates. Furthermore, less urgent explorations of power structures in relation to seniority and regulatory compliance may be of significant interest.

- Finally, it generalised ISO 13485 design QMS functions to begin the mitigation of risks arising from an increasingly stringent regulatory environment.

Those eight main contributions have the potential to directly impact on hospital staff beyond those who participated in the research, on design engineers or biomedical engineers in industry, and on researchers working in or between the two major contexts. They have already impacted on practice at the institute through the refinement and consolidation of internal quality management procedures and forms. Beyond the direct application of the intervention, or its underlying evidence, the existence of a standard process between designer and surgeon may have educational and training benefits, by encouraging trainees to learn more about anatomy and design possibilities as experienced by Roser et al. (2010). Collectively, these impacts would not be limited to the UK NHS. Indeed, in insurance-driven healthcare systems or other scenarios where cost might not be as significant a barrier as in the NHS, the regulatory compliance, design evidence provision, and design process structuring benefits could have even wider benefits.

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Appendices

A1 – Collated ISO 13485 Requirements

Section of Standard:	Relevant Requirements:
4 – Quality Management System	a) Document the **roles** undertaken by the organisation under applicable regulatory requirements. b) Determine the **processes** required to establish, apply, sequence, support, record, analyse, and maintain a QMS. c) Document: a quality **policy** and quality **manual** including QMS scope, and references to the determined procedures. d) **Document**: determined procedures; determined forms, and determined records necessary for effective planning, operation and control of the QMS. e) Establish and maintain a **medical device file** for every product or product family; including a description, intended use statement, instructions, specifications, measuring and monitoring procedures, and installation requirements. f) **Control all documents** by documenting procedures that: review and approve documents before use; review, update, and re-approve documents as necessary; ensure identification of current document statuses; ensure that relevant document versions are available at the point of use; prevent deterioration or loss of documents; and prevent unintended use of obsolete documents. g) **Control** and maintain **records** in the same way as above, and retain records for at least the lifetime of the device.
5 – Management Responsibility	a) Evidence top management's commitment to the QMS by: communicating its importance to the organisation; establishing quality objectives; ensuring that customer and regulatory requirements are met; and ensuring the availability of resources. b) Ensure the quality policy: provides a framework for reviewing quality objectives; is communicated and understood within the organisation; and is reviewed for continuing suitability. c) Define, document, and communicate responsibilities, authorities, and interrelation of all personnel who affect quality.

	d) Appoint a management representative with responsibility and authority for documenting processes, reporting on QMS effectiveness, ensuring awareness throughout the organisation. e) Document procedures for, and implement management review at planned intervals to assess: feedback; complaints; reporting to regulatory authorities; audits; monitoring processes; monitoring product; corrective action; preventative action; QMS changes; improvement; changing regulatory requirements; and resource needs.
6 – Resource Management	a) Document process(es) for: determining the necessary competences for staff; providing training where required; evaluating the effectiveness of training; ensuring staff are aware of the importance and relevance of their quality-related actions; and for maintaining records of training, skills, and experience. b) Document infrastructure requirements including: buildings, workspaces, and utilities; hardware required for processes; software required for processes; supporting services required for processes; and maintenance requirements. c) Document work environment requirements which could affect product safety or performance.
7 – Product Realisation	a) Document process(es) for risk management in product realisation and maintain records of this activity. b) Determine requirements specified by the customer. Review these requirements before committing to supply. c) Determine product requirements not stated by the customer, but which are necessary to satisfy the product's intended use. Review these requirements before committing to supply. They should include: functional and safety requirements; and information derived from previous similar designs. d) Determine applicable regulatory requirements relating to the product. e) Document plans for customer and regulatory authority communications. f) Document design and development procedures including: stages; reviews; verification activities; validation activities; design transfer activities; responsibilities and authority; traceability; necessary resources; and necessary staff competencies. g) Produce outputs which: are verifiable; are approved prior to release; meet requirements; and have specified characteristics for safe and proper use. h) Document arrangements for systematic design and development review to assess the output(s) against the requirements and to propose corrective actions where necessary. i) Document appropriate design verification plans, including: methods; acceptance criteria; and (where appropriate) statistical techniques with rationale for sample size.

j) (With custom devices being unique one-offs, it is not feasible to validate each product as being capable of meeting the performance requirements for a given use).

k) Document procedures for: transfer of design and development outputs to manufacturing; ensuring the outputs are verified as being suitable for manufacturing; and for checking that production capability can meet product requirements.

l) Document procedures to control design and development changes. The changes should be: reviewed, verified, and approved; in light of their effects on function, performance, usability, safety, regulatory compliance, and risk management.

m) Maintain a design and development file for each medical device, including reference to: records generated to demonstrate conformity to requirements; and records of design and development changes.

n) Document procedures to ensure purchased product conforms to specified purchasing information, and to monitor suppliers. Criteria: supplier's ability to provide product which meets requirements; supplier performance; effect of product on medical device quality; risk implications.

o) Create purchasing information template to cover: specification(s); requirements for product acceptance; supplier personnel qualification; supplier QMS requirements.

p) Document procedures for production to ensure: that product conforms to specification; proper qualification of infrastructure; monitoring and measurement of process parameters; availability of monitoring and measuring equipment; and product release through to post-delivery activities.

q) Document procedures for validating processes, including: review and approval criteria; qualification of equipment and personnel; methods; rationale for sample sizes; records requirements; revalidation criteria; process change approvals; and the application of software (initial use and after updates).

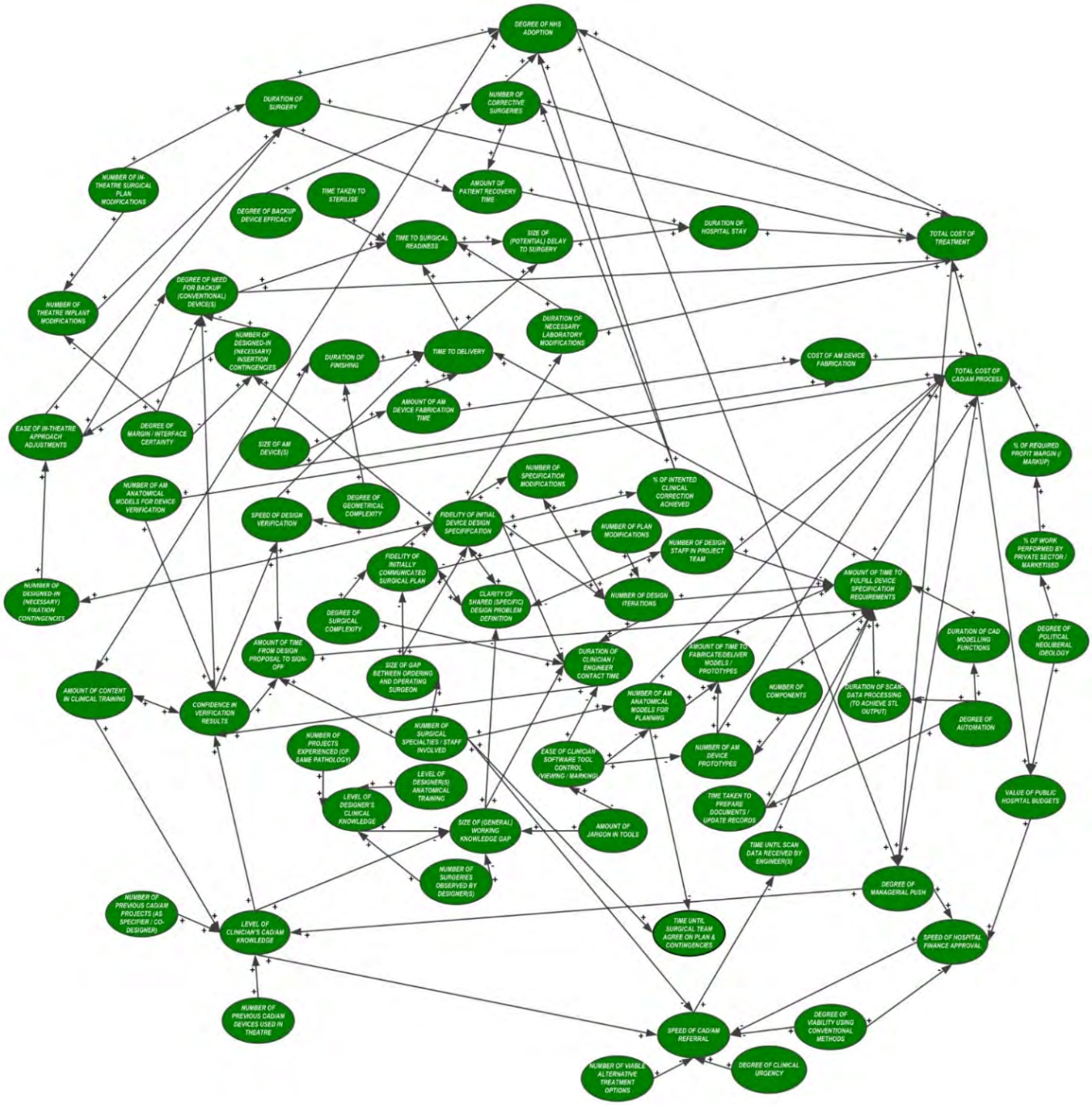
r) Document procedures for product identification throughout product realisation, and for segregating any returned devices.

s) Document processes for product traceability through; distribution, delivery, return of customer property, and preservation of product.

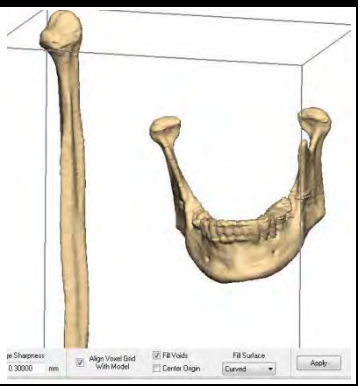
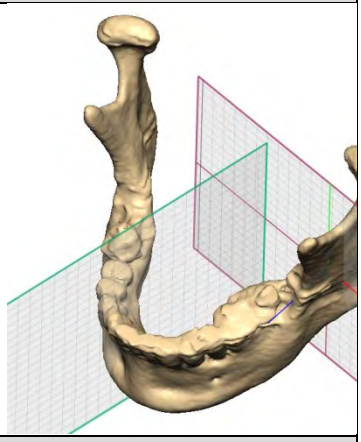
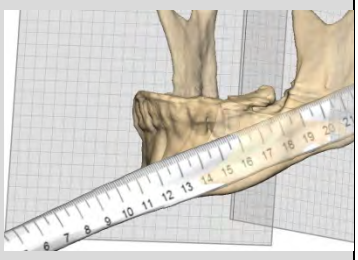
t) Determine and document necessary monitoring and measurement – and the equipment required to undertake it. Measuring equipment will: be calibrated or verified at defined intervals; be readjusted as necessary; be identifiable by calibration status; be safeguarded against accidental adjustments.

