Manufacturing of custom-made medical implants for cranio/maxillofacial and orthopaedic surgery – an overview of the current state of the industry

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ABSTRACT

Extensive work has been done in the area of manufacturing implants for medical purposes, and more recently the development of customised implants. Areas of application include cranio/maxillo-facial implants, dental drill guides, hip, knee and shoulder replacements, as well as different implants for the spine. Due to their high prevalence and complex anatomical geometry the purpose of this study is to investigate the current state of the industry regarding customised medical implants for cranio/maxillofacial and orthopaedic surgery. Implant customisation has far-reaching benefits, and a collective approach to solving current difficulties will require an in-depth study of successes already achieved. Several issues in this regard are examined, including what defines customisation, regulatory issues that govern customisation and design constraints, trends in different areas of application, suitable materials, and finally which manufacturing techniques are being employed, with a focus on the use of Layer Manufacturing technologies and their role in custom-made medical implants.

Keywords: Medical models, Customised implant, Layer Manufacturing

1 INTRODUCTION

Over the last decade there has been a growing interest among physicians in the technology of medical models for the purpose of facilitating diagnosis, pre-operative planning and communication between colleagues and patients. An ability to create tangible models from medical imaging data (e.g. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)) has proven highly advantageous, especially within the field of craniofacial surgery where planning and performing an operation are extremely difficult due to the complex and variable anatomy. Historically, the uses of medical models by surgeons wanting to pre-plan surgery have fallen into the following five categories [1]:

- Visualisation of the patient's anatomy before treatment or surgery.
- Surgery or treatment simulation (actual cutting or measuring on the model) before intervention.
- Creation of custom implants, templates, or guides prior to surgery.
- Enhanced communication with others involved in patient treatment and their related staff.
- Improved communication and consent by the patient and patient's family concerning the upcoming procedure.

Many successful case studies have been done in these areas, with prominent examples from work by the Phidias Network [2] and others. The RP4Baghdad project, initiated in June 2005, has through its contributions also documented an extensive case study base of medical models produced [3]. What is however evident from these case studies, is the fact that the majority relate to applications in the cranio/maxillo-facial areas, and that medical models were produced for either surgical planning and communication or for the purposes of producing an implant through indirect methods [12, 14, 15]. With the advent and growth of the ability to produce end-use metal components using Layer Manufacturing (LM), direct methods for implant manufacturing have gradually emerged. These improvements in materials and manufacturing methods have been well supported by a growth in necessary software to convert, simulate and prepare imaging data for medical modelling. In addition, they have enhanced the process of implant manufacturing by facilitating the design stage to enable customised implant geometry to match the relevant anatomy interfaces. This powerful combination – to develop customised CAD (Computer-Aided Design) models and subsequently produce complex geometry in final use materials by means of Layer Manufacturing – has enabled wide and far-reaching potentials for future implant manufacturing.
Before medical implants are approved, they are required to comply to a stringent set of regulations. With the continuous growth and demand for new medical devices, the need for corresponding regulations has also increased, [4, 5, 6, 7, 11], and while current regulations are making provision for new medical devices, there is still some work to be done to accommodate the growth in, especially, the use of customised medical implants, [8, 9, 10].

2. CLASSIFICATION FOR IMPLANT CUSTOMISATION AND REGULATORY ISSUES

2.1 General Classification

The Food and Drug Administration (FDA) of the United States of America has recognised three classes of medical devices based on the level of control necessary to assure the safety and effectiveness of the device. The classifications are assigned according to the risk the medical device presents to the patient and the level of regulatory control the FDA determines is needed to legally market the device.

As the classification level increases, so does the risk to the patient, and also FDA regulatory control. Class I devices have the least amount of regulatory control and present minimal potential for harm to the user. Class I devices are typically simple in design, manufacture and have a history of safe use. Examples of Class I devices include tongue depressors, arm slings, and hand-held surgical instruments.

