A SYSTEMATIC FRAMEWORK FOR PATIENT-SPECIFIC IMPLANT DESIGN AND PERSONALISED MEDICAL PRODUCT DEVELOPMENT

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Abstract - This paper presents a systematic framework for the innovative design and development of patient-specific implants and personalised products for healthcare and medical applications. The framework focuses particularly on cranio-maxillofacial surgery, and it is applicable to other fields, including orthopaedic and dental surgery, and medical rehabilitation. The proposed framework integrates the latest advancements in medical image processing, biomaterials, innovative design and product development, and emerging manufacturing technologies, including additive manufacturing and 3D bioprinting, to provide a systematic approach for the cost-effective and innovative development of personalised implants and medical devices, alongside solutions for medical diagnosis, treatment, and rehabilitation. Successfully conducted clinical cases of patient-specific implant design and development are presented, showcasing successful outcomes and improved quality of medical treatments for complex bone reconstruction, and demonstrating the effective application of the proposed framework in clinical practice. The framework emphasises the importance of multidisciplinary collaboration among clinicians, biomedical engineers, and designers, while also addressing challenges related to cost-effectiveness, technology transfer, and resource limitations within healthcare systems. It provides pathways to improve healthcare quality, strengthen the adoption of personalised healthcare and medicine, and leverage artificial intelligence-driven design, data-informed decision-making, and emerging medical image processing to simplify development processes and shorten the time required to produce patient-specific implants and personalised medical products.

Keywords: Patient-specific implant, Personalised products, Framework, Medical additive manufacturing, 3D bioprinting, Biomedical engineering, Cranio-maxillofacial surgery.

1. Introduction

Personalised products play an important role in improving the quality of medical diagnosis, treatment, and rehabilitation in healthcare and medicine. The innovative design and development of personalised products represent one of the core foundations of personalised healthcare and medicine, providing optimal solutions to meet both clinical and technical requirements for patients. Specifically, these products address the limitations of traditional standardised products, particularly implants, surgical guides, and medical devices, which can lead to complications or poor-quality diagnosis, treatment, and rehabilitation due to anatomical variations. Significant advancements have been achieved in recent decades in two-dimensional (2D) and three-dimensional (3D) medical image

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processing (MIP), biomaterials, 3D computer-aided design (CAD) and modelling, artificial intelligence (AI)-driven design and decision-making, reverse engineering (RE), and innovative manufacturing technologies, including CNC machining, advanced sheet metal forming (SMF) such as hydroforming, incremental forming, and superplastic forming, additive manufacturing (AM), and 3D bioprinting. These advancements have enabled a paradigm shift in transferring emerging technologies to hospitals, enhancing medical diagnosis, surgical outcomes, and treatment quality, especially through advanced medical image processing, AI-powered medical diagnosis and data-informed decision-making, and patient-specific implants and personalised products, promoting a patient-centric approach to healthcare and medicine [1-4, 6-9].

Despite these notable advancements, challenges remain that require cost-effective and innovative solutions. These challenges are not only related to scientific and technological innovations but also encompass practical applications, knowledge management, and technology transfer to hospitals. Particularly, there are the challenges related to limited human resources in biomedical engineering and innovative design and product development, which necessitate effective multidisciplinary teamwork and collaboration among radiologists, medical doctors (MDs), surgeons, and engineers. The following are the key challenges that have been identified in patient-specific implant design and personalised medical product development:

- ***Multidisciplinary collaboration barriers***: While multidisciplinary collaboration is essential, it is often hindered by skill gaps and ineffective communication among engineers (biomedical engineers and designers) and clinicians (radiologists, MDs, and surgeons).

- ***Economic and technological constraints***: High software costs and data processing complexity limit the adoption of innovative solutions and advanced treatments in hospitals.

- ***Cost-effectiveness considerations for patients***: Unlike conventional medical products that are mass-produced, personalised products are typically designed and developed in limited quantities or as single-use items using personalisation and patient-specific design methods to achieve optimal treatment solutions. This approach provides greater adaptability to the unique anatomical and functional needs of each patient, particularly for patient-specific implants, surgical guides, and medical devices. However, personalisation results in higher treatment costs, and cost-effectiveness must be carefully considered, especially in low-income and developing countries.

In previous studies, we have presented and discussed methods and innovations in the design and manufacture of patient-specific implants, surgical guides and medical devices, especially for clinical applications in cranio-maxillofacial surgery and medical rehabilitation [1-9]. For patient-specific implants in cranio-maxillofacial surgery, the personalised design and development process begins with medical imaging acquisition, in which computed tomography (CT) and magnetic resonance imaging (MRI) data from a patient are collected as the main inputs for 2D and 3D MIP, to construct 3D CAD models of anatomical structures for pre-operative planning and personalised design of implants, surgical guides and medical devices. CAD and RE tools are then used for 3D CAD design and modelling of patient-specific implants, with the best fit to the defective areas and meeting both technical and clinical requirements based on mirroring intact skull regions onto defective areas or using standard design databases [6-9].

Depending on the implant types as well as clinical and technical requirements, a biomaterial is selected for implant fabrication, such as bone cements, polymethyl methacrylate (PMMA), polyether ether ketone (PEEK), high-density porous polyethylene (HDPE), polycaprolactone-hydroxyapatite (PCL/HA), bioceramics, titanium alloys and carbon composites.

Based on the 3D CAD models of patient-specific implants and selected biomaterials, optimal manufacturing methods are applied to fabricate patient-specific implants, including CNC machining, advanced SMF, AM, and rapid tooling [1, 3-5].

In this study, we present a systematic framework with specific workflows and solutions for the innovative design and development of personalised products, with a focus on patient-specific implants in cranio-maxillofacial surgery, taking into account the latest developments in MIP, biomaterials, 3D CAD design and modelling, AI-driven design and decision-making, and innovative manufacturing technologies, including 3D bioprinting. Typical clinical cases are demonstrated and discussed to highlight the key phases and successful implementation of the proposed systematic framework.

The remaining sections of the paper are organised as follows. Section 2 presents the methods of the study, in which a systematic framework with specific workflows and solutions for innovative design and development of personalised products was presented and discussed. Section 3 presents clinical cases that were successfully conducted to demonstrate the successful applications of the proposed systematic framework in clinical practice. Finally, discussion and conclusions are presented in Section 4, to summarise the key points of the study, with discussions about the study outcomes as well as further research directions and emerging trends in innovative design and development of patient-specific implant design and personalised medical product development.

2. A framework for Patient-specific Implant Design & Personalised Medical Product Development

Figure 1 presents a systematic framework for patient-specific implant design and personalised medical product development. The key steps for innovative development of patient-specific implants, as well as surgical guides or tools and medical devices based on medical imaging data include the following: Data collection, data processing: Data collection (CT/MRI scanning), 2D and 3D medical image processing, 3D CAD design and modelling, design analysis – optimisation – medical evaluation, manufacture, and sterilisation and product packaging for medical applications.