8 – Measurement, Analysis and Improvement	a) Document procedures for the feedback process to establish whether the organisation has met customer requirements. The information will serve as inputs to risk management, product requirements, and documented product realisation processes. b) Document procedures for timely complaints handling, including responsibilities for: receiving and recording information; evaluating whether feedback constitutes a complaint; investigating complaints; determining need to report to regulatory authorities; handling of product; corrective and preventative action; and justification for any non-investigations. c) Document procedures for notifying regulatory authorities of complaints. d) Document a procedure for planning, conducting, recording, and reporting internal audits in terms of: scope, interval, methods, corrective actions, and their verification. e) Monitor the QMS processes for ability to deliver planned results – implement corrective action where required. f) Monitor and measure product characteristics throughout the product realisation process, including the identity of staff undertaking inspection. g) Document a procedure to identify, document, segregate and (where appropriate) correct, nonconforming product. h) Document a procedure for issuing advisory notices. i) Document procedures for rework which consider the effect of the rework on the product, and which subject the product to the same reviews and approvals as the original procedure. j) Document procedures to determine, collect, and analyse appropriate data to evaluate the effectiveness of the QMS. This will include: feedback, conformity to requirements, trends of process and product characteristics, opportunities for improvement, suppliers, and audits. k) Document procedures for: reviewing nonconformities; determining causes; evaluating need for action; implementing actions; verifying corrective actions impact on safety and performance; and reviewing the effectiveness of corrective actions. l) Document a procedure for: determining potential nonconformities; evaluating the need for action; implementing actions; verifying preventative actions impact on safety and performance; and reviewing the effectiveness of preventative action.

A2 - Initial Conceptual Framework



A3 - Fibula Flap Standard Operating Procedure - Extract

STAGE	DESCRIPTION	NOTES	ILLUSTRATION
1	Import the fibula and mandible models at the same time. Set-up saved view (level & square-on). Set-up mid-line / mirror plane.	0.3mm clay coarseness. Fill holes. Do not move the pieces in relation to each other. Rename the folder as 'original'.	
2	Use the paint clay, project image tool to wrap the calibrated ruler around the fibula.	Ensure the text is legible on the lateral side. 0cm should be at the distal end. Verify the scale by taking 'manual' measurements with the ruler function.	
3	Duplicate the original fibula & mandible. Set up the cut edge planes on the duplicated mandible.	(These determine the amount of mandible to be removed).	
4	Orientate the duplicated fib on the longest side of the recon first. Make mandible translucent. Duplicate the finalised fibula position – name 'fibula plan master'.	Take note of surgeon's guidance on the positon in relation to the inferior edge of the mandible (usually offset by around 5mm so the fib is positioned correctly for dental implants).	

A4 – Anonymised Participant Information and Consent Sheets for Investigation A1

Service Audit – NHS Professional Consent Form

Participant name: [redacted]

Title of Project:

Name of Researcher: Sean Peel

Participant to complete this section:

1. I confirm that I have read and understand the information sheet for the above audit. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☑
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. ☑
3. I agree to observation in the above audit. ☑
4. I agree to the audit being audio recorded. ☑
5. I agree to the audit being photographed. ☑
6. I agree to the use of anonymised quotes in publications. ☑

Signature of Participant — Date: 16/01/13

Name of person taking consent — Date: 16/01/13

Signature of person taking consent

Service Evaluation – NHS Professional Consent Form

Participant name [redacted]

Title of Project: Service Evaluation – Lab-Based Implant Fabrication

Name of Researcher: Sean Peel

Participant to complete this section:

1. I confirm that I have read and understand the information sheet for the above service evaluation. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☑
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. ☑
3. I agree to observation in the above service evaluation. ☑
4. I agree to the service evaluation being audio recorded. ☑
5. I agree to the service evaluation being photographed. ☑
6. I agree to the use of anonymised quotes in publications. ☑

Signature of Participant — Date: 20/2/13

Name of person taking consent [redacted] — Date: 20/2/13.

Signature of person taking consent

Service Audit – NHS Professional Consent Form

Participant name: LAUREN [illegible]

Title of Project: Service Au[redacted]

Name of Researcher: Sean Peel

Participant to complete this section:

1. I confirm that I have read and understand the information sheet for the above audit. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☑
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. ☑
3. I agree to observation in the above audit. ☑
4. I agree to the audit being audio recorded. ☑
5. I agree to the audit being photographed. ☑
6. I agree to the use of anonymised quotes in publications. ☑

26/02/14

Signature of **Participant** **Date**

SEAN PEEL 26/02/14

Name of person taking consent Date

Signature of person taking consent

A5 – Calculations and Raw Data for Investigation A1

Conventional Cranioplasty

COSTING CALCULATIONS - "CHARGE-TO-NHS"

Time Reduction.

NHS STAFF COSTS

NAME	JOB TITLE	ANNUAL SALARY	HOURLY SALARY	NO. HOURS	COST
[redacted]	MAXILLOFACIAL LAB MANAGER.	£1 500	£1 500 ÷ 2080 = £9.57.	1.	£9.57.
	PRINCIPAL MANAC PROSTHETIST.	£30 500	£30 500 ÷ 2080 = £14.66.	(6)?	(£87.96)?

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3RD PARTY STAFF COSTS

(INCLUDED IN 3RD PARTY COMPONENT / SERVICE CHARGE)

NHS RAW MATERIALS COSTS

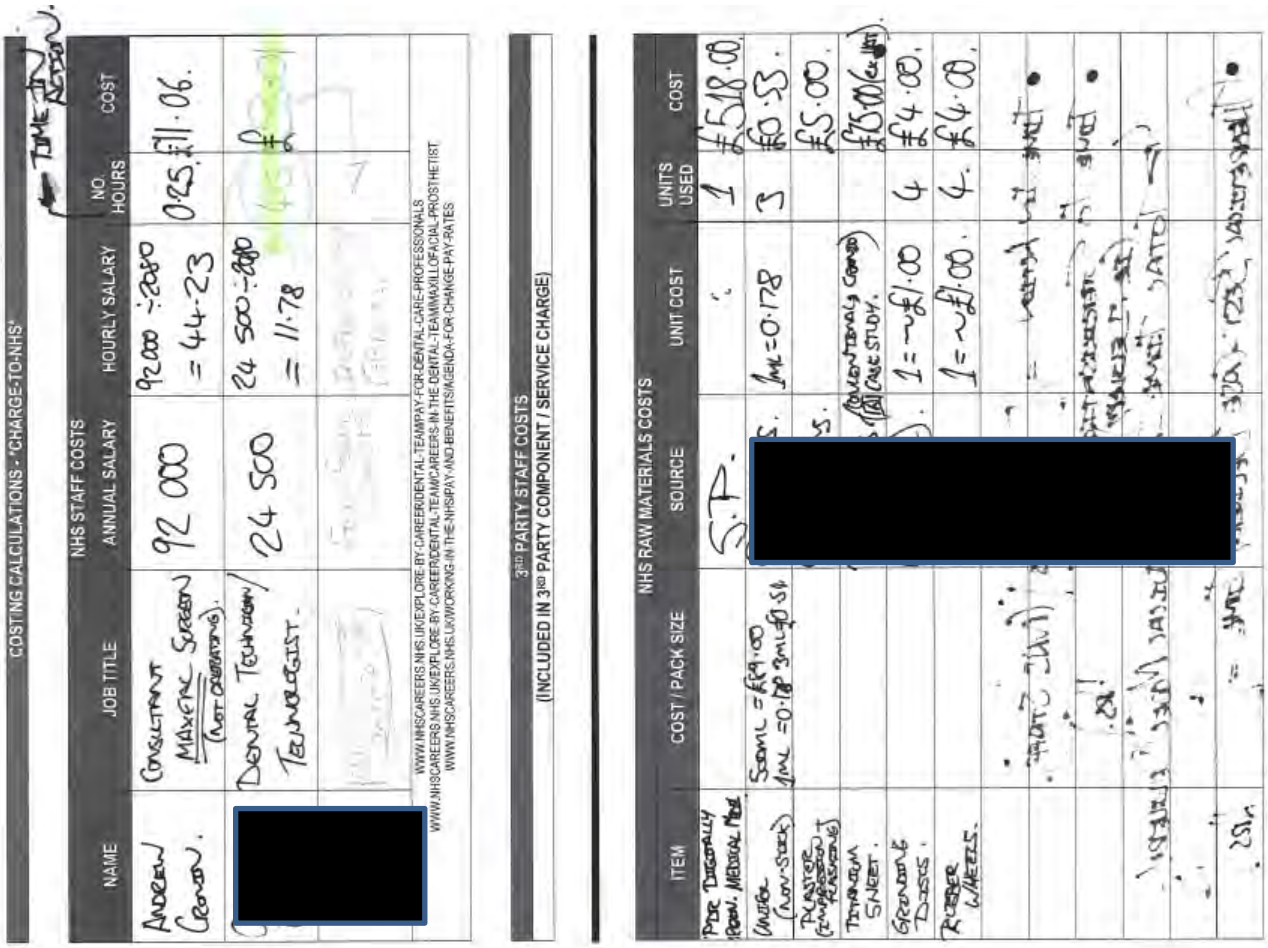
ITEM	COST / PACK SIZE	SOURCE	UNIT COST	UNITS USED	COST
Unifast (Non-Sterile)	500ml = £59.00 1ml = £0.118	[redacted]	1ml £0.118	5	£0.53
Dentsply (Impression) + Plaster					£5.00
Medical Model					£2.00
CLAY.					£0.50
Lubricant Fluid.					£150 (Count)
Titanium Sheet.					
Removable Partial Dentures					
Plaster Models.					

3RD PARTY PRODUCT / SERVICE CHARGES

ORGANISATION	PRODUCT / SERVICE	CHARGE TO NHS (INCL. VAT)	NOTES
	(MEDICAL MODEL INCL. ON PREVIOUS PAGE).		

TOTAL COST TO NHS

Raw Materials + NHS Staff + 3rd Party = £805.
£687. + £118



COSTING CALCULATIONS - "CHARGE-TO-NHS"

NHS STAFF COSTS

NAME	JOB TITLE	ANNUAL SALARY	HOURLY SALARY	NO. HOURS	COST
Andrew Cronin.	Consultant Maxfac Surgeon (not operating).	92 000	92 000 ÷ 2080 = 44·23	0·25	£11·06.
[redacted]	Dental Technician/ Technologist.	24 500	24 500 ÷ 2080 = 11·78		

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3RD PARTY STAFF COSTS
(INCLUDED IN 3RD PARTY COMPONENT / SERVICE CHARGE)

NHS RAW MATERIALS COSTS

ITEM	COST / PACK SIZE	SOURCE	UNIT COST	UNITS USED	COST
PDC Digitally Rapid Medical Mod.		S.P.		1	£518·00
Undyed (Non-Sterile)	50ml = £19·00 1ml = 0·78 3ml = £0·54	[redacted]	1ml = 0·178	3	£0·53.
Plaster (Impression Material)					£5·00.
Titanium Sheet.			(Voluntarily donated for case study).		£500 (ex VAT).
Grounds Dress.			1 = ~£1·00	4	£4·00.
Rubber Wheels.			1 = ~£1·00.	4.	£4·00.

COSTING CALCULATIONS - *CHARGE-TO-NHS*

NHS STAFF COSTS

NAME	JOB TITLE	ANNUAL SALARY	HOURLY SALARY	NO. HOURS	COST
[redacted]	CONSULTANT MAXFAC SURGEON... NOT NEURO	92000	92000 ÷ 2080 = 44.23	0.5	£22.12.
	DENTAL TECHNOLOGIST.	24500.	24 500 ÷ 2080 = 11.78.	1.0	£11.78.