Class II medical devices are devices where general controls are not sufficient to assure safety and effectiveness and existing methods/standards/guidance documents are available to provide assurances of safety and effectiveness. In addition to compliance with general controls, Class II devices are required to comply with special controls. Special controls include for example, special labelling requirements, mandatory performance standards and post-market surveillance. Examples of Class II devices include physiologic monitors, x-ray systems, gas analysers, pumps, and surgical drapes.

Class III medical devices have the most stringent regulatory controls. They usually support or sustain human life, are of substantial importance in preventing impairment of human health, or present a potential unreasonable risk of illness or injury to the patient. General or specific controls are not sufficient to regulate Class III devices, and a Pre-Market Approval (PMA) submission to the FDA is typically required to allow marketing of a Class III medical device. Examples of Class III devices that require a PMA are: replacement heart valves, silicone gel-filled breast implants, and implanted cerebella stimulators.

The classification of medical devices in the European Union (EU) is outlined in Annex IX of its Medical Devices Directive 93/42/EEC [4]. The European classification depends on rules that involve the medical device's duration of body contact, its invasive character, its use of an energy source, its effect on the central circulation or nervous system, its diagnostic impact or its incorporation of a medicinal product. Similar to the FDA classification, the EU basically defines four classes (Class I, IIa, IIb, and III), ranging from low risk to high risk. Medical implants will fall into Class III for both FDA and EU classification.

Within the context of medical devices, the Active Implantable Medical Devices Directive (90/385/EEC) defines a custom-made device as “any active implantable medical device specifically made in accordance with a medical specialist's written prescription which gives, under his responsibility, specific design characteristics and is intended to be used only for an individual named patient” [5]. This definition is also supported by the Medicines and Healthcare products Regulatory Agency (MHRA) that regulates medical devices in the UK under European legislation [6] and the FDA according to its Code of Federal Regulations, Title 21, Volume 8 [7].

Conventional procedures for implant design have in the past been limited to a process of selecting standard size replacement parts from a range provided by manufacturers based on anthropomorphic data. This works satisfactorily for some types of procedures, but there are always patients outside the standard range, between sizes, or with special requirements caused by disease or genetics. Therefore as technology increases to provide more options to surgeons, so there is a growing need for producing custom-made implants. The authors suggest that implant customisation may largely be divided into two main groups, namely:

- Custom-size and
- Custom-fit implants

Custom-size refers to the custom manufacture of “in-between-size” implants that have been manufactured from the same original implant design, but scaled appropriately per patient. Custom-fit implants on the other hand denote redesign and manufacture of part geometry to match a patient's specific anatomy. The term “custom-made” then refers to the process or action of producing either a custom-size or custom-fit medical implant.

The degree to which implant customisation takes place is largely dictated by the area of application. Cranio/maxillo-facial implants, for example, by virtue of their complex geometry, require tailored designs to fit at the implant location, and this implies a need for custom-fitting. A hip replacement on the other hand, may require less customisation to the implant design while its function remains the same for different patients. Nevertheless, custom-sizing is still justified due to wide variability in patients' anatomy.

2.2 Regulatory issues

Although implants can now be manufactured so that their geometry matches the geometry of anatomical features, the importance of implant function and efficacy is a consideration that cannot be overlooked. Customisation may in fact pose opportunities to improve functional restoration in addition to geometric fit. Within this context, international quality standards, protocols and medical regulations are in place to ensure safety for patients regarding any undue practices. In cases where custom sizing is involved, conventional procedures demand a set of rigorous testing and clinical trials to be conducted before an implant design may be commercialised. In cases where one-off custom fit implants for individual patients are produced and inherently differ from previously tested existing designs, a situation arises where extended rigorous testing and clinical trials becomes impractical. A question therefore arises as to how to balance the design and manufacture of custom-fit implants while at the same time performing adequate testing prior to implantation.

The medical device market is unfortunately not very well regulated in South Africa. Medical equipment – other than electro-medical devices – including disposable or single use devices, are not regulated. The Hazardous Substances Act (Act 15 of 1973) of the Department of Health is used to regulate electro-medical devices that fall within a so-called Group III classification (note that Group III classification here differs from Class III previously mentioned). If any product does not appear on the current Schedule of Listed Electronic Products [10], such products are under no legal requirement from the South African Department of Health in terms of importing, manufacturing or distribution [8, 9]. Currently, medical implants do not appear on this schedule [10], and are therefore at this stage exempt. The Department of Health is in the process of drafting the necessary policy documents and has indicated that these may become available in the near future. In the absence of local regulations, international regulations should therefore be considered and adhered to.

