Polymeric materials and processes to produce facial reconstruction implants: A review

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Abstract. Many patients are affected by facial deformities due to trauma or congenital disorders. Reconstruction using bone transplants has been the standard procedure to address many of these defects. In modern times, synthetic materials such as polymers have become widely used in facial reconstruction as medical implants to reconstruct the defective facial bony features. Conventional manufacturing methods can be used to produce polymeric implants, but literature has shown them to be limited in their applications. Many of these limitations can now be overcome by additive manufacturing technologies. This review paper presents an overview of different processes and polymeric materials that can be used to produce cosmetic facial implants.

1 Introduction

The human face is the basis of what society generally defines as a person's physical attraction and beauty [1]. A perfect balance of our facial features, and how each feature is uniquely configured, forms the standard of a harmonious beautiful face [2]. Any defect and abnormality that affects and impedes the function of each of these features and/or any feature around the head region, can have a tremendous impact on our self-perception, and how others come to view us [1-3]. Facial defects may result from various causes including physical trauma such as car accidents or diseases [4]. Congenital disorders also contribute significantly to facial defects, and it has been reported that one in every 500-700 new-born babies may suffer from facial abnormalities leading to their need of cranio-maxillofacial reconstructive surgery [3-6]. Facial defects may include tissue malformations of the ear, nasal region, and bony regions of the face including the jaw, orbital floor, as well as the oral, and cheek bones, amongst others [7, 8]. A depiction of some of these defects is presented in Figure 1. Synthetic facial implants may be used to augment missing tissue via reconstructive surgery. These implants may either be loadbearing or non-loadbearing depending on where they are used. A jaw implant will, for example, be load bearing while a cheek bone augmentation for cosmetic purposes will be non-loadbearing. For this review, implants produced through additive manufacturing (AM) and other techniques using different polymers will be considered as medical solutions to reconstruct the non-loadbearing bony

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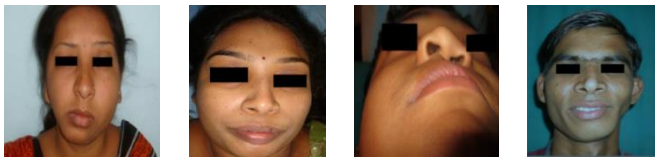
features that are affected by facial abnormalities. Note that silicone prosthetics that are worn externally by a patient are excluded from this review.



(a) (b) (c) (d)

Fig. 1. Examples of facial abnormalities: (a) undeveloped one side of the face deformity; (b) chin deformity; (c) cleft nasal anomaly; (d) jaw abnormality [7].

2 Cranio-maxillofacial augmentation methods

The end goal of cranio-maxillofacial augmentation surgery is to optimize cosmetic results irrespective of the nature of the facial deformity that needs reconstruction [9]. The desired cosmetic result depends largely on an accurate surgical plan formulation. Surgical planning includes understanding the human face anatomyand the assessment of the defected area, the surrounding hard and soft tissue, as well as the selection of the appropriate type of augmentation solution needed together with its size, and shape to achieve a positive surgical outcome [2, 9, 10]. Biologic tissue implants and synthetic implant devices have proved capable of augmenting non-loadbearing bones and their predominance will be explored in the following two subsections.

2.1 Biologic tissue implants: Bone grafts

Biologic tissue implants can be taken to mean any implantable device derived from the natural living tissue of organisms. These types of implants are available in many forms and their application depend on the type of tissue that needs augmentation [2]. Biologic tissue implants which are usually used to augment facial non-loadbearing bony features are bone grafts. Bone grafts can be broadly divided into three groups viz., autografts, allografts, and xenografts [2, 11, 12]. Autografts, which are bone grafts harvested from a patient's own biologic bone tissue, have been the go-to method of augmentation for bone deformities for decades [2, 4, 12]. These type of bone grafts are normally harvested from non-essential bones of the face and head regions such as those bones around the rib, iliac crest, fibula, skull, chin and the jawbones [12]. Autografts can supply structural support, scaffolding necessary for cell distribution during bone ingrowth, and exhibit the needed osteoinduction bone property. Osteoinduction is the recruitment process of unspecialised and immature cells of the body and their differentiation and stimulation into cells that encourage bone growth. [2, 12, 13]. Autografts require a secondary operation where the bone is removed and relocated to the primary site. This means blood loss, the duration of the surgical procedure, postsurgical discomfort, and the patient's hospital stay are increased [12, 13]. In the 1980s, autografts had failure rates approximating to 25%, and over the passing decade, their failure rates are still above 20% [4, 11, 14].