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3RD PARTY STAFF COSTS

(INCLUDED IN 3RD PARTY COMPONENT / SERVICE CHARGE)

NHS RAW MATERIALS COSTS

ITEM	COST / PACK SIZE	SOURCE	UNIT COST	UNITS USED	COST
DRILL BITS (FOR REMOVAL).					

3RD PARTY PRODUCT / SERVICE CHARGES

ORGANISATION	PRODUCT / SERVICE	CHARGE TO NHS (INCL. VAT)	NOTES
PDR.	VERIFICATION MODEL (CLEANUP TIME INCL. IN QUOTE).	£289.	(DEFECT EDGE ONLY).
	DESIGN TIME (INCL. PAPERWORK)	£180	3 HRS.
FIT	IMPLANT COST.	£1055.89	
PDR	IMPLANT PROFIT (20%)	£213.18	
	=	£1748.07.	

TOTAL COST TO NHS

NHS STAFF £33.90 + RAW MATERIALS + SERVICES £1748.07. = £1781.97.

Conventional Orbit

COSTING CALCULATIONS • *CHARGE-TO-NHS*

@ TIME OF MOTION.

NHS STAFF COSTS

NAME	JOB TITLE	ANNUAL SALARY	HOURLY SALARY	NO. HOURS	COST
[redacted]	Principal Maxfac Prosthetist	30 500.	30 500 ÷ 2080 = 14.66	2.	£29.32.
	Maxfac Lab Manager.	61 500	61 500 ÷ 2080 = 29.57.	0.5 (equipment consultation)	£14.76.
	Consultant Maxfac Surgeon	92 000	92 000 ÷ 2080 = 44.23	1 (Consultancy with surgeon)	£67.

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WWW.NHSCAREERS.NHS.UK/WORKING-IN-THE-NHS/PAY-AND-BENEFITS/AGENDA-FOR-CHANGE-PAY-RATES

0.083

3RD PARTY STAFF COSTS

(INCLUDED IN 3RD PARTY COMPONENT / SERVICE CHARGE)

NHS RAW MATERIALS COSTS

ITEM	COST / PACK SIZE	SOURCE	UNIT COST	UNITS USED	COST
Unifor (non-stick)	500ml = £89.08 1ml = £0.178	[redacted]	1ml = £0.178	1	£0.178.
PLASTER (impression + plasters)					£2.00.
MEDICAL MODEL					£119. (ex VAT)
CLAY					£0.50
0.25mm Ti SHEET.					£9.00.
WAX SHEET					£0.22
GENERIC DISC			1=£1.00.	1	£1.00.
"KENDA QUICK" (GLUE).			1=£1.00.	1	£1.00.
SPEEDY MIX.					£0.10
IMPRESSION PUTTY.					£0.42

3RD PARTY PRODUCT / SERVICE CHARGES

ORGANISATION	PRODUCT / SERVICE	CHARGE TO NHS (INCL. VAT)	NOTES
	(MEDICAL MODEL INCL. ON PREVIOUS PAGE).		

TOTAL COST TO NHS

Raw Materials £193.42. + NHS Staff £47.75. = £241.17.

COSTING CALCULATIONS - *CHARGE-TO-NHS*

NHS STAFF COSTS

NAME	JOB TITLE	ANNUAL SALARY	HOURLY SALARY	NO. HOURS	COST
[redacted]	PRINCIPAL/MAXFAC PROSTHETIST.	30,500.	30,500 ÷ 2080 = 14.66.	0.967	£14.17.
	CONSULTANT MAXFAC (ORAL SURGEON)	92 000	92000 ÷ 2080 = 44.23	0.083	£3.67.

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3RD PARTY STAFF COSTS
(INCLUDED IN 3RD PARTY COMPONENT / SERVICE CHARGE)

NHS RAW MATERIALS COSTS

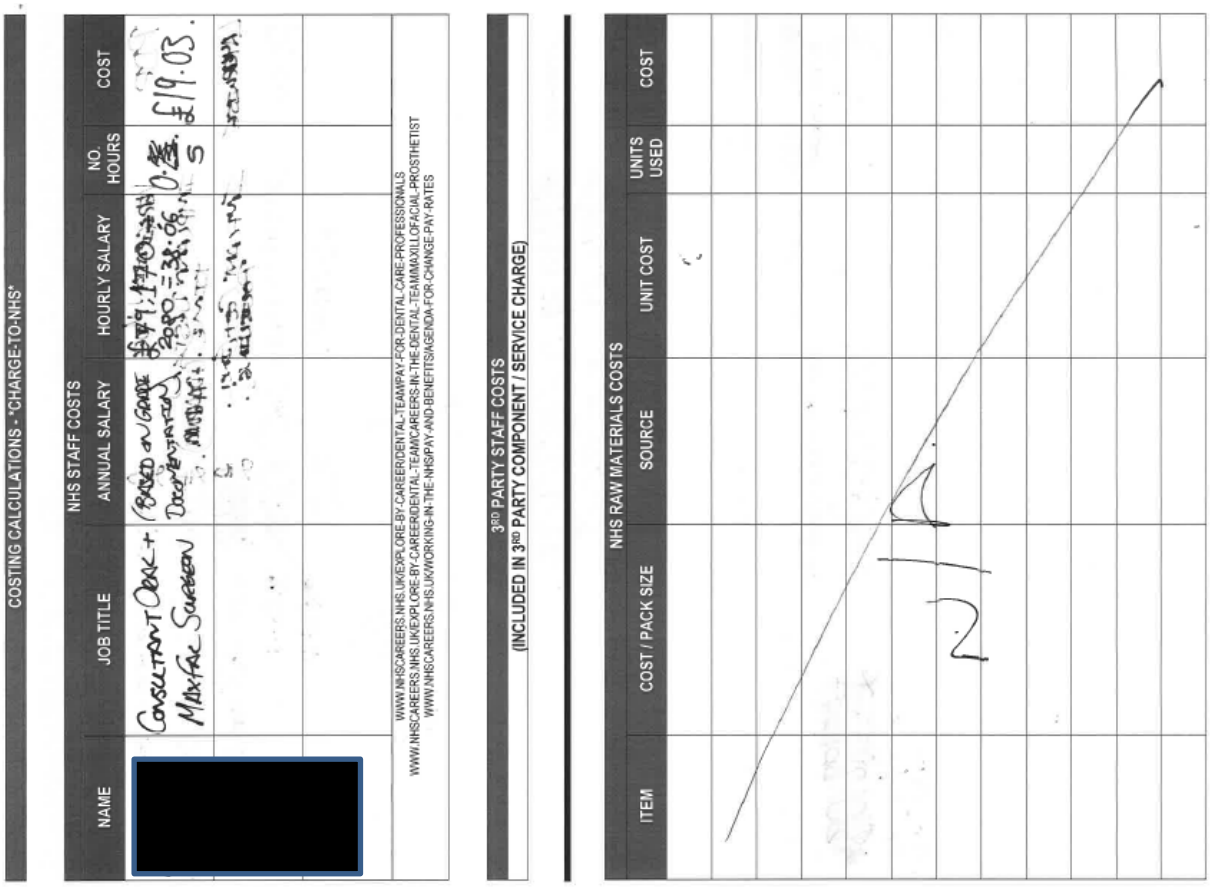
ITEM	COST / PACK SIZE	SOURCE	UNIT COST	UNITS USED	COST
MEDICAL MODEL + REGION MODEL.	INCLUDES DESIGN TIME + DELIVERY.	[redacted]			£306.
UNIFOR (NON-STICK)	SCALE = £89.00 1ML = £0.178.		1ML = £0.178.	1	£0.178.
PLASTER (IMPRESSION + CASTING).					£2.00.
0.25mm Ti SHEET.					£9.00.
GRINDING DISCS.			1 = £1.00	1	£1.00.
PRESH TOOL.	"KENDA QUEEN" (CURE).		1 = £1.00.	1	£1.00.
SPEEDY MIX.					£0.10.

3RD PARTY PRODUCT / SERVICE CHARGES

ORGANISATION	PRODUCT / SERVICE	CHARGE TO NHS (INCL. VAT)	NOTES
	(MEDICAL MODELS		
	INCL. ON PREVIOUS		
	PAGE).		

TOTAL COST TO NHS

RAW MATERIALS £319.28. + NHS STAFF £17.84. = £337.12.



COSTING CALCULATIONS - 'CHARGE-TO-NHS'

NHS STAFF COSTS

NAME	JOB TITLE	ANNUAL SALARY	HOURLY SALARY	NO. HOURS	COST
[redacted]	Consultant Oral + Maxfac Surgeon	(Based on Grade Documentation)	£49.17 (£100,000 ÷ 2080 = 38.06)	0.5	£19.03

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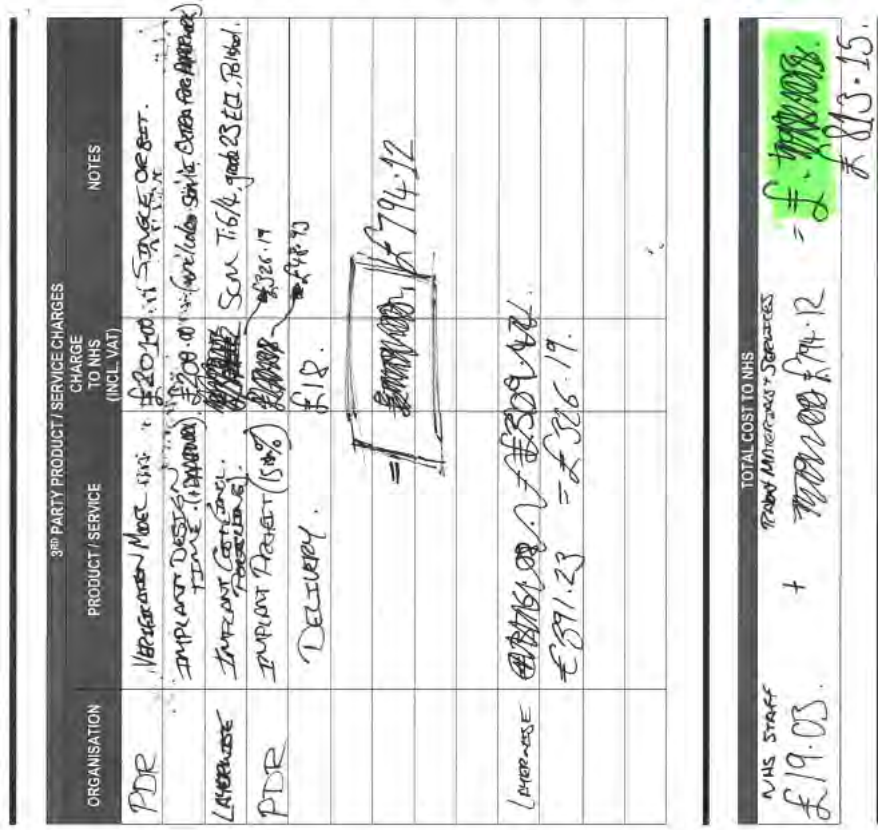
3RD PARTY STAFF COSTS
(INCLUDED IN 3RD PARTY COMPONENT / SERVICE CHARGE)

NHS RAW MATERIALS COSTS

ITEM	COST / PACK SIZE	SOURCE	UNIT COST	UNITS USED	COST



3RD PARTY PRODUCT / SERVICE CHARGES

ORGANISATION	PRODUCT / SERVICE	CHARGE TO NHS (INCL. VAT)	NOTES
PDR	Verification Model	£20.00	Stage One set.
	Implant Design Time (1 hour)	£98.00	(we include Sim's & Extra for Another).
Lighthouse	Implant Control Procedure.	[illegible]	Scan T.6/4, grade 23 £12.78/hol.
PDR	Implant Project (15%)	[illegible] £326.17	[illegible] £48.90
	Delivery.	£18.	
			= £794.12
Lighthouse	[illegible] £309.47.		
	£391.23 = £326.17.		