In order to simplify the process of approval for product developers, international efforts towards collaboration in regulating medical devices are making progress. In 1992 an international forum, the Global Harmonization Task Force (GHTF), was formed, embarking on a number of regulatory initiatives designed to move the participating countries closer to achieving the goal of mutual recognition of regulatory processes. As regulations are continuously being updated to reflect new developments in this industry, custom-made devices are becoming more recognised and incorporated in these documents. In its most recent update, the European Commission has published an important amendment to the Medical Devices Directive [11]. This amendment Directive 2007/47/EC gives member states an opportunity to comply and doesn't come fully into force until 21 March 2010. It introduces more than 150 changes that range from simple text corrections, to introduction of new requirements. Directive 2007/47/EC is the fifth document that introduces amendments to the original text of the Medical Devices Directive 93/42/EEC [4].

In review of current regulations, provision is therefore made for the design and manufacture of custom-made implants. Further requirements for custom-made devices are set out in Annex I of the Medical Devices Directive 93/42/EEC [4], of which the details fall beyond the scope of this article.

3. METAL PROCESSING LM TECHNOLOGIES

Over the last decade several LM technologies have emerged that are showing notable promise in their ability to directly manufacture customised implants in final, end-use materials. Direct metal fabrication processes can be grouped into three categories [1]. The first group describes systems that use a laser to heat powder to form metal parts. All of the systems in this group produce parts in a powder bed, such as for example, Direct Metal Laser Sintering and LaserCusing.

The second group includes systems that use a powder deposition head to deposit the metal powder, such as Direct Metal Deposition. The third group consists of systems that use special approaches to produce metal parts and that do not fit into the first two groups, e.g. Direct Metal Printing (from ProMetal).

LM System developers are investing a lot of effort to improve the quality of metal parts produced according to these systems in order to meet customer requirements and deliver components by means of Rapid Manufacturing (RM). Specific emphasis has been placed on the ability to deliver 100% dense, high strength parts with superior surface finish for engineering applications. Apart from the need for high strength parts, medical implants however do not always share the same emphasis on part quality requirements. The essential material issues in the medical field relate mostly to biocompatibility. In many cases poor surface finish and porosity is a desirable feature for implants to allow bone ingrowth. In other cases where articulating surfaces (such as knee or hip joints) are involved, surface roughness must be very low. Also, accuracy in medical terms is usually quantified in millimetres with only selected situations (e.g. some dental applications) requiring more narrow tolerances. What is of more interest is an ability to create very detailed features. In medical models for example, the inclusion of fine features such as arteries, nerves and small bones are critical for accurate and proper representation during pre-surgical planning.

A selection of metal fabrication LM technologies have been taken from Wohlers [1] and placed in Table 1 with a comparison of characteristics and key areas for medical application.

System [1]		Characteristics [1]		Key Application Area			
Key Process	**Company**	**Materials**	**Detail Ability (mm)**	**Cranio/ maxillofacial**	**Dental**	**Orthopaedics (Hip, Knee, Shoulder)**	**Other**
Direct Metal Laser Sintering (DMLS)	EOS GmbH	Metal powder blends	0.6	√	√	√	√
Electron Beam Melting (EBM)	Arcam	Powder metals	0.25	√	√	√	√
LaserCUSING	Concept Laser	Powder metals: SS; Tool steels; Ti; Al	0.4	√	√	√	√
Selective Laser Melting	F&S/ MCP	Non proprietary; SLM processes any metal powder (10 to 75 micron particles)	< 0.2	√	√	√	√

Table 1: Metal fabrication comparison matrix suitable for medical applications

4. AREAS OF APPLICATION

The following section describes a number of examples for different areas of applications that can serve to illustrate how custom implants are currently being used. The cases shown do not cover all possible applications and are not necessarily the best examples in each application sector. Rather they serve to illustrate the processes involved and technological capabilities available.