2.1 Data Collection

Data collection is the initial and crucial phase in the innovative design and development of

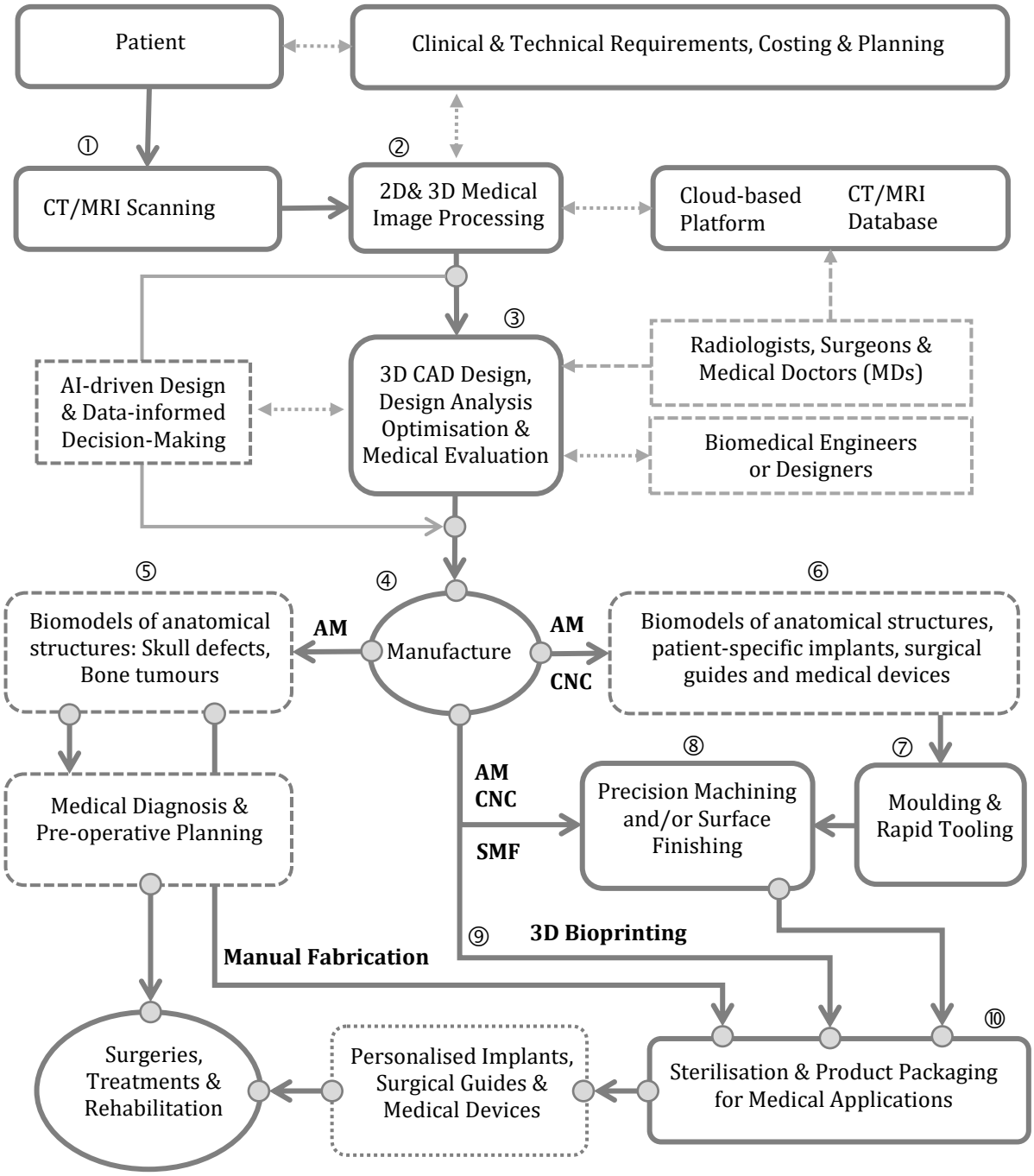

Figure 1: A systematic framework for patient-specific implant design and personalised medical product development. AM: Additive Manufacturing, CNC: CNC machining, and SMF: Sheet Metal Forming

personalised medical products, such as implants, surgical guides, and medical devices (Figure 1, Step 01). This phase involves gathering DICOM-formatted CT and MRI images from hospitals. Fundamentally, CT images are used for bone reconstruction, while MRI images are used for soft tissue reconstruction.

During this stage, a patient must be thoroughly advised by clinicians. Issues related to costing must be carefully considered, as an optimal solution for design and manufacturing needs to meet the patient's financial constraints in addition to clinical and technical requirements. Biomedical engineers and designers involved in the product development process must establish clinical and technical

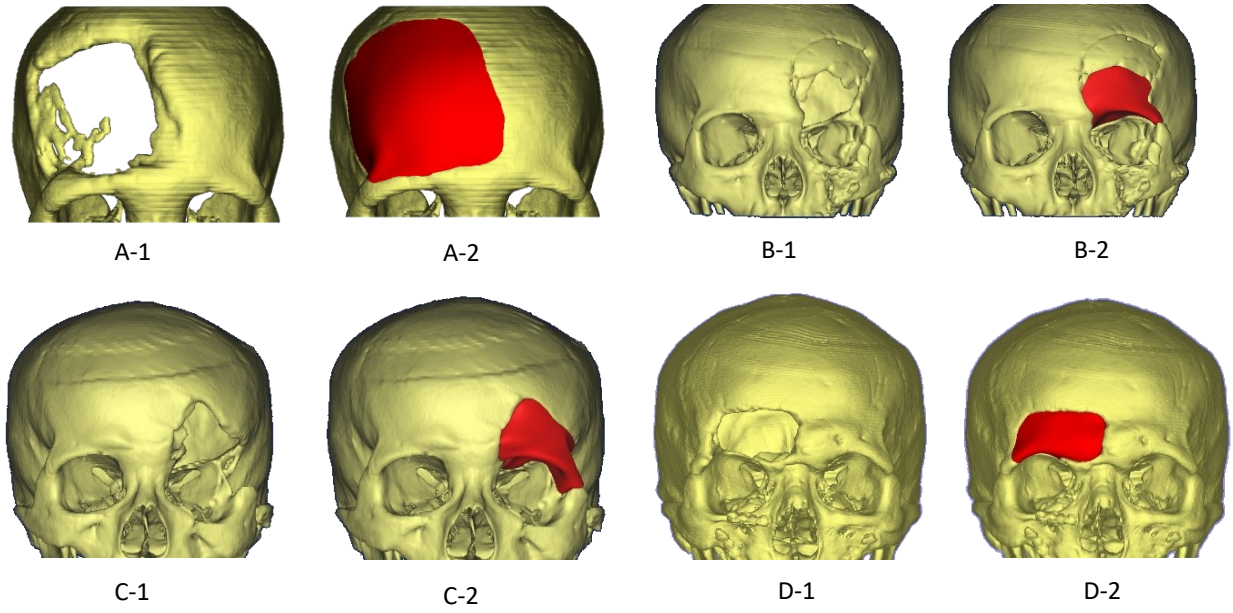

Figure 2: Typical designs of patient-specific implants for bone reconstruction of skull defects. A-1, B-1, C-1, and D-1 show 3D models of skull defects. A-2, B-2, C-2, and D-2 show 3D models of the personalised implants assembled with the skull defects, respectively