Despite autografts still being the go-to method of augmentation for facial bone defects, the past couple of years have seen a substantial rise in the number of valid alternatives which can be used for facial augmentation [11, 12]. Biologic alternatives to autografts are allografts, and xenografts. Allografts are the type of bone grafts made from a donor patient's bone tissue other than the person who will receive the graft. Xenografts on the other hand are bone grafts derived from species other than the human species such as bovine bones which are obtainable

from non-essential bones of cows [11, 12, 15, 16]. Similar to autografts when using a patient's own bone tissue, allografts and xenografts also have associated problems. These include scarcity of donor's bone tissue supply, undesired implant failure rates, and infections [4, 12]. The implant failure history associated with bone grafting has called for alternative solutions over autografts, allografts, and xenografts as means for augmenting facial non-loadbearing bony features affected by facial defects [4].

2.2 Synthetic implant devices

Synthetic implant devices, normally referred to as medical implants, have shown promising clinical outcomes when considered as suitable alternatives to bone grafts [4, 11]. These implant devices can be used where the function of bone grafts needs to be enhanced, extended, or totally replaced [2, 17]. Synthetic implant devices ideally need to be capable of encouraging cell proliferation and distribution, providing scaffolding during cell attachment and tissue ingrowth, and providing mechanical support necessary for withstanding the effect of the possible formation of hard and soft tissue stresses [2, 12, 17, 18]. For successful facial augmentation, synthetic implant devices need to remain integrated and fixed at the implantation site, retain their original form, and not degrade [2].

Synthetic implant devices need to be made with materials which are compatible to the human biological environment and do not cause any harmful and inflammatory response upon the device's implantation in the human body [2, 4, 12]. These materials can be classified into five categories viz., materials of natural origin, alloplastic materials (also called man-made or synthetic materials), composite materials, materials combined with growth factors, and materials that contain living cells [4, 11, 19]. The current paper is mainly concerned with the use of alloplastic materials as alternatives to bone grafts to augment non-loadbearing bony features affected by facial defects. A review on each of the synthetic implant material categories is beyond the scope of this paper. However, [19] can be consulted for a review on material categories other than the category of alloplastic materials. Alloplastic materials can be further classified into three subcategories viz., ceramics, metals, and polymers [4].

Ceramic materials such as bioactive glass, hydroxyapatite, and tricalcium phosphate have been used as facial augmentation implants [4, 20]. This is because ceramics are known to have excellent corrosion resistance, and some of them have characteristics similar to the ceramic component of the natural bone. Despite these advantages, the clinical use of ceramic materials is limited, and this is mainly due to their poor mechanical properties such as their intrinsic brittleness which makes them susceptible to breaking when used as implants [4, 21]. Moreover, some ceramic materials are difficult to process and cannot be reshaped and modified during the surgical procedure for an acceptable patient fit [20].

Metallic materials such as gold, silver, aluminium, titanium and its alloys have also been used to fabricate facial synthetic implant devices. However, the use of many of them has been cast aside because of the complications they caused [20]. The metallic material that remains in wide clinical use today and offers competitive qualities to bone grafts is an alloy called Ti6Al4V extra low interstitial [20, 22-24]. Ti6Al4V alloy has the needed prerequisites of implant materials of high specific strengths, high impact resistances, high corrosion resistances, biocompatibility as well as non-biodegradability which all make it particularly suitable for implants where loads are applied. Some patients, however, complain of Ti6AI4V implants being felt as cold during the winter season and the possible visibility of the implant under the facial skin of light skin individuals is also a concern. Medical implants made from Ti6Al4V are known to be opaque to radiation during medical imaging and may cause artifacts which reduces the quality of the images that are often needed for postoperative follow-up checks, and possible radiotherapy planning [20, 25]. Despite the disadvantages associated with Ti6Al4V, this alloy remains the "gold standard" of synthetic materials for the fabrication

of synthetic implant devices for use during facial augmentation. Therefore, the performance of suitable synthetic materials for use as facial augmentation implants is often judged in comparison first to autografts (for their inherent likelihood of being readily compatible to the human biological environment) and then Ti6Al4V alloy (since it yields lower complication rates compared to other synthetical materials) [2, 14].