TOTAL COST TO NHS

NHS STAFF	3RD PARTY MATERIALS + SERVICES	
£19.03. +	[illegible] £794.12	= £ [illegible] £813.15.

A6 – Anonymised Participant Information and Consent Sheets for Investigation C

Participant Information and Consent Form

Thank you for agreeing to take part in this study. It consists of three parts:

1) (15 minutes) introduction, computer setup, consent.
2) (180 minutes) design and CAD modelling exercise.
3) (45 minutes) interview questions and discussion about the design exercise, and design practice in your institution.

For the design exercise, a simulated scenario has been created. A patient has been diagnosed with a meningioma in their frontal / orbital / temporal region, having presented with headaches, exophthalmos, and a black spot in their vision at extreme lateral gaze. They have been booked-in for surgery in three weeks from now.

In this simulated scenario, the surgical team have decided to excise the diseased portion of bone, and reconstruct the resulting defect using titanium alloplastic implants. Your task is to proceed with the design of the patient-specific implants in the allotted time. For this study, in the interest of brevity, assume that patient-specific cutting guides and medical models have already been designed. The STL file with which you have been provided shows the residual healthy anatomy, after the tumour has been excised. The implant, or implants should be "in-lay" in nature (as opposed to "on-lay"), and be based on a mirror-image of the contralateral healthy anatomy. It is not necessary to replace the full thickness of excised bone.

Sean will be fulfilling the role of prescribing and operating surgeon with regards to answering device-design related questions during the design and modelling exercise. While this design and modelling exercise is time limited, your working speed is not being judged. Please work at a normal pace. Where possible, this study should be uninterrupted. However, the study can be paused at any time – at your request.

In this second study, please use, to the fullest degree possible, sections 1, 2, and 3 of the printed design framework (provided with this form). This is essentially an instructional form intended to deliberately structure the design process, and prompt consideration of key design issues. Sections 4, 5, and 6 of that framework are for use after completion of the design and modelling work and are provided for reference only.

Video and audio of the study will be recorded – over the course of the design and modelling exercise. Please explain your working as you proceed through the modelling stages, where possible. Audio will be recorded of the interview. Additionally, notes will be taken throughout. These data will be analysed, evaluated, and presented for inclusion in a thesis, and in potential journal papers or conference presentations. This will include video stills and direct quotations. They will however, be anonymised.

Please print your name, sign, and date the fields below to signify your understanding of, and consent to the above:

NAME: [redacted] **SIGNED:** [illegible] **DATE:** 22-02-17

Participant Information and Consent Form

Thank you for agreeing to take part in this study. It consists of three parts:

1) (15 minutes) introduction, computer setup, consent.
2) (180 minutes) design and CAD modelling exercise.
3) (45 minutes) interview questions and discussion about the design exercise, and design practice in your institution.

For the design exercise, a simulated scenario has been created. A patient has been diagnosed with a meningioma in their frontal / orbital / temporal region, having presented with headaches, exophthalmos, and a black spot in their vision at extreme lateral gaze. They have been booked-in for surgery in three weeks from now.

In this simulated scenario, the surgical team have decided to excise the diseased portion of bone, and reconstruct the resulting defect using titanium alloplastic implants. Your task is to proceed with the design of the patient-specific implants in the allotted time. For this study, in the interest of brevity, assume that patient-specific cutting guides and medical models have already been designed. The STL file with which you have been provided shows the residual healthy anatomy, after the tumour has been excised. The implant, or implants should be "in-lay" in nature (as opposed to "on-lay"), and be based on a mirror-image of the contralateral healthy anatomy. It is not necessary to replace the full thickness of excised bone.

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In this first study, please follow the design process you would usually undertake for an enquiry from one of your surgeons / customers (including any documentation you would normally complete during this activity). If there are any deviations from your normal practice, because they are impractical or unachievable thanks to this experimental setup, please simply explain them as they are encountered.

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Please print your name, sign, and date the fields below to signify your understanding of, and consent to the above:

NAME: [redacted] **SIGNED:** [illegible] **DATE:** 09/02/17

Participant Information and Consent Form

Thank you for agreeing to take part in this study. It consists of three parts:

1) (15 minutes) introduction, computer setup, consent.
2) (150 minutes) design and CAD modelling exercise.
3) **(30 minutes) break.**
4) (45 minutes) interview questions and discussion about the design exercise, and design practice in your institution.

For the design exercise, a simulated scenario has been created. A patient has been diagnosed with a meningioma in their frontal / orbital / temporal region, having presented with headaches, exophthalmos, and a black spot in their vision at extreme lateral gaze. They have been booked-in for surgery in three weeks from now.

In this simulated scenario, the surgical team have decided to excise the diseased portion of bone, and reconstruct the resulting defect using titanium alloplastic implants. Your task is to proceed with the design of the patient-specific implants in the allotted time. For this study, in the interest of brevity, assume that patient-specific cutting guides and medical models have already been designed. The STL file with which you have been provided shows the residual healthy anatomy, after the tumour has been excised. The implant, or implants should be "in-lay" in nature (as opposed to "on-lay"), and be based on a mirror-image of the contralateral healthy anatomy. It is not necessary to replace the full thickness of excised bone.

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Please print your name, sign, and date the fields below to signify your understanding of, and consent to the above:

NAME: [redacted] **SIGNED:** **DATE:** 5/4/17.

Participant Information and Consent Form

Thank you for agreeing to take part in this study. It consists of three parts:

1) (15 minutes) introduction, computer setup, consent.
2) (150 minutes) design and CAD modelling exercise.
3) **(30 minutes) break.**
4) (45 minutes) interview questions and discussion about the design exercise, and design practice in your institution.

For the design exercise, a simulated scenario has been created. A patient has been diagnosed with a meningioma in their frontal / orbital / temporal region, having presented with headaches, exophthalmos, and a black spot in their vision at extreme lateral gaze. They have been booked-in for surgery in three weeks from now.

In this simulated scenario, the surgical team have decided to excise the diseased portion of bone, and reconstruct the resulting defect using titanium alloplastic implants. Your task is to proceed with the design of the patient-specific implants in the allotted time. For this study, in the interest of brevity, assume that patient-specific cutting guides and medical models have already been designed. The STL file with which you have been provided shows the residual healthy anatomy, after the tumour has been excised. The implant, or implants should be "in-lay" in nature (as opposed to "on-lay"), and be based on a mirror-image of the contralateral healthy anatomy. It is not necessary to replace the full thickness of excised bone.

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Please print your name, sign, and date the fields below to signify your understanding of, and consent to the above:

NAME: [redacted] **SIGNED:** **DATE:** 20/3/17

Participant Information and Consent Form

Thank you for agreeing to take part in this study. It consists of three parts.

1) (15 minutes) introduction, computer setup, consent.
2) (150 minutes) design and CAD modelling exercise.
3) **(30 minutes) break.**
4) (45 minutes) interview questions and discussion about the design exercise, and design practice in your institution.

For the design exercise, a simulated scenario has been created. A patient has been diagnosed with a meningioma in their frontal / orbital / temporal region, having presented with headaches, exophthalmos, and a black spot in their vision at extreme lateral gaze. They have been booked-in for surgery in three weeks from now.

In this simulated scenario, the surgical team have decided to excise the diseased portion of bone, and reconstruct the resulting defect using titanium alloplastic implants. Your task is to proceed with the design of the patient-specific implants in the allotted time. For this study, in the interest of brevity, assume that patient-specific cutting guides and medical models have already been designed. The STL file with which you have been provided shows the residual healthy anatomy, after the tumour has been excised. The implant, or implants should be "in-lay" in nature (as opposed to "on-lay"), and be based on a mirror-image of the contralateral healthy anatomy. It is not necessary to replace the full thickness of excised bone.

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In this second study, please use, to the fullest degree possible, sections 1, 2, and 3 of the printed design framework (provided with this form). This is essentially an instructional form intended to deliberately structure the design process, and prompt consideration of key design issues. Sections 4, 5, and 6 of that framework are for use after completion of the design and modelling work and are provided for reference only.

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Please print your name, sign, and date the fields below to signify your understanding of, and consent to the above:

NAME: [redacted] **DATE:** [illegible]

Participant Information and Consent Form

Thank you for agreeing to take part in this study. It consists of three parts:

1) (15 minutes) introduction, computer setup, consent.
2) (150 minutes) design and CAD modelling exercise.
3) **(30 minutes) break.**
4) (45 minutes) interview questions and discussion about the design exercise, and design practice in your institution.

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In this simulated scenario, the surgical team have decided to excise the diseased portion of bone, and reconstruct the resulting defect using titanium alloplastic implants. Your task is to proceed with the design of the patient-specific implants in the allotted time. For this study, in the interest of brevity, assume that patient-specific cutting guides and medical models have already been designed. The STL file with which you have been provided shows the residual healthy anatomy, after the tumour has been excised. The implant, or implants should be "in-lay" in nature (as opposed to "on-lay"), and be based on a mirror-image of the contralateral healthy anatomy. It is not necessary to replace the full thickness of excised bone.

Sean will be fulfilling the role of prescribing and operating surgeon with regards to answering device-design related questions during the design and modelling exercise. While this design and modelling exercise is time limited, your working speed is not being judged. Please work at a normal pace. Where possible, this study should be uninterrupted. However, the study can be paused at any time – at your request.

In this first study, please follow the design process you would usually undertake for an enquiry from one of your surgeons / customers (including any documentation you would normally complete during this activity). If there are any deviations from your normal practice, because they are impractical or unachievable thanks to this experimental setup, please simply explain them as they are encountered.

Video and audio of the study will be recorded – over the course of the design and modelling exercise. Please explain your working as you proceed through the modelling stages, where possible. Audio will be recorded of the interview. Additionally, notes will be taken throughout. These data will be analysed, evaluated, and presented for inclusion in a thesis, and in potential journal papers or conference presentations. This will include video stills and direct quotations. They will however, be anonymised.

Please print your name, sign, and date the fields below to signify your understanding of, and consent to the above:

NAME: [redacted] **DATE:** 29/03/2017

DESIGN FRAMEWORK

COMPLEX CRANIOFACIAL RECONSTRUCTIONS

VERSION 2.0

DOCUMENT REVISIONS

List in date-ascending order:

REVISION:	DATE:	AUTHOR:	SUMMARY OF CHANGES:
V1	13/12/16	SP	First draft completed.
V2	15/12/16	SP	Edited to remove repetitions, and context or software-specific elements.