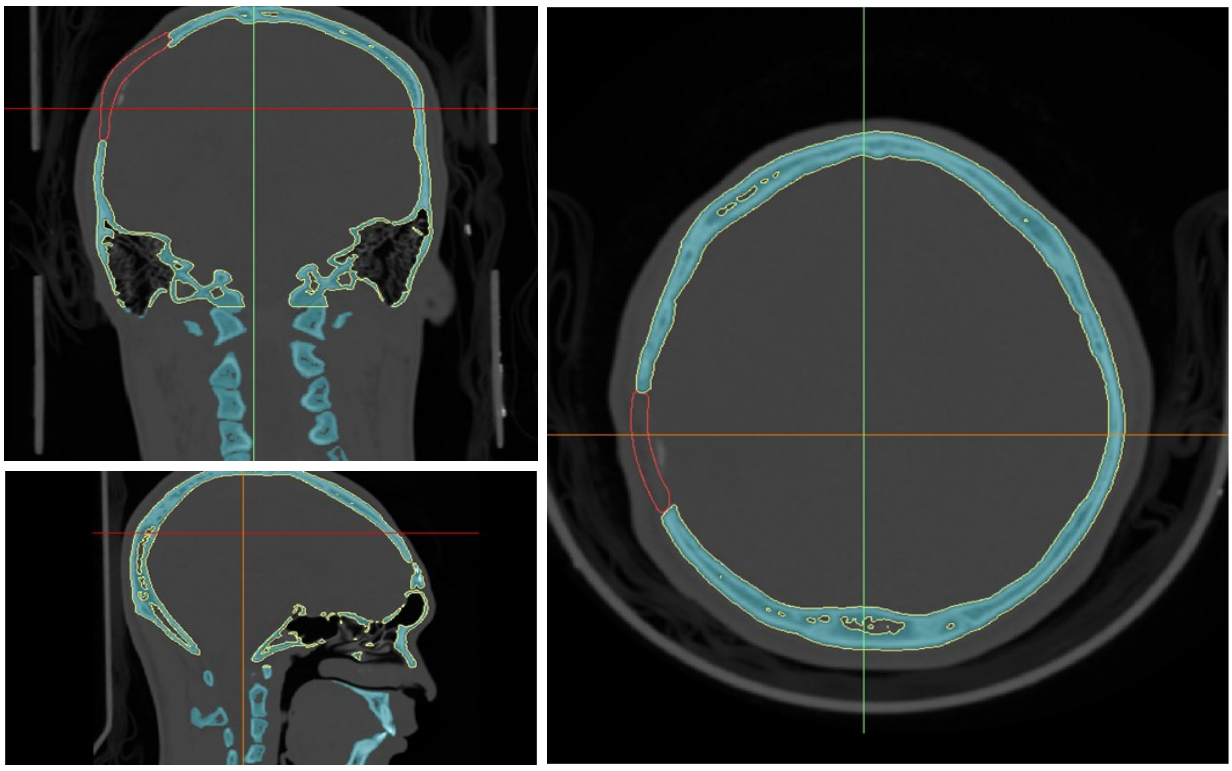

Figure 3: Medical evaluation and verification of the personalised cranioplasty implant using MIP software platforms. The 2D profile of the implant and CT images at each slice are examined to ensure optimal implant thickness design and proper contact interface between the implant and bone defect window

requirements in close collaboration with MDs or surgeons. These requirements, combined with the financial constraints, serve as the primary inputs for the design and development of personalised medical products. The CT/MRI imaging data are stored on secure, cloud-based servers to ensure optimal data management, facilitate medical image processing, data-informed decision making, and enable collaborative design and product development.

2.2 2D and 3D Medical Image Processing

Medical imaging data in the form of CT or MRI images are used as inputs for 2D and 3D medical image processing (Figure 1, Step 02). 2D and 3D MIP software and platforms are used for 3D modelling of anatomical structures, based on 2D and 3D segmentation in which regions of interest (ROI) are identified and converted into 3D models. The 2D and 3D segmentation can be performed automatically with editing tools, such as 2D and 3D region-growing methods, to separate a 2D digital image or a 3D volumetric space (volume pixels or voxels) into different regions or 3D volumes, from which 3D models of anatomical structures defined by ROI are constructed. In 2D segmentation, individual 2D images are analysed and processed independently using techniques such as thresholding, clustering, edge detection, region-based methods, and artificial neural networks; meanwhile, 3D segmentation processes the entire 3D volumetric space [10]. Due to the nature of 2D and 3D segmentation, CT data provide better results for bone reconstruction compared to MRI images, which are fundamentally suitable for soft tissue modelling [1-3].

Typical commercial MIP software includes Mimics (Materialise NV, Leuven, Belgium), Simpleware (Synopsys Inc., Mountain View, CA, USA), 3D-Doctor (Able Software Corp., Lexington, MA, USA), and Amira (Thermo Fisher Scientific, Waltham, MA, USA) [11]. When the requirement is limited to reconstructing 3D models of anatomical structures from CT or MRI data for further development or analysis, cost-effective software and platforms as well as open-source MIP packages may be used, such as 3D Slicer (Slicer Community) and MedINRIA (INRIA Sophia Antipolis, France) [12].

2.3 3D CAD Design, Design Analysis – Optimisation and Medical Evaluation

The outputs of the "2D & 3D Medical Image Processing" phase are typically 3D models of anatomical structures in the form of triangle meshes (STL or VRLM format) or 2D slice contours.

Depending on clinical and technical requirements as well as biomaterial selection, 3D CAD models of patient-specific implants, surgical guides, or medical devices are designed, analysed and clinically evaluated, based on reconstructed 3D models of anatomical structures from CT/MRI images. In the case of patient-specific implants for bone reconstruction in cranio-maxillofacial surgery, the intact area is typically used as the reference for 3D design and modelling of implants [6-9]. Biomedical engineers and designers play a key role in the 3D design and modelling of implants, surgical guides and medical devices. During the phase of 3D CAD design, design analysis and optimisation, and medical evaluation (Figure 1, Step 03), especially for the tasks of 3D CAD design, design analysis and optimisation, it is essential to consider the issues related to main implant function, biomaterial selection, and Design for Manufacture (DfM), which determine the optimal implant type for bone reconstruction treatments.

Figure 2 presents typical designs of patient-specific implants for bone reconstruction of skull defects. The design requires analysis and optimisation to meet both technical and clinical requirements. Finally, the 3D CAD models of personalised products (patient-specific implants, surgical guides, and medical devices) must be evaluated and reviewed by medical doctors or surgeons to obtain approval before they are transferred to the manufacturing phase. In the case of personalised cranio-maxillofacial implants for bone reconstruction, a 3D CAD model of the implant is imported into MIP software or platforms for medical evaluation and verification, as illustrated in Figure 3. The 2D profile of the implant and CT images at each slice are examined to ensure that the implant thickness and the contact interface between the implant and bone defect window are optimally designed and clinically evaluated.

Types of patient-specific implants for bone reconstructions in cranio-maxillofacial surgery need to be carefully considered when working on 3D CAD design and modelling of implants: on-lay implants and in-lay implants. On-lay implants are positioned on top of existing bone to augment or reshape the area and restore anatomical contours (Figure 5); these implants are commonly used in cases requiring aesthetic enhancement and contouring, functioning as structural support without replacing the underlying bone. In-lay implants are placed within a defect or cavity in the bone (Figures 2, 3, 9 and 10), essentially replacing the missing bone structure; these implants fit seamlessly within the boundaries of the defect to restore structural integrity and function, and are commonly used when the bone defect is well-defined and enclosed.

In cases of online meetings for medical evaluation and verification, the use of cloud-based MIP and collaborative design platforms provides an effective communication solution for multidisciplinary teams, including radiologists, MDs, surgeons, biomedical engineers and designers, to conduct comprehensive medical evaluation and verification of personalised

products (patient-specific implants, surgical guides, and medical devices).