From the three classes of alloplastic materials, polymeric materials offer competitive qualities which has enabled their clinical use as suitable alternatives to bone grafts for facial augmentation [2, 4, 20]. This is essentially due to their compatibility and adaptation to the human biological environment, as well as their excellent mechanical properties. The choice of a particular polymeric material for use as facial implants depends on its solubility, degradation rate, molecular weight, crystallinity, melting point, and the location where it will be implanted [4]. Polymeric materials are flexible, diverse, extensive, easy to process and modify, and can be used in a wide array of applications for the fabrication of synthetic implants. The diversity of material properties seen in polymeric materials showcases their flexibility and qualifies them to be suitable for wide use as facial implant devices for augmentation of non-loadbearing bony features affected by facial defects [2, 4, 20]. These synthetical materials are therefore considered as suitable alternatives to bone grafts over ceramics and metallic materials and will be discussed further in this paper.

3 The use of polymeric synthetic implants in cranio-maxillofacial augmentation surgery

Polymeric materials such as polymethylmethacrylate, polyether etherketone, silicone rubber, expanded polytetrafluoroethylene, and high-density polyethylene have been used extensively as non-degradable facial implants in cranio-maxillofacial surgery [2, 4, 11, 17, 20]. Degradable polymeric materials such as polycaprolactone, polylactic acid, poly-L-lactic acid and polyglycolic acid are commonly used to produce scaffolds for bone growth where bone augmentation is required but this falls outside the scope of this paper. In the below subsections, the extent to which non-degradable polymeric materials have been used in craniomaxillofacial surgery is discussed as well as areas that need improvement and more research.

3.1 Polymethylmethacrylate

Polymethylmethacrylate (PMMA) is a non-degradable, high strength and rigid polymeric material which is normally produced through polymerization of methylmethcrylate monomers, and it is mostly used in craniofacial reconstruction [2, 17]. PMMA is compatible to the human biological environment and has low toxicity rates when used as an implant material. Compared to hydroxyapatite, PMMA has better compressive strength [2, 11, 17].

PMMA is used conventionally for implant fabrication when the material is still in the plastic phase of polymerization. Implants are usually prepared by applying the PMMA material directly over the bony defect which hardens by polymerization. After the polymerisation process, the implant is removed from the defect site, trimmed, sterilized, and fixated at the implantation site with titanium plates and screws [26]. When using this technique to produce PMMA implants, the duration of the surgical procedure is increased. The exothermic reaction, which takes place during the polymerization process, also gives off heat which may burn the patients and toxic fumes are caused by the curing process. Moreover, the uncured resin in PMMA once in contact with the operating area during polymerization may be toxic and cause allergic reactions [2, 11, 17, 26].

3.2 Polyether etherketone

Polyether etherketone (PEEK) is a semi-crystalline thermoplastic material from the polyaryletherketone family. It is chemically inert, compatible to the human biological environment and does not elicit inflammatory responses when implanted into the human body [2, 11, 17]. PEEK as an implant material has high strength, and elasticity which are close to the properties of cortical bone and offers qualities which are comparable to metallic materials [11, 17, 27]. In contrast to most metallic materials, PEEK implants are, firstly, non-magnetic and translucent to X-rays thus they cannot create artifacts during medical imaging procedures for post-surgical re-examinations and evaluations. Secondly, they are less dense and lightweight thus patients can be comfortable when using them and thirdly, PEEK implant are not good conductors of heat [11, 27, 28]. PEEK implants can be fabricated using conventional manufacturing methods such as computer numerical control milling machines for use in craniofacial augmentation.

Major limitations of PEEK implants include the high manufacturing costs of the material compared to PMMA and the possibility of the implant slipping and extrusions where the implant starts showing and piercing through the skin. Since PEEK is not porous, no ingrowth of surrounding tissue takes place which will act as a means of implant fixation. Screws therefore need to be used for this purpose [11, 28].