4.1 Cranio/maxillo-facial

4.1.1 Cranioplasty

Cranioplasty is the surgical correction of skull defects. The two major purposes of performing a cranioplasty operation are to protect the brain and to provide restoration for cosmetic purposes. In this field, medical models are used for pre-operative planning, as a template for preparing implants, and as a master implant for making a mould from which the implant is fabricated.

Current cranioplasty materials include autologous or homologous bone grafts (a bone transplant from either the same patient or another person respectively), wire mesh and methyl methacrylate, plastics, and metals, either alone or in combination [12]. The ideal material for cranioplasty prostheses construction must be resistant to corrosion and abrasive wearing, biocompatible, eliminate the risk of inflammation, rejection and infection, and must be integrable with the living bone structure to the point of becoming a part of it, promoting osteoblast migration (migration of cells that are responsible for the forming of bone) [14]. Over the past quarter-century, the popularisation of numerous alloplastic materials has favoured them over autologous bone because of the absence of need to harvest donor bone, and particularly because of bone's tendency to resorb or scar [13].

As an alternative, hydroxyapatite-based ceramics, which may induce bone growth into the implant, are increasingly being used because polymethylmethacrylate (PMMA), high density ceramics, titanium and other resin and alloy types do not fully meet the material target requirements [14]. Apart from their own study which involved a review of 25 cases over a period of seven years, Staffa et al. [14] include an epidemiological study of post-surgical cranial defects and its reconstructive treatment which was conducted in Italy, in an attempt to link human health effects to specified causes. This was accomplished through a questionnaire sent to all Italian neurosurgery departments in the year 2000. With 47% response, these departments indicated that comminuted fracture (a fracture in which there are two or more bone fragments) (41%) and decompressive operculectomy (the surgical removal of the operculum) due to oedema (swelling due to fluid under the skin) (28%) are the main causes of post-surgery craniolacunae (disorganised formation of collagen).

Trauma is involved in more than 60% of all procedures to remove parts of the skull [14]. Despite the growth towards using alloplastic materials and hydroxyapatite-based ceramics, the most common material reportedly used (Figure 1) was still heterologous PMMA (i.e. an implant not derived from the patient's body).

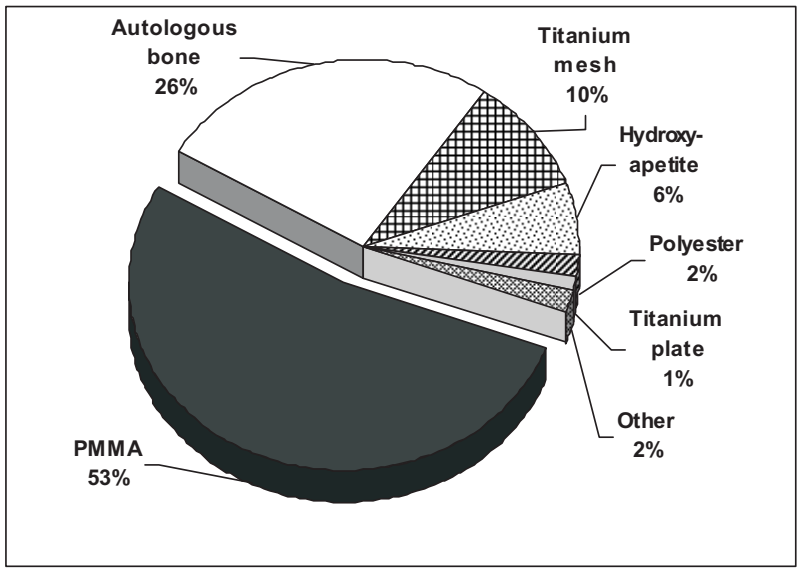
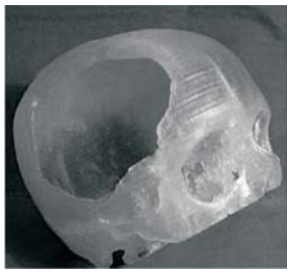