2.4 Manufacture

The selection of manufacturing methods fundamentally depends on the following: complexity of a 3D CAD model of personalised products (patient-specific implants, surgical guides, and medical devices), selected biomaterials, and technical and clinical requirements. The financial constraints from the patient also need to be taken into account, especially when selecting biomaterials for a product. In the case of patient-specific implants for bone reconstructions in cranio-maxillofacial surgery, the following biomaterials are commonly used [13-15]: Bone cements, PMMA, PEEK, HDPE, PCL/HA, bioceramics, titanium alloys and carbon composites. It should be noted that bone cements for bone reconstruction in cranio-maxillofacial surgery are typically PMMA-based, containing PMMA polymers, radiopaque agents, initiators, and potentially antibiotics or colorants.

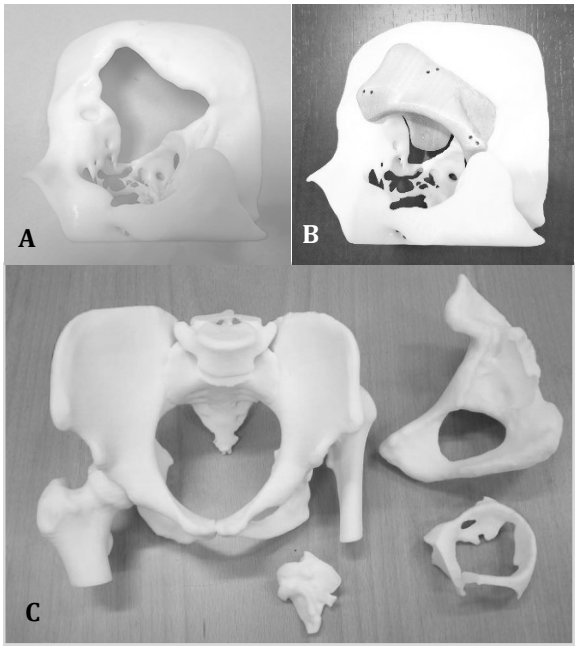

Figure 4: Biomodels of anatomical structures used for surgical planning and fabrication of personalised implants. A and B: Biomodels of a skull defect and pre-fabricated personalised implant. C: Biomodels of a hip system and bone grafts for pre-operative planning of hip reconstruction surgery

For the simple case of cranio-maxillofacial surgery, biomodels of anatomical structures can be fabricated by AM directly from the STL files exported from the MIP process. These biomodels can be used for medical diagnosis and surgical planning (Figure 4), as well as pre-fabrication of implants in which biomodels can be used as a reference for forming and shaping a patient-specific implant [6-8]. The types of patient-specific implants for bone reconstructions in cranio-maxillofacial applications also need to be considered.

For on-lay implants, sheet metal forming and AM, as well as rapid tooling, are normally required for implant fabrication. A 3D CAD model of an on-lay implant is used as a reference for designing the mould for sheet metal forming to fabricate patient-specific implants. The moulds for sheet metal forming can be manufactured using CNC machining, or AM, in combination with rapid tooling methods (Figure 1, Steps 06, 07 and 08).

For in-lay implants, due to the complexity of the implant geometry, they normally require CNC machining and AM as well as rapid tooling for implant fabrication [6-9]. In the case of using AM, firstly, the biomodel of a patient-specific implant is fabricated, which is then used as the template for creating the mould that serves as the rapid tooling mould for fabricating patient-specific implants made of biomaterials such as PMMA and bone cements (Figure 1, Steps 04 and 05, 06 and 07). For the case of using CNC machining, a 3D CAD model of an implant is used for Computer Aided Process Planning (CAPP) to create toolpaths for CNC machining of implants or the mould for fabricating implants (Figure 1, Steps 06, 07, 08) [9, 16]. Precision machining and/or surface finishing are normally required for personalised implants fabricated by CNC machining, AM and rapid tooling to enhance quality and meet required technical product specifications (Figure 1, Step 08). With the rapid advancement of AM, biomaterials, and 3D bioprinting in recent years, personalised implants made of PEEK and other biomaterials can be directly fabricated using AM, eliminating the need for rapid tooling methods (Figure 1, Step 09). Surface finishing is normally required for 3D bio-printed implants to meet clinical and technical requirements.

2.5 Sterilisation and Product Packaging for Medical Applications

Patient-specific implants manufactured through CNC machining, AM, rapid tooling, and 3D bioprinting for cranio-maxillofacial surgery require sterilisation, packaging, and transport to surgical facilities prior to implantation. Sterilisation and packaging of implants are critical processes that ensure implant functionality, long-term biocompatibility, patient safety, and infection prevention. The sterilisation process eliminates all microbiological contamination, including viable microorganisms such as bacteria, fungi, and viruses, while packaging maintains sterility until implantation in accordance with stringent medical standards.

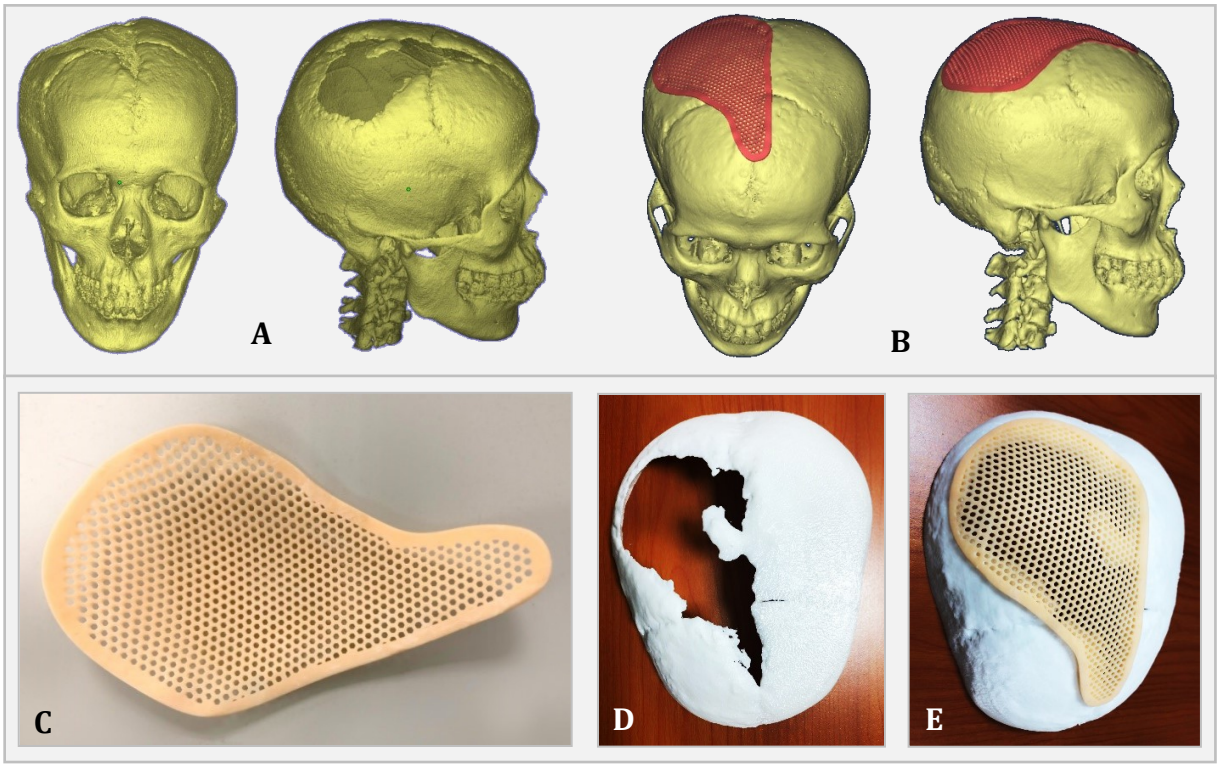

Figure 5: A and B: A skull defect in a 44-year-old male patient resulting from a traffic accident (A) and a patient-specific implant (B) designed and validated for bone reconstruction surgery. C, D and E: A biomodel of a patient-specific implant (C), a biomodel of a skull defect (D), and both assembled together (E)