3.3 Silicone rubber

Silicone rubber (polysiloxane) is a soft polymeric material which is stable, non-toxic, chemically inert, and consists of silicon and oxygen elements alternating with organic side groups [2, 17, 29]. Silicone rubber is the only non-carbon chain polymer suitable for clinical use today as a synthetic implant for use during facial augmentation [2]. This is because silicone is easy to modify, compress, and expand as a facial implant during the surgical procedure. Silicone rubber is non-degradable and has low permeability rates thus it can be used for the fabrication of long-acting facial implants [17].

Major challenges with the use of silicone rubber implants includes difficulty of fixating the implant to the implantation site [2, 30]. This has led to concern over the use of silicone rubber implants which may include possible implant slipping and extrusions. As a result of silicone rubber having low permeability rates, the use of this material for implants lacks the ability to allow cell proliferation, and tissue ingrowth to assist with implant fixation [30, 31]. Medical-grade silicone rubber material for use as medical implants is available as prefabricated standard shapes which may need further carving and modifications for an acceptable patient fit [30, 32].

3.4 Expanded Polytetrafluoroethylene

Expanded polytetrafluoroethylene (ePTFE) is a non-biodegradable and biocompatible material which has been extensively used for facial augmentation especially for lip enhancement, chin and cheek augmentation, and facial contouring as well as filling of soft tissue defects. ePTFE is also useful as an injectable implant material where the function of the face needs to be restored by improving its movements and symmetry [2]. In contrast to silicone, ePTFE implants allow cell distribution and tissue ingrowth. Implant slipping as well as implant shrinkage, and extrusion, are some of the major challenges experienced when ePTFE is adopted for use as a facial implant material [2, 17, 31]. ePTFE implants are also available as prefabricated standard shapes which may need further carving and modifications for an acceptable patient fit [32]. ePTFE implants can be strengthened by the addition of silicone rubber which will help overcomeshrinkage issues associated with ePTFE [17].

3.5 High-density polyethylene

High-density polyethylene (HDPE) is widely used in facial augmentation surgery. HDPE is a semi-crystalline, biocompatible, and non-biodegradable thermoplastic material with excellent mechanical properties which make it particularly useful for facial augmentation in non-loadbearing applications [4, 7, 31]. HDPE has been successfully used in vivo, as MEDPOR® implants, since the 1970s [4]. In comparison to PMMA, PEEK, silicone rubber and ePTFE, HDPE implants allow very good cell infiltration and tissue ingrowth. As a result, when they are clinically applied, they seldom suffer from extrusions, and implant slipping [2, 4]. Rai *et al.* [7] reported 16 successful cases in which HDPE was used *in vivo* to reconstruct the facial regions affected by deformities including hemifacial microsomia (a defect where one side of the face is not well developed), nasal tip correction, cheek bone deformities, and orbital floor reconstruction.

HDPE that is certified for use as medical implants is commercially available as sheets and blocks. These needs to be carved by the surgeon manually in theatre to fit the defect area on the patient [33, 34]. Standard shapes [33] used in facial augmentation are also available such as those shown in Figure 2. These standard shapes also need to be modified in theatre through carving for a good patient-specific fit. Using sheets, blocks, and standard shapes that needs further modification extends the operating theatre time with associated risk and the fit of the implant may not be perfect.

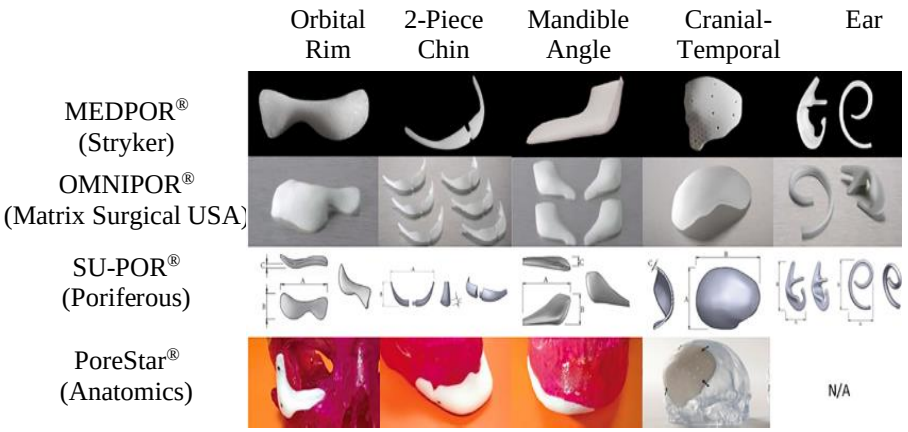


Fig. 2. HDPE implants from various manufacturers with their respective clinical applications in the facial and head regions [4].