DESIGN PRO-FORMA

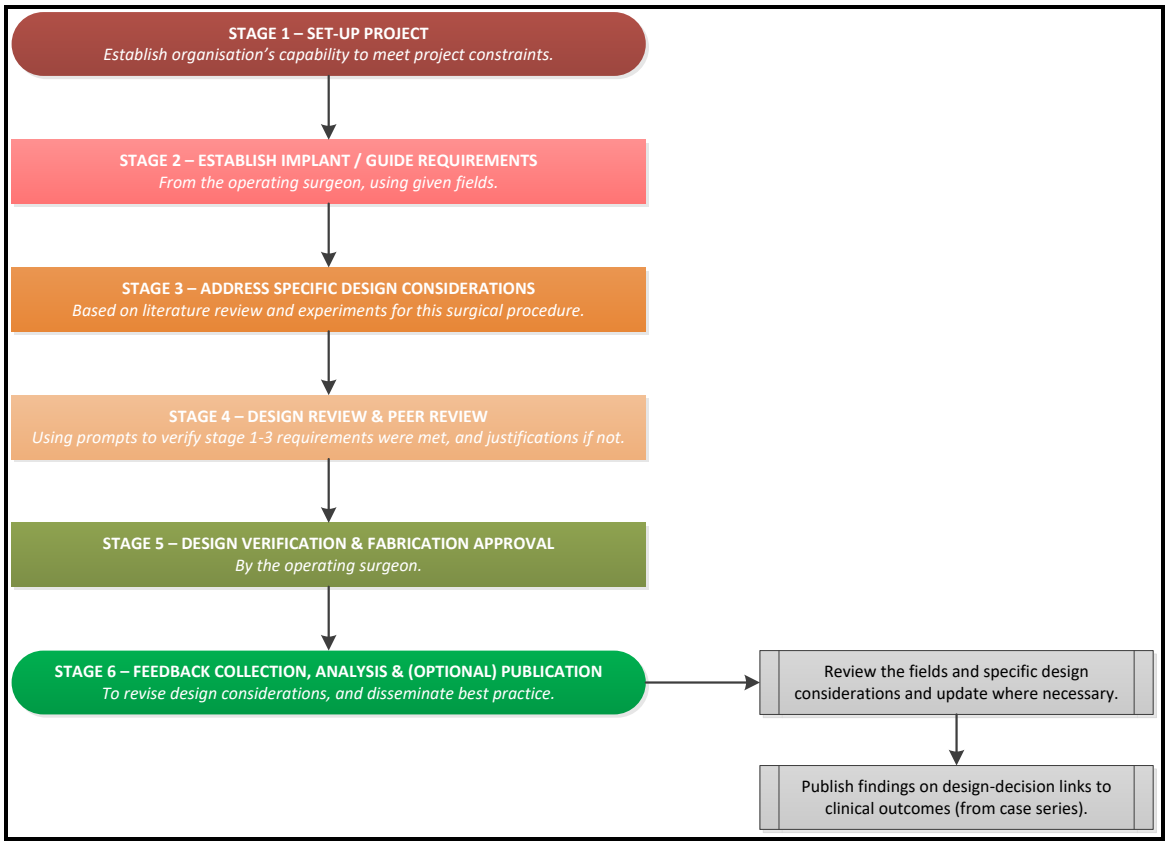
PURPOSE / SCOPE

This framework is for use by design engineers, biomedical engineers, and clinicians who are undertaking computer-aided **design** of patient-specific 3d-printed (titanium) or machined (PEEK) complex craniofacial reconstructive implants. Missing information, required to populate the fields, should always be sought from the operating surgeon (not an intermediary). Fabrication should be controlled separately. Production quality control should be addressed separately.

This form prompts consideration of routine, and overlooked key factors – with a view to minimising design iterations, minimising risks, and improving patient outcomes - based on evidence and informed risk-management. It also ensures good record keeping. **This version of the framework tool is constrained to orbito-temporal disease excision and reconstruction**. In future, it will be expended – with evidence based prompts for other procedures.

This framework can contribute to meeting the requirements of ISO 13485 for the **design** of medical devices – when used as part of an organisation's own Quality Management System. It is intended for continuous referencing and updating throughout project activity (including after surgery and during clinical follow-up). For best results, do not progress to the next project stage(s) until the current section has been completed.

Stages 1 and 2 establish the project and product requirements by prompting, and making explicit, answers to key fields – information which will be required during the 3D modelling of implants and guides. **Stage 3** prescribes specific considerations for some of those fields based on published evidence. **Stage 4** prompts reviews of the design by the project manager and by a relevant peer. **Stage 5** prompts the processes of obtaining "customer" (or, operating surgeon) sign-off. **Stage 6** prompts the collection of useful feedback – and encourages later publication. The flow diagram below provides an overview of the stages in this framework.



STAGE 1: SET-UP PROJECT

STAGE 1: SET-UP PROJECT (PRE-SCAN-DATA PROCESSING / PRE-DESIGN):

Establish the fundamental project details, and evaluate yours / your organisation's ability to deliver within the stated constraints.

PROJECT SETUP	
Patient / project name / identifier:	F.L. (Patient Left) or P.R. (Patient Right)
Your name: ***[Acting as project manager / project designer]:***	
Your employed role:	Project Manager / ————————
Operating clinician name: ***[If different to you]:***	Sean Peel
Operating clinician role: ***[If different to you]:***	Consultant Maxillofacial Surgeon
(Operating clinician) email address(es):	speel@pdronline.co.uk
(Operating clinician) phone number(s):	02920 416 723
(Operating clinician) typical meeting availability:	Mon-Thurs 1200-1300 / Emails every weekday evening after 2000.
DEADLINES	
Today's date: ***[Project starts]:***	09/02/17 10/02/17 21/02/17 22/02/17 28/03/17 29/03/17 05/02/17 06/02/17
Finished (clean, not sterile) devices required on or before:	3 weeks from today.
Estimated fabrication and post-processing timescale:	5 working days.
Full delivery address / restrictions:	e.g. Maxillofacial Laboratory Morriston Hospital Morriston Swansea SA6 6NL

STAGE 1: SET-UP PROJECT

AIMS

Patient condition / procedure / background / future: ***[including, e.g. scheduled radiotherapy]:***	A patient has been diagnosed with a meningioma in their frontal / orbital / temporal region, having presented with headaches, exophthalmos, and a black spot in their vision at extreme lateral gaze. Surgery will excise the disease, and reconstruct the defect with alloplastic implant(s). No post-operative therapy is scheduled.
Service(s) required:	***Digital surgical planning meeting:*** X ; ***Custom implant design:*** X ; ***Custom guide design:*** X ; ***Medical model design:*** X
Ideal custom device(s): ***[Item(s) & purpose]:***	*Surgical guides to transfer the planned excision margin into theatre.* Titanium implant based on the healthy side. Probably need to split it into multiple parts to make it easier to insert.
Ideal clinical outcome(s):	Single stage procedure. Disease fully excised. Exopthalmos and black spot in vision, corrected.
Billing arrangements in-place? ***[Where necessary, detail]:***	Use the usual billing route.

CAPABILITY CHECK

Capable of delivering device design services? ***[In terms of: timeframe / capacity / technical capability / skills.]***	***Yes:*** X	***Yes:*** ***[With support which is achievable within the deadline]:***	***No:*** ***[Abandon project]:***

STAGE 2: ESTABLISH IMPLANT / GUIDE REQUIREMENTS (PRE-SCAN-DATA PROCESSING / PRE-DESIGN):

Request specific details about the operating clinician's implant and guide requirements – and note them against all of the relevant fields. Where the clinician prompts or agrees to requirements updates through the project (perhaps after design review, further discussion, a design experiment, or a change in project circumstances), note any refined requirements in the third column.

CUSTOMER & IMPLANT / GUIDE REQUIREMENTS

Requirements:	Design Implications & Requirements Version 1:	(Optional) Version 2: *[If refined / changed]:*
	Context	
Any accommodation required for potential defect alterations between the scan and surgery?	No – scan was taken recently.	
Any scan-data modifications required before design work? *[E.g. Remove existing devices / grafts?]*	No – no existing reconstructions to remove.	
Any requirements from surgeon experience (and therefore expectations) from using analogous devices?	Frequent users of 3D printed implants. Less experience of using them for this particular procedure.	
Any project requirements from the surgical team having relevant additional needs? *[E.g. accommodating colour blindness?]*	One of surgical team is colour blind – so make sure that any contrasting colours in project documents (or in-theatre references) are approved as being suitable.	
	Material and Texture	
Device(s) materials:	Titanium, because the surgical team are used to, and confident with this material. Just the outermost contours of the missing bone need to be reconstructed – not the full bone thickness. Cost is also a consideration.	
Device(s) surface finish(es): *[Including desirability of osseointegration]:*	Polished finish – as the surgeon is used to. The inside surfaces can be satin, if asked.	

STAGE 2: ESTABLISH IMPLANT / GUIDE REQUIREMENTS

	Basic Geometry	
Device(s) extents:	Reconstruct the entire defect, except for the orbit – in which case, do not extend the implant the full distance posteriorly. Because – easier insertion, and less dangerous.	
Device(s) thickness:	0.5mm.	
Device(s) shape:	Based on the contralateral healthy anatomy.	
	Morphology and Safety	
Device(s) fit: ***[Including inlay vs.onlay]:***	Inlay design for all parts - aiming to avoid a bulbous reconstruction.	
Device(s) insertion paths:	Defect site will be fully exposed. Main concern during surgery will be to protect the globe. Cranium part would be inserted more from a superior direction. Other part or parts would be inserted from anterior direction.	
Device(s) soft-tissue considerations:	Temporalis muscle will be dissected for the excision and needs to be anchored to a part of the implant after insertion. Soft tissue tends to hollow around the temporal region – a small over-correction may be desirable. The skin flap cannot be under too much tension upon completion – so a bulbous reconstruction must be avoided.	
Number of components / nature of the interface between components:	At least 2 components.	
Device(s) fixation methods: ***[Incl. specify screws]:***	1.5mm screws in all cases. Screws should avoid the frontal sinus.	
Delicate anatomy handling / manipulation:	Globe / optic nerve important to avoid. Avoid frontal sinus.	
Device handling:	Parts should not be so small as to be difficult to handle / easy to drop.	