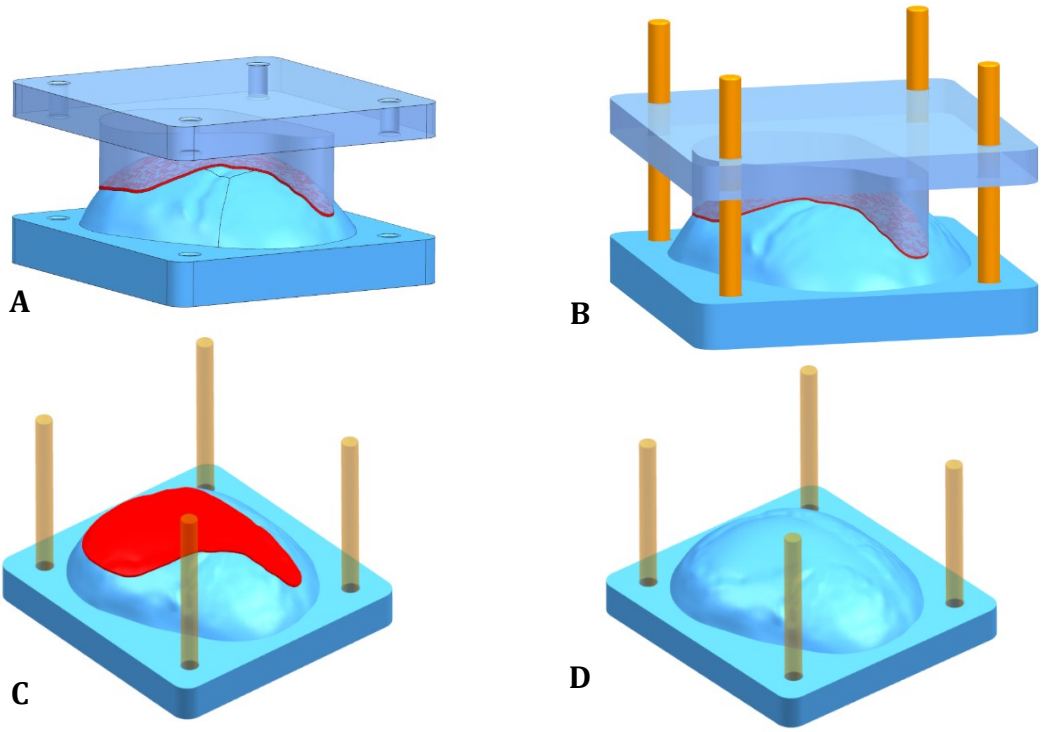

Figure 6: Innovative design of the mould with upper and lower cavities as the core forming module to fabricate personalised cranioplasty implants from titanium meshes. A and B: 3D CAD assembly model of the upper and lower cavities with an implant and guide pins. C and D: 3D CAD assembly model of a lower cavity and guide pins, with and without an implant model

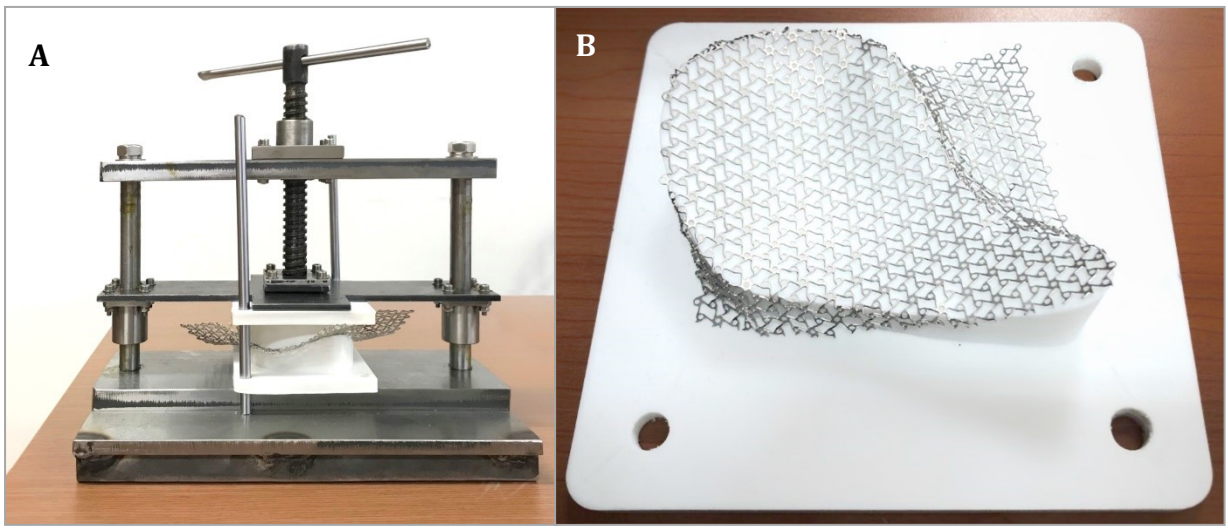

Figure 7: A titanium mesh forming system for fabricating patient-specific implants from titanium meshes. A: The titanium mesh forming system with a 3D-printed mould in operation. B: The successfully formed titanium mesh ready for finishing operations to produce a personalised cranioplasty implant