Figure 1: Materials commonly used to create cranioplasty implants [14]

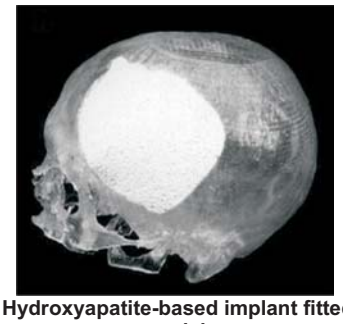
Staffa et al. [14] present a case study of their process using hydroxyapatite as implant material. The process that they follow requires firstly the manufacture of a medical model of the existing skull and fracture (Figure 2.a) – in their case using Stereolithography (SL). Secondly, an initial sample implant equal to the patient's bone defect is produced (Figure 2.b), which is used to craft an implant equal to the approved model from a block of porous hydroxyapatite (Figure 2c), which is then surgically implanted (Figure 2d).

All patients underwent clinical follow-up and a 3D CT scan 6–9 months after surgery. Follow-up indicated that there were no infective complications, reabsorption, rejections or spontaneous fractures. The mean time in the operating theatre was reduced from around 150 min (with implants produced in the operating theatre) to 90 min for the pre-manufactured hydroxyapatite prosthesis.



(a) Medical model using Stereolithography

(b) Medical model with initial sample implant



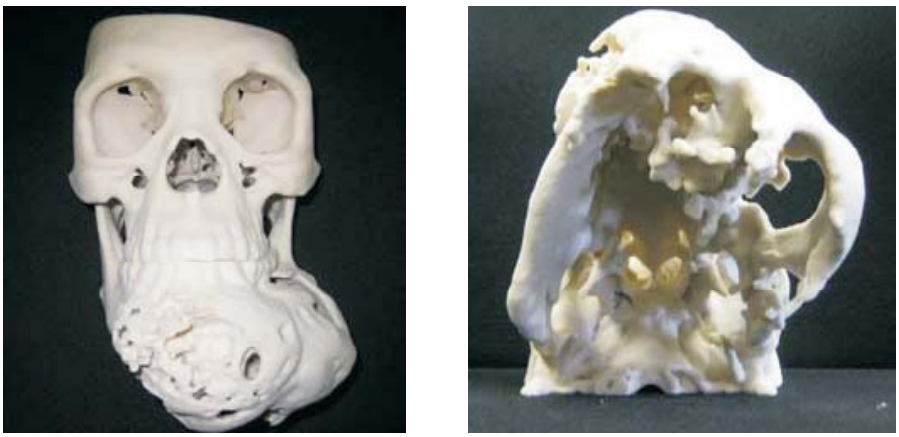
(c) Hydroxyapatite-based implant fitted to model

(d) Surgical implantation

Figure 2: Preparation and surgery of hydroxyapatè-based ceramic cranial implant [14]

4.1.2 Reconstructive surgery

Another area in which medical models and custom implants have proven very beneficial is facial reconstructive surgery. A number of causes – notably bone tumours or congenital defects – may result in situations requiring surgical intervention. Singare et al. [18] combined rapid prototyping (RP) and investment casting techniques to fabricate a customised titanium-alloy mandible substitute and filled it with autograft to repair the damaged mandible. Another recent case involved a local male patient with a bone tumour causing severe damage to his mandible (Figure 3). Conventional surgical procedures were followed, making use of bone grafts and plates to reconstruct the lower jaw. A retrospective case study is however being performed in collaboration with the surgical specialist, Dr Jean Morkel, head of the Department of Maxillo-Facial and Oral Surgery & Anaesthesiology and Sedation of the University of the Western Cape, to investigate the benefits obtained from having a medical model prior to surgery for planning or as a template on which a graft may be directly shaped intra-operatively. With this approach, the operating time can be dramatically reduced because the surgeon can shape the bone graft on the biomodel while the assistant simultaneously prepares the exposure of the donor site.