STAGE 2: ESTABLISH IMPLANT / GUIDE REQUIREMENTS

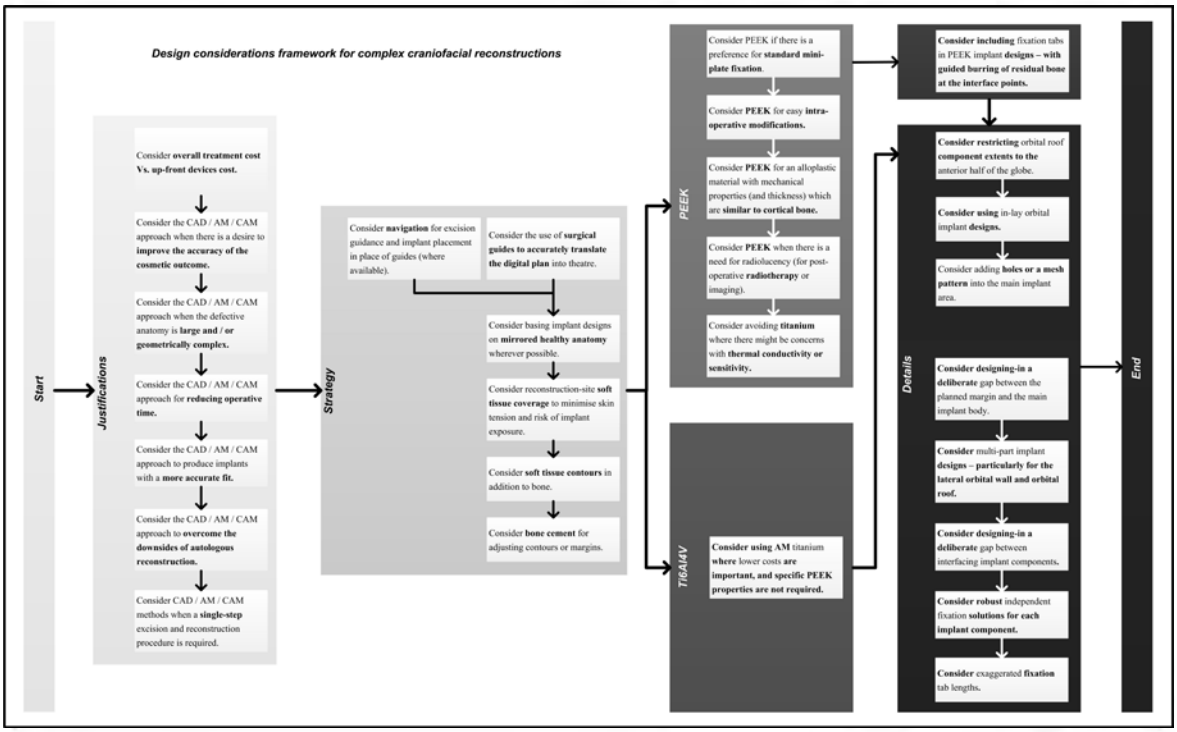
Anatomical engagement:	Parts must engage with anatomy confidently, or where this isn't possible, a positioning guide (s)should be designed.	
Clinician / support-staff safety:	Normal considerations – avoid sharp corners.	
Intuitive? **[Or functional labelling?]**	Minimise ambiguity. Labelling not essential on parts themselves, but clear instructions should be provided in order to communicate with the rest of the surgical team.	
	Other	
Other product requirements:	Coronal approach in-theatre. These parts will be the only reconstructive option in-theatre (meaning that no laboratory-produced or pre-shaped stock implants will be prepared as emergency alternatives). ➢ Therefore, they must be able to accommodate changes to the surgical plan / excision margin.	

STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS

STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS (PRE-DESIGN / DURING DESIGN):

After defining and refining the operating surgeon's product requirements during **STAGE 2**, address the specific design considerations listed in the table on the following page below. Check the boxes when each issue has been addressed, or note a justification for those which are deliberately overlooked, or deemed irrelevant.

For ease-of-reference, the flow-diagram below presents the considerations in summary form. The table however, provides details on evidence and justifications.



STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS

SPECIFIC DESIGN CONSIDERATIONS CHECKLIST

Consideration / Outcome:	Evidence / Source:	Implemented?	Notes / Justifications:
	Design Decisions		
Consider multi-part implant designs – particularly for the lateral orbital wall and orbital roof. *To enable easy manipulation of the components into the correct (pre-planned) positions.*	PDR-SPD study in partnership with surgeons from the University Hospital of Wales: Peel, S., Bhatia, S., Eggbeer, D., Morris, D., Hayhurst, C. "Evolution of design considerations in complex craniofacial reconstruction using patient-specific implants", Journal of Engineering in Medicine, (2017 – In Press)		Yes – requirement listed in written instructions.
Consider robust independent fixation solutions for each implant component. *To build-in functional independence in case one component is omitted from the final reconstruction.*			Required – judge against this. Requirement not listed in written instructions.
Consider exaggerated fixation tab lengths. *To provide margin flexibility when excisions are larger than planned.*			Required – judge against this. Requirement not listed in written instructions. Check whether alternative solutions achieve the same result.
Consider designing-in a deliberate gap between the planned margin and the main implant body. *To provide margin flexibility when excisions are smaller than planned.*			Required – judge against this. Requirement not listed in written instructions. Check whether alternative solutions achieve the same result.
Consider designing-in a deliberate gap between interfacing implant components. *To provide positioning flexibility and avoid chain-tolerance errors in the event that one or more components is fixed sub-optimally.*			Required – judge against this. Requirement not listed in written instructions. Check whether alternative solutions achieve the same result.
Consider using in-lay orbital implant designs. *To lower the risk of reducing the orbital volume.*			Yes – requirement listed in written instructions.
Consider restricting orbital roof component extents to the anterior half of the globe. *To lower the risk of reducing the orbital volume.*			Desirable (more evidence needed) – judge partially against this. Requirement not listed in written instructions. Check whether alternative solutions achieve the same result.
~~Consider including fixation tabs in PEEK implant designs – with guided burring of residual bone at the interface points.~~			N/A

STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS

~~*To offer a more stable fixation option – or when preferred over mini plates.*~~			
Consider using AM titanium where specific PEEK properties are not required. *To achieve similar benefits at lower cost.*			Yes – requirement listed in written instructions.
Consider providing extra holes in the temporal region. *To provide suturing points for the temporalis muscle.*			Required – judge against this. Requirement not listed in written instructions. Check whether alternative solutions achieve the same result.
Consider slightly flattening the reconstruction contours. *To produce a plate which is not overly bulbous – therefore ensuring good skin flap coverage.*	Literature review – part of a publication which is in development. *"Additively manufactured vs. conventionally pressed cranioplasty implants – an accuracy comparison"*		Desirable (more evidence needed) – judge partially against this. Requirement not listed in written instructions. Check whether alternative solutions achieve the same result.
~~Consider removing plate material around areas of potential temporalis muscle-dura fusion.~~ ~~*To maintain implant viability in the event of muscle-dura fusion in the weeks and months following craniotomy.*~~	~~Peel S, Eggbeer D. Additively manufactured maxillofacial implants & guides – achieving routine use *Rapid Prototyping Journal*. 2016; 22: 189 – 99.~~		N/A – temporalis will be dissected in this instance.
	Manufacturing (Metal AM)		
Consider adhering to the supplier's minimum part thickness guidelines (Renishaw PLC = 0.4mm). *To prevent the need to redesign areas or components downstream.*	Renishaw PLC correspondence.		Required. Judge based on this, if Morriston have had the same instructions from Renishaw.
Consider the differences in surface finish achievability for: where a grit blast stream can reach, and where a polishing tool can reach, and where a polishing tool can reach. *To prevent the need to reduce the range of available surface finishes downstream.*			Required. Judge against this.
Consider ensuring the residual material remaining after modelling countersinks in device designs is at least 0.3mm thick.			Required. Judge against this.

STAGE 3: ADDRESS SPECIFIC DESIGN CONSIDERATIONS

To adhere to the supplier's guidelines and guarantee the integrity of the fixation solution.			
Consider making transitions between part thickness values smooth. *To mitigate issues with distortion and stress during part cooling.*			Required. Slightly less important. Judge less harshly against this.
Consider chamfering or smoothing sharp corners where possible. *To mitigate issues with support structure modelling.*			Required. Judge against this.
Manufacturing (Machined PEEK)			
~~Consider adhering to the supplier's minimum part thickness guidelines (DePuy Synthes = 3-4mm except for slight local thinning for onlay implants).~~ ~~*To prevent the need to redesign areas or components downstream.*~~	~~DePuy Synthes Correspondence.~~		~~N/A~~
~~Consider the ability of a machine tool to access undercut areas of a PEEK device design.~~ ~~*To prevent the need to redesign areas or components downstream.*~~			~~N/A~~
Regulatory Requirements			
Consider how to minimise contamination opportunities through the design of the devices. *By, e.g. improving the ease of cleaning, sterilisation, packaging damage prevention.*			More a question of avoiding bad designs / obvious dirt traps, rather than designing FOR this issue.
Consider how to minimise risks of leakage from the designed device(s). *By, e.g. ensuring the designed geometry has unintended gaps filled.*			N/A
Consider how to minimise risks of substance ingress into the designed device(s). *By, e.g. ensuring the designed geometry has unintended gaps filled.*			N/A
Consider how to ensure part identification and traceability. *By, e.g. ensuring packaging is labelled if labelling the devices physically is difficult.*			Required. Labelled packaging OR part are acceptable.

STAGE 4: DESIGN PEER REVIEW (POST-DESIGN)

Now, the proposed design(s) must be reviewed by you, and by another member of the technical or design team against the requirements list which was compiled in **STAGE 2**, and against the recorded considerations in **STAGE 3**. Use the checkboxes to verify the design solution(s) and confirm that each requirement and relevant consideration has been accommodated. Where a requirement has been deliberately overlooked, or a relevant consideration omitted, note the justification in the spaces provided.

PEER REVIEW		
Peer- reviewer:		
Peer-reviewer job role:		
	Designer Review	Peer Review
Date of reviews:		
Name(s) of reviewed file(s): *[Finished device STL's / IGES]:*		
Do the design outputs match the requirements from **STAGE 2** and the justifications from **STAGE 3**?	*Yes:* ☐ *No:* ☐	*Yes:* ☐ *No:* ☐

STAGE 5 DESIGN REVIEW & PEER REVIEW

If not, why not?	*Not enough detail in recorded notes:*	*Changes to design required:*	*Not enough detail in recorded notes:*	*Changes to design required:*
	Recorded notes are not current:	*Other: [Detail below].*	*Recorded notes are not current:*	*Other: [Detail below].*
If not, recommended corrective actions:				
Corrective actions undertaken satisfactorily?		*Yes:*		*Yes:*

DESIGN APPROVAL

The design outputs address STAGE 2 requirements and STAGE 3 considerations, or have omissions justified.	*Project manager signature:*		*Reviewer signature:*

STAGE 5: DESIGN VERIFICATION & FABRICATION APPROVAL (POST-DESIGN)

Present the peer-approved final designs to the operating clinician for approval. If requirements have changed, or modifications are requested, update the previous sections of this form, and undertake the revisions. After obtaining a verification signature from the operating surgeon, begin an appropriately controlled and certified fabrication process.

VERIFICATION MATERIAL

Checklist – have you documented and communicated these details to the operating surgeon?

List of final product requirements:	*Images of the 3D reconstructions of the processed scan-data:*	*Multiple views of designed devices:*	*Images showing device contours overlaid against key scan-data slices:*
List of specifically addressed design considerations from stage 3:	*Images of scan-data modifications /digital anatomical repairs:*	*Multiple views of designed devices in-situ on virtual model of anatomy:*	

CHANGE REQUESTS

Operating clinician design verification? *Yes:* *No:*

If not, requested modifications:

Corrective actions undertaken satisfactorily? *Yes:*

DESIGN VERIFICATION & FABRICATION APPROVAL

The design outputs address STAGE 2 requirements and STAGE 3 considerations, or have omissions justified.

Operating surgeon signature: *Date:*

STAGE 6 – FEEDBACK COLLECTION, ANALYSIS & (OPTIONAL) PUBLICATION (POST-DESIGN TRANSFER)

Gather feedback on the designed devices, their design details, their performance, and any links to surgical outcomes - by prompting the operating clinician for thorough comments after key milestones. Record this feedback under your own organisation's systems. Where a case study or a case series demonstrates new design considerations, or require revisions of existing considerations, consider updating this framework (after peer-review in your organisation). Wherever possible, this new evidence should be disseminated through conferences or journal papers to advance the development of design rules across the field.