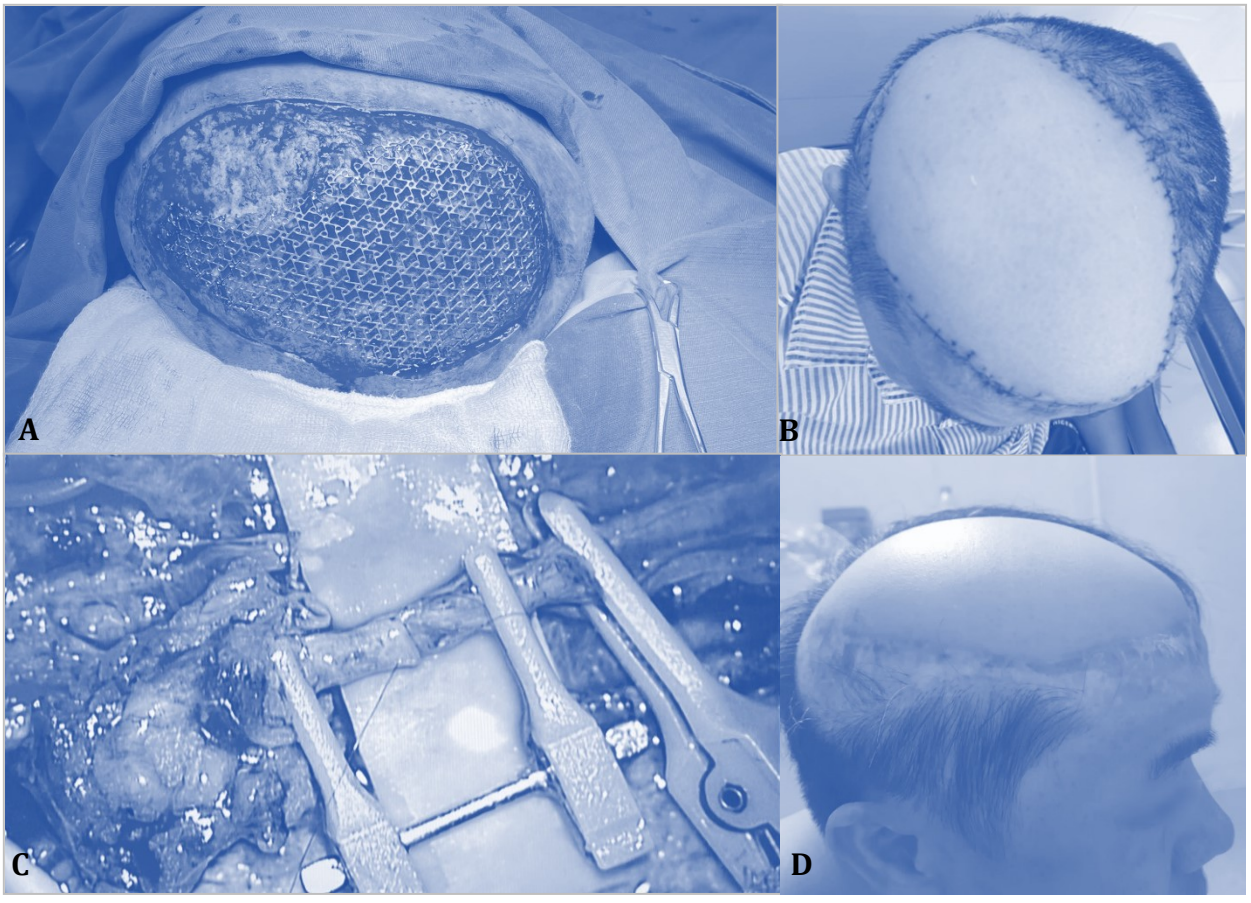

Figure 8: Soft and hard tissue reconstruction in cranial surgery. A: A personalised cranioplasty implant fabricated from titanium mesh, secured to the skull with optimal fit to the cranial defect following scalp exposure. B: Scalp reconstruction performed using skin grafting, wherein a skin layer harvested from the thigh was utilised for grafting. C: Microsurgical technique used for microvascular anastomosis, during which blood vessels were connected to enable vascularisation and integration of the grafted skin with surrounding tissue. D: A patient one-year post-surgery

Sterilisation methods for cranio-maxillofacial implants fundamentally include steam autoclaving, gamma radiation, and ethylene oxide sterilisation [17]. Steam sterilisation, involving high-pressure saturated steam at 121–141°C, is widely utilised due to its accessibility, cost-effectiveness, and efficacy in eliminating microorganisms. Gamma radiation employs high-energy gamma rays to inactivate microorganisms, including bacteria, viruses, and fungi. Gamma rays can penetrate dense materials and sterilise products whilst they remain in their final sealed packaging, thereby preventing re-contamination post-sterilisation. However, it is important to note that gamma radiation can alter the properties of certain materials, particularly polymers, potentially leading to changes in mechanical strength, colour, or other physical characteristics.

Ethylene oxide sterilisation is a widely employed method for sterilising medical devices, including implants for cranio-maxillofacial surgery. This method operates by exposing devices to ethylene oxide gas, which destroys microorganisms by disrupting their cellular metabolism and reproductive processes. Since sterilisation occurs at low temperature with minimal impact on material properties, ethylene oxide sterilisation is compatible with heat-sensitive materials such as certain polymers and plastics such as PMMA, PEEK and HDPE.

Following sterilisation, implants are packaged to maintain sterility and provide protection during transport and storage. Packaging serves multiple functions: mechanical protection, ease of handling and integration with surgical workflows. All packaging must comply with regulatory standards and facilitate traceability whilst ensuring safe transport to the surgical facility.

3. Clinical Cases

3.1 Innovative & Cost-effective Development of Personalised on-lay Cranioplasty Implants

Figure 5A presents a skull defect in a 44-year-old male patient resulting from a traffic accident. Based on the framework presented in Figure 1, a patient-specific implant was designed and validated, as shown in Figure 5B. Figures 5C, 5D, and 5E present a biomodel of the patient-specific implant, a biomodel of the skull defect, and both components assembled together. These biomodels were fabricated using AM for preoperative planning, effective discussions and

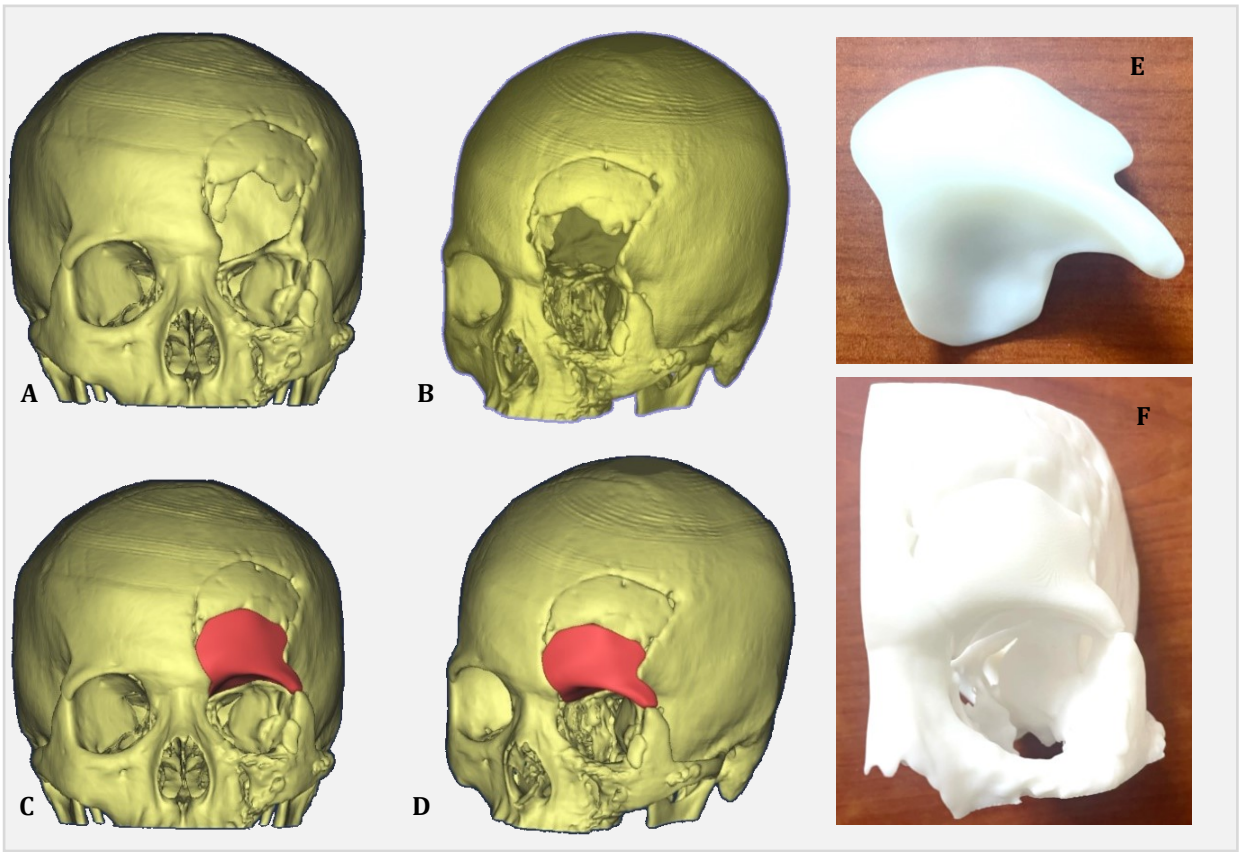

Figure 9: A and B: A skull defect in a 20-year-old male patient resulting from a traffic accident. C and D: A patient-specific implant designed and validated with optimal fit to the bone defect. E: The biomodel of a patient-specific implant. F: The biomodel of a skull defect and patient-specific implant assembled together

communication among the patient, radiologists, MDs and surgeons, as well as biomedical engineers and designers involved in the design and manufacturing of the patient-specific implant. Besides the clinical and technical requirements for a cranioplasty implant, the on-lay implant type was selected for this case for the following reasons. First, the scalp in the defected areas was missing or insufficient for covering the entire skull defect. Second, the implant cost must be reasonable for the patient.