(a) Anterior view (b) Inferior view

Figure 3: Medical model of patient case with large bone tumour

Alternatively, when the graft requires a fairly complex shape, acrylic, or a similar material, can be used pre-operatively to create a master implant to serve as a guide for shaping the bone graft intra-operatively. The surgeon can minimise surgery time by pre-operatively moulding the acrylic to the exact shape required, using the biomodel as a template [15].

4.2 Hip and knee replacements

The science of hip and knee replacements (arthroplasty) has certainly come a long way since the first successful ivory implants of Dr San Baw in the 1960s. With the development of material processing technologies, a range of substitutes for load-bearing components have been created by combining different materials and advanced engineering techniques. Some researchers coated calcium phosphate onto metallic implants using plasma-spraying techniques and *in vivo* studies have shown good fixation to the host bone and increased bone ingrowth to the implants [16, 17]. Another example of improved techniques using advanced engineering methods is a case presented by He et al. [19]. They show a custom design and fabrication method for a novel composite hemi-knee joint implant, which consists of a titanium-alloy hemi-knee joint component and a porous-bioceramic artificial bone, using a dog as research subject. The process that was followed (Figure 4) included data collection through CT scanning and image reconstruction of this data to create a 3D model of the femur bone (Figure 4a-c). A Reverse Engineering (RE) process was performed to derive surface recreations of the model for further design and customisation. These RE models were then used to design two 3D models (Figure 4e-f and Figure 4g-i) that were later reproduced using Stereolithography (SL).

One was a negative model from which to create the porous-bioceramic artificial bone, and the other a solid model of the hemi-knee implant itself. Figures 5a and c show these SL models respectively. The negative SL pattern of the artificial bone was further processed by filling it with porous beta-tricalcium phosphate (β-TCP), which is a biocompatible and biodegradable material. The β-TCP-filled pattern was then sintered into a porous bioceramic scaffold (Figure 5d), burning out the resin material. The other SL pattern of the hemi-knee implant was used to produce the final hemi-knee implant (Figure 5b) by means of investment casting in Ti-6Al-4V.

Postoperative results are reported to be very successful. After two months, the normal function of the damaged joint began to restore and the composite prosthesis maintained its original shape, which indicated sufficient mechanical strength. These results suggest that this fabrication method could create a composite hemi-knee joint prosthesis for individuals with enough mechanical strength and it can potentially be applied to the fabrication of other customised artificial implants such as the hip or shoulder too.

Although He et al. [19] and other researchers are reporting successful results in applying RP and RM technologies for implant manufacture, it is important to keep in mind some limitations which will influence a selected process. Cost is one such important consideration. Even where there are obvious benefits in terms of improving the medical service, the approach may still be cost prohibitive. RM can be an option for high-cost, customised, complex-geometry parts, and ideally RP technologies are suited to situations where it would be difficult or impossible to produce the component using more conventional manufacturing techniques. In addition to cost, material properties are another important consideration.

Very few RP materials are presently biocompatible while many are not even fit to be sterilized and taken into operating theatres. But researchers into RP and RM processes are aiming to develop components to include multiple materials (and/or functional gradients of multiple materials) as well as electronic components and features. Should this be achieved, a significant contribution will be made to create medical devices with intelligent sensors while at the same time matching an individual patient's body and needs.