4 Medical implant stability and porous synthetic implant structures

The use of porous implant structures in tissue engineering as solid tissue scaffolds offers the opportunity to improve implant stability and fixation with the surrounding tissues over the use of screws and bone cements [21, 35]. Porous synthetic implant structures, also referred to as lattice structures, are complex geometry design structures that allow fixation and bonding of the implant with the surrounding tissue by providing pathways for cell proliferation and tissue ingrowth [4, 36]. Naturally, bodily tissues and organs, each contain a unique non-cellular support structure called the extracellular matrix [37]. The extracellular matrix of tissues and organs also helps with initiating cues for cell proliferation and tissue

ingrowth during tissue rehabilitation. In this context, porous synthetic implants are designed to act as and mimic the extracellular matrix of tissues to augment facial defects [4, 37, 38].

Porous structures are characterized by the distribution and arrangement of approximately equal open pores which are interconnected to each other as shown in Figure 3 below. The position of open pores, how they are interconnected, as well as their shape and their sizes are what essentially makes cell infiltration and the surrounding tissue ingrowth into lattice structures possible [21, 37, 38]. Lattice structures are optimised through controlling these internal geometry designs, and in this way mechanical properties of implants can also be tailored for [18]. Lattice structures should be easy to handle during the surgical procedure, and their mechanical behaviour should be consistent with the bone with which it will interact and be integrated [36, 39]. In the context of non-degradable materials and permanent implants, the use of porous implant structures is preferred over solid implant structures with stiffness that is a lot higher than that of the surrounding bones as is often the case with many metallic materials. Solid structures with high stiffness compared to the host bone are known to give rise to the stress-shielding phenomenon. During stress shielding, the surrounding bone is gradually broken down into its constituents which will be scattered around and allow the bone to remodel into new bone resulting in implant loosening and displacement [21].

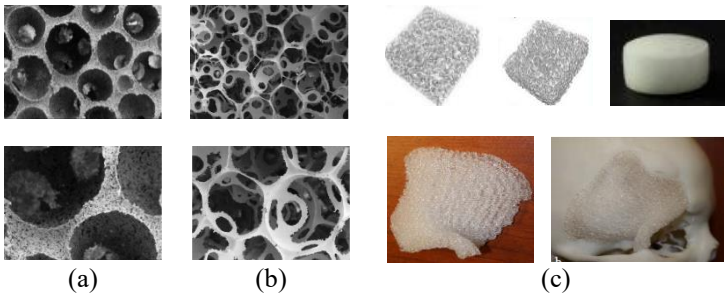


Fig. 3. Porous lattice structures with approximately equal, and same shaped interconnected pores: (a) Spherical pore scaffolds with porosity range of 250–420 µm; (b) Scaffolds with porosity range of 420–500 µm; (c) Three-dimensional (3D) polymeric structures with varying porosities [39-41].

As mentioned before, polymeric materials are flexible, formable and can thus be easily fine tuned into structures with desirable mechanical properties suitable for use as facial implants in the medical field [38, 39]. The challenges of implant slipping, and extrusions associated with the use of polymeric implant materials in facial reconstruction can be overcome when they are used as porous structures. Since porous HDPE implants allow superior cell infiltration and tissue ingrowth, the range of available porous HDPE structures can be used as a guideline when fabricating the other polymeric materials. MEDPOR®, for example, has pore sizes that range between 150 µm and 400 µm and have shown clinical success when used as an implant since its first use in the 1970s [4].

5 Alternative manufacturing processes for polymeric synthetic implant devices

The control and regulation over porous implant structures depend largely on the implant fabrication process. Several methods have the potential to control the geometry, and porosity of implant structures and can be employed to manufacture synthetic implant devices which can be used in facial augmentation surgery.