Based on the implant type and geometry, titanium mesh was used for fabricating the cranioplasty implant. The use of titanium mesh for repairing cranial defects has been well-documented, and it is valued for its biocompatibility, mechanical strength, ductility and low infection risk. Titanium mesh is often preferred in resource-limited settings as a cost-effective solution for cranioplasty applications.

Figure 6 presents the innovative design of the mould which includes the upper and lower cavities as the core forming module to fabricate personalised cranioplasty implants from titanium meshes. Figure 7 presents the complete sheet metal forming system for fabricating patient-specific implants from titanium meshes, in which the upper and lower cavities were fabricated by AM. The sheet metal forming system and cavities were innovatively designed, taking into account the issues related to DfAM and Design for CNC machining. The sheet metal forming system can be cost-effectively used for multiple clinical cases, and it is manufactured by CNC machining. For specific clinical cranioplasty cases, the upper and lower cavities are specifically designed to meet the required clinical and technical requirements.

Figure 8 presents images of a successful surgery for the skull defect case shown in Figure 5. It is important to note that the scalp in the defected areas was missing or insufficient to cover the entire skull defect; therefore, an additional surgical procedure of scalp reconstruction using skin grafting [18] was required, wherein a skin layer harvested from the thigh was utilised for grafting. For the scalp reconstruction, a microvascular anastomosis procedure was performed in which blood vessels were connected to enable vascularisation and integration of the grafted skin with the surrounding tissue (Figures 8C and 8D). The total operative time for both soft and hard tissue reconstruction was approximately 7 hours.

3.2 Innovative Design & Development of Personalised In-lay Implants for Cranio-Maxillofacial Surgery

Figure 9 presents a clinical case of a skull defect in a 20-year-old male patient resulting from a traffic accident. The complex defect is located in the zygomatic and frontal bones. The patient experienced an inability to open his eye due to the frontal and zygomatic bone defects. Bone reconstruction surgery was recommended to meet cosmetic requirements and restore eye movement.

Based on the framework presented in Figure 1, a patient-specific implant was designed and validated, as shown in Figures 9C-F. The biomodels of a patient-specific implant and a skull defect were fabricated using AM for preoperative planning, effective discussion and communication among the patient, radiologists, MDs, surgeons, biomedical engineers and designers involved in the design and manufacturing of the patient-specific implant.

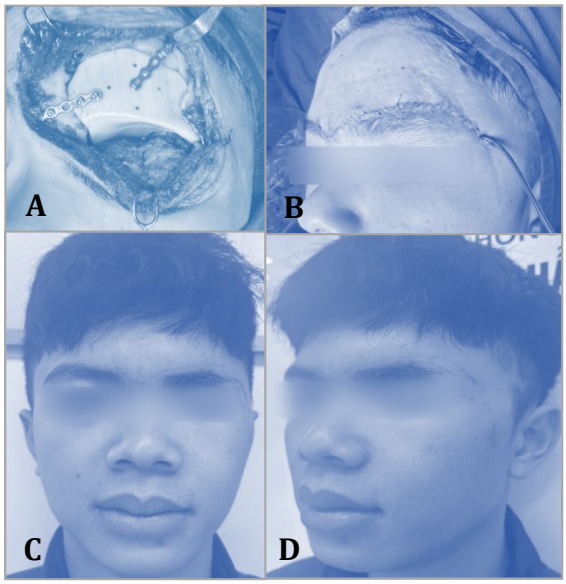

Figure 10: A: The personalised cranioplasty implant fabricated from PEEK biomaterial, secured to the skull with optimal fit to the frontal and zygomatic bone defects following scalp exposure. B: The patient immediately after successful surgery. C and D: The patient 22 days post-surgery

For cost-effectiveness and reduction of fabrication time, PEEK biomaterial was selected for fabricating the patient-specific implant. The 3D CAD model of the patient-specific implant, approved by the surgical team, was transferred to the manufacturing phase to produce an implant using AM, in which Fused Deposition Modelling technology and PEEK biomaterial were employed for fabrication. This approach eliminated the need for rapid tooling to fabricate moulds from which patient-specific implants are manufactured using biomaterials such as bone cements and PMMA.

The 3D-printed patient-specific implant was subsequently finished, sterilised, and packaged for surgical use. Figure 10 presents images of a successful surgery for the skull defect case shown in Figure 9 and a patient after 22 days of the surgery. The total operative time for this case was approximately 2 hours.

4. Discussion and Conclusions

Personalised design and development of products for applications in healthcare and medicine play an important role in improving the quality of medical diagnosis, treatment and rehabilitation. With the advancement of 2D and 3D medical image processing, as well as innovative design and manufacturing technologies, patient-specific implants, surgical guides and medical devices can be designed and manufactured to meet specific clinical and technical requirements. In the areas of cranio-maxillofacial surgery, the rapid advancements in innovative design and product development, biomaterials, AM and 3D bioprinting, have generated significant impacts on enhancement of quality in surgical planning and treatments of bone defects, especially to reduce operative time and improve safety and accuracy in surgery.

The methods for innovative design and development of patient-specific implants, surgical guides and medical devices based on medical imaging data were well-documented in our previous studies [1-9]. In this study, an integrated method with a systematic framework for the innovative and cost-effective design and development of patient-specific implants and personalised products for applications in healthcare and medicine is presented and demonstrated, taking into account the latest developments in MIP, biomaterials, 3D CAD design and modelling, AI-driven design and decision-making, and innovative manufacturing technologies, including 3D bioprinting. The systematic framework shows detailed workflows for innovative design and development of patient-specific implants and personalised products with a focus on applications in cranio-maxillofacial surgery; and it is applicable to other fields, including orthopaedic and dental surgery. Within this systematic framework, the most important phases with the direct involvement of biomedical engineers or designers include the following: (i) 2D and 3D medical image processing, (ii) 3D CAD design, design analysis and optimisation, and medical evaluation, and (iii) manufacture.

During the phase of 2D and 3D medical image processing, biomedical engineers or designers need to effectively collaborate with radiologists, MDs or surgeons to define the clinical and technical requirements, and to optimally process medical imaging data to generate 3D models of anatomical structures which serve as the key inputs for the innovative design and development of personalised products.