FEEDBACK PROMPTS

Have you requested feedback after:

Surgery: ☐ *3 months:* ☐ *6 months:* ☐

12 months: ☐ *Longer:* ☐

RECEIVED FEEDBACK

Feedback receipt date:

Feedback medium: *Letter:* ☐ *Form:* ☐ *Email:* ☐ *Verbal:* ☐

Original (or transcribed) correspondence attached (or filed)?

[Details]:

FEEDBACK CLASSIFICATION

Complaint? (If yes, follow your organisation's procedure). ☐

[- A device failure related to the design of the device, - a criticism of the product or service for which the customer requests compensatory action, - or something requiring an immediate response]:

Feedback? ☐

[- Information which can be used to formulate new or revised considerations, form frameworks, or work instructions]:

DISSEMINATION

Does this project demonstrate potential for inclusion in a presentation or publication?

[Details]:

A8 – Investigation C Field Notes Pro-Forma

Design Exercise Pro-Forma

TRACK: questions / actions / behaviours / emotions / design details / iterations.		
KEY TIMESTAMPS (MINS):	(DURING) NOTES / TALLY:	(AFTER) ACCURATE KEY QUOTE TRANSCRIPTIONS / ANALYSIS:

Interview Questions / Notes

QUESTION / TOPIC: + FOLLOW-UPS!	TIMESTAMP:	(DURING) NOTES / FOLLOW-UP QUESTIONS / TOPICS	(AFTER) ACCURATE KEY QUOTE TRANSCRIPTIONS:
		Specific Task / Outputs:	
Please describe your designed solution in the context of the project and product requirements.			
Please describe how you would have finished the design, and its key design details.			
How do you rate the ease (or difficulty) of the design exercise?			
		Regular Working:	
What is the biggest barrier (or barriers) during everyday design work. *Did that (or they) manifest themselves in this exercise?*			
How is quality controlled (if at all) is your design process? *To what degree do you follow these controls?*			

How prescriptive is the structure of your design process? *To what degree do you follow this structure? (As you go? Or retrospectively?)*			
How are projects managed? *Including intra-team arrangements?*			
What were your emotional reaction(s) to using your conventional processes to work on this exercise?			
To what degree, and how, is your regular design process documented and recorded?			
To what degree are design procedures supported by evidence? *How? Sources?*			
To the degree that any exist, how are disagreements between you and your clients regarding designed solutions resolved?			
To what degree are regulatory requirements considered in your regular design work? *Where required.*			
How are new design approaches or ideas evaluated and approved? *How often do you try something new?*			
How often are you presented with an unusual design problem?			
Is feedback on your designed device performance collected? How? *How is this used?*			

Framework Working:			
Please describe the effects, if any, the framework had on your design process – relative to your conventional methods.			
What where your emotional reaction(s) to using the framework in this design exercise?			
How, if at all, did section 1 of the framework (project set-up) affect your working?			
How, if at all, did section 2 (establishing implant requirements) affect your working?			
How, if at all, did section 3 (specific design considerations) affect your working?			
Does your conventional practice include an activity analogous to section 4 (peer review)?			

How does / could this affect your design work?			
Does your conventional practice include an activity analogous to section 5 (fabrication approval)? How does / could this affect your design work?			
Does your conventional practice include an activity analogous to section 6 (feedbak)? How does / could this affect your design work?			
What effects, if any, did using the framework have on the success of your designed outputs (or at least the design direction)?			

A9 – PDR SPD IT & Data Handling Policy

IT SECURITY POLICY

Scan data is provided to PDR-SPD on the basis that the patient is informed that a custom device(s) will be made (based on a virtual model of their anatomy) and that their data is being sent to a third party for that purpose.

PATIENT INFORMATION HANDLING

PDR-SPD does not need any patient-identifying information (such as age: date of birth, address, clinical condition etc.) in order to produce models other than information deemed necessary to guide the extents required.

It is advised the provider is aware of local and country-specific guidelines such as connecting for health. http://www.connectingforhealth.nhs.uk/systemsandservices/infogov/security/encryptionguide.pdf

PDR-SPD processes personal data in accordance with the Data Protection Act 1998. Data is held confidentially and will only be used for the task specified by the provider.

Physical data (such as scan data arriving on a CD and cover letters) arriving at PDR will stored in an office which is locked overnight and has strict access control (limited to authorised visitors who must sign in). Data on CD will be returned by courier with the model, or sent back via tracked delivery. Raw DICOM scan data is stored for 12 months from receipt, before being destroyed. Records and design files are stored maintained for five years (in the case of non-implantable devices), or for seventeen years (implantable devices) beyond the end of the marketable life of the product category. Digital data pertaining to each case is stored securely with access limited to authorised staff. Regular data backups are taken to a secure server.

PDR-SPD IT COMPLIANCE STATEMENT

Access to the desktop computers and the network require authentication with the relevant Cardiff Metropolitan University (CMU) personal account. Password policies are in place to ensure passwords used comply with best practice (complex, maximum age of 90 days, restrictions on re-use). 802.1x is used on the wireless network to prevent unauthorised access.

Cardiff Metropolitan University has firewall protection on its network and uses relevant access control to limit access to secure server systems. Penetration testing is used, when necessary, to assess system and service security and to identify any vulnerabilities.

An Incident Response Procedure is established, which documents relevant processes for the University to address security incidents. Disaster Recovery Plans are in place to document relevant business continuity actions for IT systems and services.

IMAGE EXCHANGE PORTAL DATA

Secure online hospital-PACS-to-PDR transfer service data is accessed directly on the service portal and downloaded to PDR-SPD's secure server. Desktop and laptop computers based in the PDR-SPD office, access the data from the server; so no downloads occur to the end user equipment. All computers are protected with up to date endpoint protection (anti-virus and anti-malware).

Staff who have access to the Image Exchange Portal and any personal data that originates from this have been trained on the Data Protection Act 1998 and fully comply with its instructions. They have also undertaken IT Security training and are aware that they need to abide by the measures documented in CMU's Electronic Communications Policy (copy available on request).

The secure online hospital PACS-to-PDR transfer service's local storage location is not used to store large data sets for long periods. Once SPD staff have read the data into scan-data processing software, DICOM data is deleted promptly from the immediate download location. This removes excess copies of retained sensitive information – and reduces the burden on the PDR-SPD server.

APPROVING AND REVOKING ACCESS TO SENSITIVE DATA

PDR Staff members who have access to Project Folders are approved by the head of PDR-SPD and granted access by the CMU Information Services Division (ISD). In the event of a staff member leaving, or their role changing (in relation to the need to access sensitive data), or being suspended, the head of PDR-SPD liaises with ISD to revoke or alter access appropriately.

STAFF ROLE / GROUP:	ACCESS JUSTIFICATION
Head of PDR-SPD	Everyday role requires access to deliver services.
Business Development Design & Research Engineer – PDR-SPD	Everyday role requires access to deliver services.
Surgical & Prosthetic Design Engineer – PDR-SPD.	Everyday role requires access to deliver services.

PHYSICAL SECURITY OF IT EQUIPMENT

The PDR-SPD server is housed by CMU's ISD department in a secure data centre area. Sensitive data received from hospitals is stored in [PDR15] Individual Project Folders. None of this data is stored locally on computers in the PDR-SPD office or on PDR-SPD laptops.

DISPOSAL OF IT EQUIPMENT

Cardiff Metropolitan University's equipment and data disposal policy (copy available on request) is followed. ISD is consulted when any device that could contain sensitive data (or the ability to access it) requires disposal.

DATA STORAGE AND BACKUP

CMU's ISD have responsibility securely backing up the contents of the PDR-SPD server. Laptops and desktop computers containing work-related (but non-confidential) data are regularly backed-up by individuals.

CARDIFF METROPOLITAN UNIVERSITY
APPLICATION FOR ETHICS APPROVAL

When undertaking a research or enterprise project, Cardiff Met staff and students are obliged to complete this form in order that the ethics implications of that project may be considered.

If the project requires ethics approval from an external agency such as the NHS or MoD, you will not need to seek additional ethics approval from Cardiff Met. You should however complete Part One of this form and attach a copy of your NHS application in order that your School is aware of the project.

The document ***Guidelines for obtaining ethics approval*** will help you complete this form. It is available from the Cardiff Met website.

Once you have completed the form, sign the declaration and forward to your School Research Ethics Committee.

PLEASE NOTE:
Participant recruitment or data collection must not commence until ethics approval has been obtained.

PART ONE

Name of applicant:	Sean Peel
Supervisor (if student project):	Dr Dominic Eggbeer
School:	PDR
Student number (if applicable):	20018919
Programme enrolled on (if applicable):	MPhil>PhD (Part Time)
Project Title:	Novel Solutions for the Patient-Specific Medical Device Design Process – PART 1 – Current Methods
Expected Start Date:	08/01/2013
Approximate Duration:	Ongoing (series of 1-2 day visits as and when appropriate case studies arise).
Funding Body (if applicable):	N/A
Other researcher(s) working on the project:	N/A
Will the study involve NHS patients or staff?	Yes
Will the study involve taking samples of human origin from participants?	No

In no more than 150 words, give a non technical summary of the project
The Ph.D aims to improve the efficiency of patient-specific implant production methods using novel design methodologies that incorporate the use of computer aided design and fabrication techniques. The first phase of the Ph.D. is a study to audit current methods of producing and using implanted

CARDIFF METROPOLITAN UNIVERSITY
APPLICATION FOR ETHICS APPROVAL

cranioplasty and other reconstructive plates produced within Morriston Hospital and University Hospital of Wales.

Methods

- Observation, process-mapping and timing of the actions undertaken by prosthetists, technicians and surgeons at Morriston Hospital and University Hospital of Wales during the specification, design and fabrication of implants.
- No direct interaction with patients or specifying of treatments.
- Recording of NHS staff actions and comments via notes, photographs and audio for later review (subject to gaining informed consent from all participants). NHS professionals.

Does your project fall entirely within one of the following categories:	
Paper based, involving only documents in the public domain	No
Laboratory based, not involving human participants or human tissue samples	No
Practice based not involving human participants (eg curatorial, practice audit)	Yes
Compulsory projects in professional practice (eg Initial Teacher Education)	No
If you have answered YES to any of these questions, no further information regarding your project is required. If you have answered NO to all of these questions, you must complete Part 2 of this form	

DECLARATION: **I confirm that this project conforms with the Cardiff Met Research Governance Framework**	
Signature of the applicant: Speel.	Date: 04/01/13
FOR STUDENT PROJECTS ONLY	
Name of supervisor: DOMINIC EGGBEER	Date: 4/1/13
Signature of supervisor:	

Research Ethics Committee use only	
Decision reached:	Project approved ☑ Project approved in principle ☐

CARDIFF METROPOLITAN UNIVERSITY
APPLICATION FOR ETHICS APPROVAL

Decision deferred ☐ Project not approved ☐ Project rejected ☐	
Project reference number: Click here to enter text.	
Name: Click here to enter text. HR MILLWARD	Date: Click here to enter a date. 8/1/2013
Signature: HR Millward.	
Details of any conditions upon which approval is dependant: Click here to enter text. N/A	

A11 – NHS Ethics Approvals / Waivers

From: Jemma Hughes (ABM ULHB - Research & Development) [mailto:Jemma.Hughes@wales.nhs.uk]
Sent: 02 January 2013 16:31
To: Eggbeer, Dominic (PDR)
Subject: RE: Audit conformation

Hi Dominic
Apologies for the delay, I'm assuming your reference to audio recording/photos of participants etc refers to the lab staff only? If that's the case, the current rules state that ethical review is not required for studies only involving NHS staff as participants, by virtue of their professional role. I have attached relevant guidance for further info.
Kind regards
Jemma

Tue 22/01/2013 00:10
Maureen Fallon (Cardiff and Vale UHB - Innovation and Improvement) <Maureen.Fallon@wales.nhs.uk>
Approval SPeel
To Peel, Sean
You replied to this message on 22/01/2013 09:14.