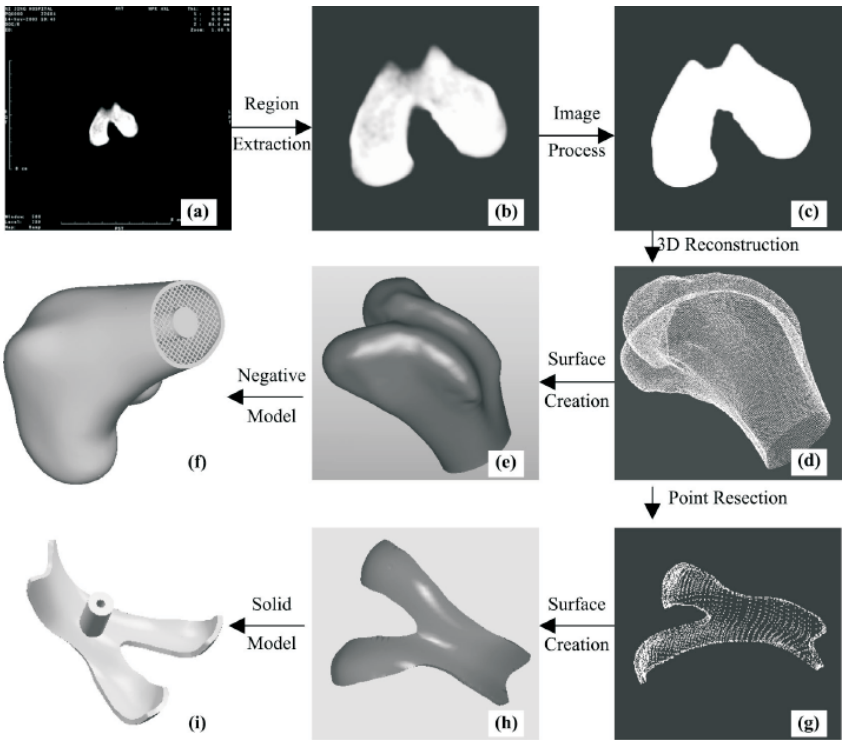
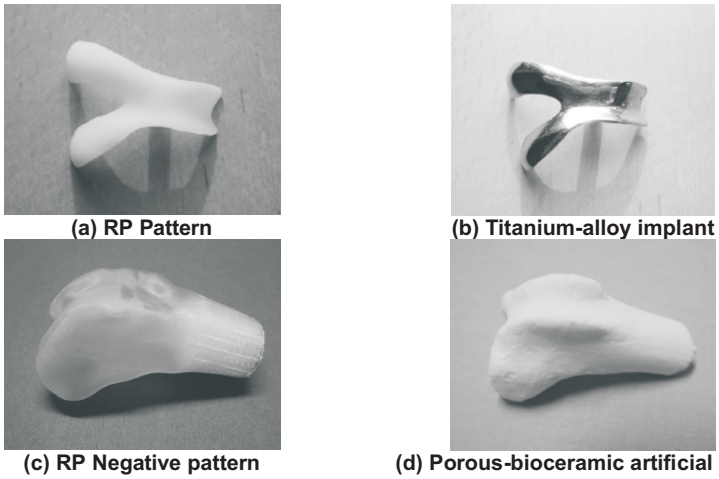


Figure 4: Process chain for custom design of composite hemi-knee joint substitute [19]



(a) RP Pattern **(b) Titanium-alloy implant**

(c) RP Negative pattern **(d) Porous-bioceramic artificial bone**

Figure 5: Hemi-knee joint implant and artificial bone before and after sintering process [19]

5. CONCLUSIONS

The use of Layer Manufacturing technologies combined with cross-cutting disciplines to serve the medical field is a highly interesting and rewarding branch of research. With the advancement of new techniques for custom fabrication of implants in combination with clinical experience and innovative developments in materials, the potential for improved surgical procedures looks very promising.

Different combinations of materials and techniques are however still being investigated and more cases, especially in the area of direct metal implant fabrication through Rapid Manufacturing, must be presented and evaluated. The technology cannot be applied for every case, and capability studies are needed to identify specific scopes of application per technology.

In parallel to a continuous drive for finding better ways to produce medical implants, the issues surrounding regulation and control of manufacturing customised implants should not be neglected. Technological advancement in the medical field must be supported by appropriate legislation, otherwise application of new technology may be restricted, or patients may potentially suffer as a result of undue practices.

Several avenues for future development in this field lie wide open. LM as an enabling technology should be seen as a tool to produce physical models for different needs. A critical factor in the successful application of LM in the medical field will be a matching and supportive development of suitable materials or combinations thereof for clinical use in the body. It is therefore not surprising that so much research effort is being applied in the area of Tissue Engineering and scaffold development. These efforts are indeed justified, and this study recommends continued further investigations into these fields.

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