The process of 3D design and modelling of personalised products such as patient-specific implants, surgical guides and medical devices requires high skill, especially when dealing with complex geometries of patient-specific implants and surgical guides. There is an important need for quality assurance protocols to ensure the safety and accuracy of the designed medical products. Therefore, the 3D CAD model of personalised products must be clinically evaluated, biomechanically analysed, and checked against the original medical imaging data, to ensure that the designed products meet well the clinical and technical requirements, with approvals from MDs or surgeons before the design is transferred to the manufacturing phase. For the case of patient-specific implants for cranio-maxillofacial surgery, the implant types and biomaterials used for fabricating implants must be determined before working on the 3D design and modelling activities.

The key steps of 3D CAD design and modelling of personalised products must be carefully recorded; this is important to support the process of clinical evaluation, and biomechanics analysis. This ensures that errors or modifications of the design can be carefully monitored and checked, and when necessary, the biomedical engineers or designers can return to previous steps for improving the design, or change the design to meet the clinical requirements or new requirements from MDs or surgeons. For the case of patient-specific implants for cranio-maxillofacial surgery, the process of 3D CAD design and modelling needs to be recorded in which the 3D geometric transformation and coordinates of reference geometries must be taken into account, so that the 3D CAD model of patient-specific implants and skull defects imported into the MIP software are accurately positioned with the 2D cross-sectional CT/MRI images or slices. In this way, the clinical evaluation and biomechanics analysis process can be conveniently and quickly implemented.

With the advancement in biomaterials and manufacturing technologies, including CNC machining, advanced SMF, AM, and 3D bioprinting as well as surface finishing, the manufacturing of personalised medical products can be conveniently accomplished. The most important consideration is the cost-effective solutions, especially for low-income and developing countries.

For the specific clinical case shown in Figures 5 and 8, in which Ti-mesh biomaterial is used for fabricating a personalised implant, the total treatment cost is approximately 2,490 USD. The cost breakdown is as follows: CT scanning (5%), personalised implant design (30%), biomodeling and manufacturing (15%), Ti-mesh biomaterial (26%), and surgery (24%). For the specific clinical cases shown in Figures 2, 9, and 10, in which AM and 3D biomodelling technologies were used for fabricating a personalised implant and biomodels, the total treatment cost ranges from approximately 2,600 to 4,877 USD for implant sizes ranging from 20 cm^2 to 130 cm^2. Table 1 presents the approximate costing and cost breakdown of personalised implants fabricated from PEEK biomaterial, using AM and 3D bioprinting. It is clearly shown that innovative and

cost-effective development using Ti-mesh biomaterial with optimal manufacturing solutions provides the most economical approach. In contrast, the use of AM and 3D bioprinting, and biomaterials such as PEEK and bone cements remains expensive, especially for patients in developing countries, in which biomaterial and manufacturing costs account for 44% to 70% of total expenses for implant sizes ranging from 20 cm^2 to 130 cm^2.

Table 1. Approximate costing and cost breakdown of personalised implants fabricated from PEEK biomaterial, using AM and 3D bioprinting

	Personalised implant sizes in cm^2			
	10-20	20-60	60-90	90-130
CT Scanning	4 %	3 %	3 %	2%
Design	29%	23%	18%	16%
Biomaterial, AM and 3D bioprinting	44%	56%	65%	70%
Surgery	23%	18%	14%	12%
Total cost in USD	2,600	3,360	4,118	4,877

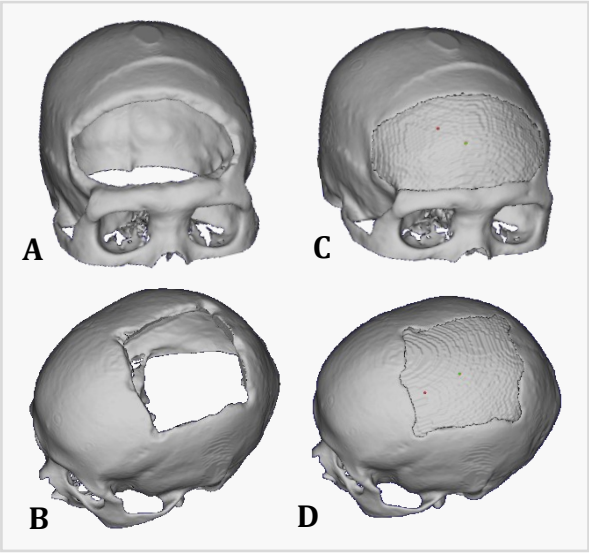

Figure 11: AI-driven design and development of personalised implants for cranio-maxillofacial surgery. A and B: The skull defects. C and D: The 3D CAD models of patient-specific implants which can be automatically or semi-automatically generated based on patient-specific and training data

In clinical practices in hospitals, financial constraints must be carefully taken into account, and the selection of biomaterials, design and manufacturing technologies needs to be optimally made, so that the clinical and technical requirements can be well-met.

In the presented systematic framework, different solutions for manufacturing of personalised products are presented, including CNC machining, SMF, AM, and 3D bioprinting, with a focus on patient-specific implants for cranio-maxillofacial surgery. With the rapid development of emerging and enabling technologies under the impact of Smart Manufacturing and Industry 4.0 and 5.0, future studies and technological trends will expand the scope of applications and integrate the emerging and enabling technologies of AI, including Machine Learning and Deep Learning (ML-DL), AI-driven design and decision-making, as well as cloud-based MIP in the systematic framework for innovative and cost-effective design and manufacturing of patient-specific implants and personalised medical product development. Figure 11 presents a promising result demonstrating AI-driven design and development of patient-specific implants for cranio-maxillofacial surgery, in which the 3D CAD models of patient-specific implants can be automatically or semi-automatically generated based on patient-specific and training data. AI-driven design and AI-based optimisation offer a promising path for rapid prototyping and rapid manufacturing, especially to help explore innovative design solutions, identify optimal design parameters, and achieve significant performance improvements. However, there are still emerging challenges related to AI-driven design and development of patient-specific implants and personalised medical product development, especially issues related to clinical validation, biomechanics analysis, monitoring the design steps and determining how to return to previous design steps to quickly and effectively refine and change the design to meet specific technical and clinical requirements from MDs or surgeons, as well as the challenging issues of the cost-effective integration of AI-driven design tools [19] into current design and manufacturing systems.

In conclusion, we have presented a systematic framework for innovative and cost-effective design and manufacturing of patient-specific implants and personalised medical product development for applications in healthcare and medicine, with a focus on patient-specific implants, surgical guides and medical devices, especially for cranio-maxillofacial surgery, taking into account the latest developments in MIP, biomaterials, innovative design and manufacturing technologies, as well as the outcomes from more than 100 clinical cases successfully conducted from 2002 to 2025 in innovative design and development of patient-specific implants, surgical guides and medical devices based on medical imaging data [1-9]. Within this study, two typical clinical cases with complexity in design and development of patient-specific implants were presented, with successful outcomes and enhanced quality of medical treatments for complex bone reconstruction. The presented systematic framework can be applied not only for applications in cranio-maxillofacial surgery, but also in other

areas such as orthopaedic and dental surgery as well as medical rehabilitation.

Future development will integrate AI-driven design and data-informed decision-making as well as emerging MIP tools in the framework to enhance medical diagnosis and surgical planning via a cloud-based collaborative MIP and design platform, leading to reduced complexity of 3D CAD design and modelling, clinical evaluation, biomechanics analysis and design optimisation, reduction of product design and development time, minimised potential risks, enhanced safety and quality of treatment, and effective technology transfer to hospitals with impactful applications. The scope of applications will also be expanded to orthopaedic and dental surgery, as well as medical rehabilitation.

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