Dear Sion

Thanks for your forbearance. Your e-mail and indeed the detailed information included within the registration document itself was helpful in terms of confirming the limitations to your PhD. As a result, I am delighted to confirm that your proposal to evaluate current production methods for cranioplasty and other reconstructive plates does meet with service evaluation approval. Please accept this e-mail as confirmatory approval.

In terms of finalising the process could you arrange for Mr. Cronin to send an e-mail of his support for the project please? Also, once the evaluation is completed I would be grateful if you could forward a copy of your findings and recommendations.

Best wishes and good luck with the project.
Maureen

Wed 23/01/2013 12:52
Andrew Cronin (Cardiff and Vale UHB - Dental) <Andrew.Cronin@wales.nhs.uk>
RE: Approval SPeel
To Peel, Sean; Maureen Fallon (Cardiff and Vale UHB - Innovation and Improvement)

Dear Sean

Just to confirm I am fully supportive of this and look forward to the results/conclusions. It would make perfect sense to save money but not at the expense of quality and perhaps your evaluation will shed light on this.

Good luck and Best Wishes

Andrew

A12 – NHS Honorary Employment Letter

GIG CYMRU NHS WALES | Partneriaeth Cydwasanaethau Gwasanaethau Cyflogaeth | Shared Services Partnership Employment Services

Ref: HONORARY/CH Date: 22nd May 2013

Private & Confidential
Mr Sean Peel
PDR - Cardiff Metropolitan University
Llandaff Campus
200 Western Avenue
Cardiff
CF5 2YB

Dear Mr Sean Peel

Appointment of: PDR Student

I am pleased to confirm your appointment with Abertawe Bro Morgannwg University Health Board to the above position. Your start date is to be agreed upon receipt of all satisfactory pre employment checks.

The conditions of your post are as follows:

- The position is offered on an honorary basis.
- Based at: Maxillofacial Laboratory - Morriston Hospital

Please note that in accordance with WHC 2005 (071) Pre and Post Appointment Checks for All Persons Working in the NHS in Wales, the offer of employment is conditional and subject to the following pre-employment checks (if applicable to the post):

- At least two suitable satisfactory references covering a minimum of the last three years of employment
- A satisfactory Criminal Records Bureau check if required. Receipt of an adverse check could result in termination of employment or withdrawal of offer of employment
- Satisfactory occupational health check from the Health Board's Occupational Health Department.
- Proof of Right to Work in the UK
- Proof of Identity
- Proof of Qualifications (if the post requires)
- Proof of Professional Registration (if the post requires)

We do not advise you to hand in your notice with your current employer until you have received verification from your appointing manager that all pre employment checks are satisfactory.

In line with the European Working Time Regulations it is the Health Board's Policy to ensure that employees do not work in excess of 48 hours per week. You are required to advise your Manager of any other post/s held with any organisation that would conflict with the European Working Time Regulation.

In order that the recruitment process runs smoothly, you will need to take the following action **within 3 working days** as outlined below:

- Telephone the Recruitment Team on 01792 703386 in order to arrange a Pre Employment Document Check meeting.

- If included in this appointment pack, complete the CRB Disclosure Form in **Black Ink** and bring it with you to your appointment, along with the necessary original documents as per enclosed Guidance.

Documents required for your Pre- Employment Document Check meeting,

You must bring:

- If required the CRB documentation as per attached guidance
- ID documentation
- Proof of Right to Work in the UK as per attached guidance
- Driving Licence if required for the job

Proof of the following information, if relevant to the job, and as outlined in your application:

- Professional Registration as per Person Specification
- Qualifications as per Person Specification

Failure to arrange or attend an appointment will delay your start date.

Failure to bring the necessary documents will result in you being asked to return at a later date, which in turn will delay your start date.

Please note that the Health Board is "Smoke Free" in all premises and within grounds in line with legislation.

If you are a new employee of the Health Board, you will automatically become a member of the NHS Pension Scheme, unless you make alternative arrangements and notify your manager accordingly. Details of the NHS scheme are given in the scheme guide which is available via the website http://www.nhsbsa.nhs.uk/pensions or a hard copy can be obtained from the Pensions Department by telephoning 01656 753440.

Finally, I would like to take this opportunity to congratulate you on your success, and hope you enjoy working for Abertawe Bro Morgannwg University Health Board. Should you have any queries, please contact Sarah Turner on 01792 703386.

Yours sincerely

Employment Services Team
NHS Wales Shared Services Partnership
(On behalf of Abertawe Bro Morgannwg University Health Board)

c.c Recruiting Manager

A13 – IMPT Associate Membership Certificate

This is to Certify that

SEAN PEEL

having satisfied the regulations, objectives, ethical and professional code of The Institute, is admitted by the authority of The Council to

Associate Membership

of

The Institute of Maxillofacial Prosthetists and Technologists

Roll No. A607

Chairman Sarah Parkinson.

Registrar Karen B Glen

Date 1st April 2013

Issued by The Authority of The Institute only and not under The Authority of any Government Department or Authority

A14 – BSI Gap Analysis Report (Extract)

bsi.

Assessment Report.

Executive Summary

Description of the Organisation:

PDR is a research institute and design consultancy at Cardiff Metropolitan University. PDR comprises seven groups – of which one is Surgical and Prosthetic Design (PDR-SPD). Three groups in PDR (including PDR-SPD) are certified to BS EN ISO 9001:2008 under a single certificate. PDR-SPD undertakes design activities to produce 3D geometries (usually STL files) representing patient-specific anatomical models, patient-specific cutting and drilling guides, and patient-specific implants. PDR-SPD is not the legal manufacturer of medical devices – this responsibility lies with manufacturing and marketing entities (usually major engineering companies, or major engineering companies via hospital customers). The files provided by PDR describe only the surface geometry of a three-dimensional object – and require further inputs and infrastructure from the legal manufacturer to enable fabrication of class 3 medical devices (in 3D-printed titanium or machined PEEK). The files contain data, and are not a software program. Our proposed BS EN ISO 13485:2016 certification will cover PDR-SPD's design activities for non-load-bearing, static implants and guides (and anatomical models). Fabrication of laboratory / office-use medical models continues to be subject to PDR's BS EN ISO 9001:2008 certification.

The objectives of the assessment were met.

Obstacles, Omissions and Reliability
There were no obstacles encountered during the course of the audit. No factors were encountered during the audit that would affect the reliability of this assessment.

All areas were covered per the assessment plan.

Identification and Dating
Audit report authors are as per the assessment team listed. The recommendation included in this assessment is based on assessment of PDR, Cardiff Met Company Ltd, Western Avenue, Cardiff, CF5 2YB, United Kingdom on 03 March 2017.

The report was finalised and issued on 06 March 2017.

Pre-certification
The results of this Pre-certification assessment confirm the management system is ready to proceed to Stage 1 assessment.

Assessment objective, scope and criteria

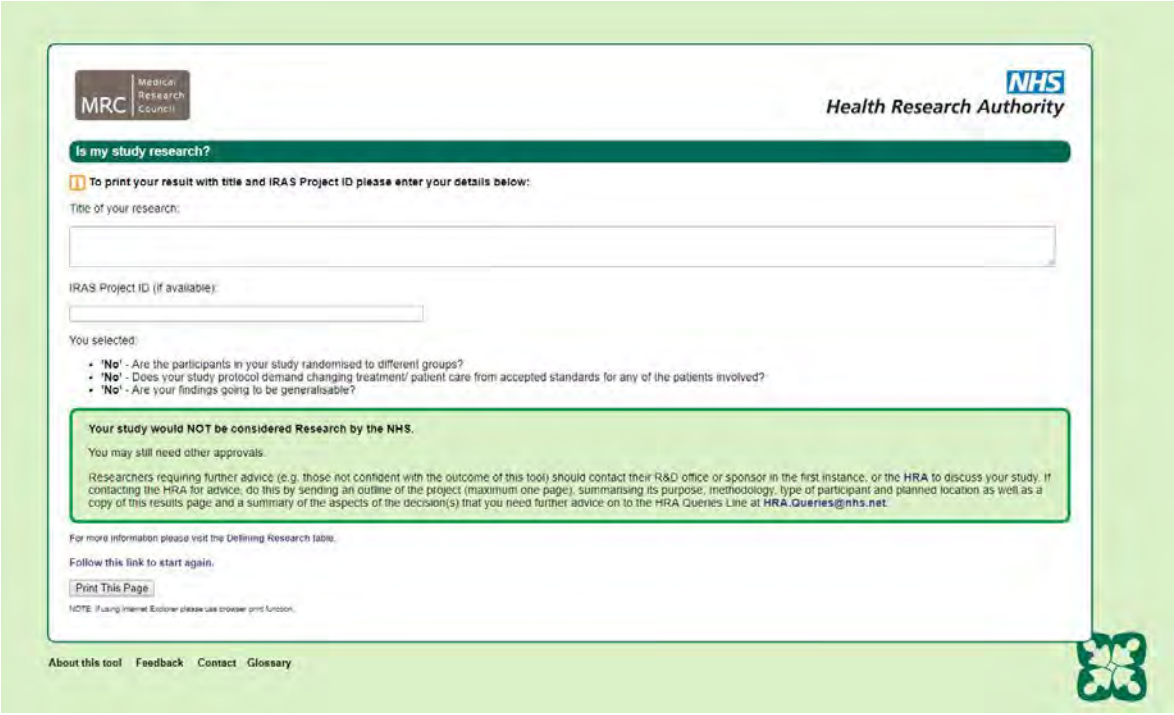
AUDIT SCOPE AND OBJECTIVES

Assessment Scope:
The management system processes at PDR, Cardiff Met Company Ltd, Western Avenue, Cardiff, CF5 2YB, United Kingdom

Assessment Objectives
PRE-CERTIFICATION ASSESSMENT

...making excellence a habit.™

A15 – Medical Research Council "Is my study research?" Result



MRC Medical Research Council

NHS Health Research Authority

Is my study research?

To print your result with title and IRAS Project ID please enter your details below:

Title of your research:

IRAS Project ID (if available):

You selected:

- **'No'** - Are the participants in your study randomised to different groups?
- **'No'** - Does your study protocol demand changing treatment/ patient care from accepted standards for any of the patients involved?
- **'No'** - Are your findings going to be generalisable?

Your study would NOT be considered Research by the NHS.

You may still need other approvals.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the **HRA** to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of this results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at **HRA.Queries@nhs.net**.

For more information please visit the Defining Research table.

Follow this link to start again.

Print This Page

NOTE: If using Internet Explorer please use browser print function.

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