5.1 Conventional Manufacturing: Electrospinning

Various conventional polymer processing methods have been used to fabricate solid porous implants, including conventional polymer foaming techniques such as gas foaming, solvent casting/particulate leaching, thermally induced phase separation, melt moulding, and freeze-drying [22, 38, 39]. However, these conventional methods have limited control over the pore size, geometry, and interconnectivity associated with porous structures as these three parameters are the most vital parameters that determines the efficiency of porous implants in the medical field [38, 39].

Another conventional manufacturing method which exhibits superior qualities of porous implants compared to other conventional methods and has been used in the past for porous polymeric implant fabrication is electrospinning which is essentially a blend of electrospraying and spinning manufacturing techniques [42]. In electrospinning, the solution of a polymer is prepared in a volatile solvent and fed into a syringe. The material is then extruded into a high voltage electric field as a solution droplet from a small diameter nozzle/die tip attached to the end of a syringe. Once the droplet of a polymeric solution is extruded from the nozzle or die, it starts narrowing leading to the evaporation of the solvent present in the droplet and the creation of ultrafine plastic fibres which are deposited onto the collector mechanism of the technology. In this way both two and three dimensional (3D) porous macroscale/solid structures can be easily manufactured through electrospinning. Flat collectors are usually used to manufacture two dimensional structures while special shaped collectors are used to fabricate three dimensional structures [42-46].

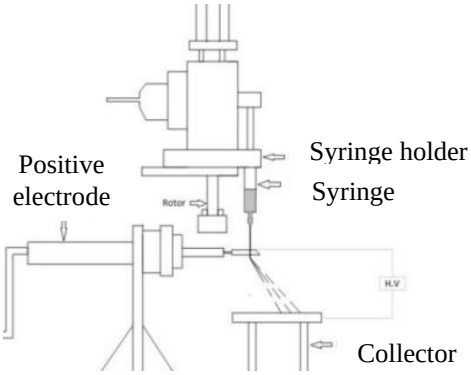


Fig. 4. Apparatus set-up of the electrospinning technology [45].

Electrospinning possesses the ability to process a wide range of polymeric structures with a high distribution of pores, micro-to-nano scale dimensions, and a high surface ratio to volume. Compared with the manufacturing methods previously mentioned, electrospinning can control the direction in which the plastic fibres are aligned/organised on the collector during the fabrication of porous structures [44]. Despite these advantages of the electrospinning technology, there is a limited range of allowed solvents which can be used in the process and the toxicity associated with most the available solvents is also a concern. Moreover, from the list of the synthetic non-degradable polymeric materials which can be used for facial augmentation which were previously discussed, only PMMA has been processed extensively in electrospinning and the other polymeric materials are yet to be tested for processability on the process [45]. Also, according to the study by Gao *et al*. [46], using special collectors to fabricate 3D porous structures in electrospinning, limits the control of the process over the external geometries of 3D structures and there is also a challenge to

position the collector mechanisms precisely to enable accurate control over the complex geometries of 3D structures. Moreover, 3D electrospun porous structures which are fabricated using special collectors still need more research to enable their commercial and clinical use. This is despite their success at the research level which has shown that they are mechanically superior and performs better than two-dimensional porous structures which inhibits cell proliferation, cell infiltration and tissue ingrowth during in vitro and in vivo animal studies [46].

5.2 Microfluidic Technologies

In layman's terms, microfluidic technologies can be taken to mean any technology capable of minute manipulations of fluids through different channels, the dimensions of which are in tens of micrometers [39, 47]. Giannitelli *et al.* [44], mentions four categories in which these technologies have thus far been applied to address some of the prevalent problems in the biomedical field. In one of these categories, they mention that microfluidic technologies can be used to fabricate polymeric materials which can be used as porous implants in tissue engineering [44]. Microfluidic technologies use polymeric materials to produce bubble or droplet templates using either a T-junction, co-flow, or flow-focusing channel geometry to fabricate porous structures as shown in Figure 5 below. The resulting bubble or droplet templates are continuously deposited into a collector plate or container. Once on the plate or inside the container, the fluid bubble or droplet template self-assembles and solidifies spontaneously into porous structures as those depicted in Figure 3 (c) above [38, 39]. After solidification, two-dimensional porous structures can be easily removed from the plate while in the case of 3D porous structures, the bubble or droplet templates need to be removed by evacuation and extraction processes to obtain the 3D structure from the container [39].

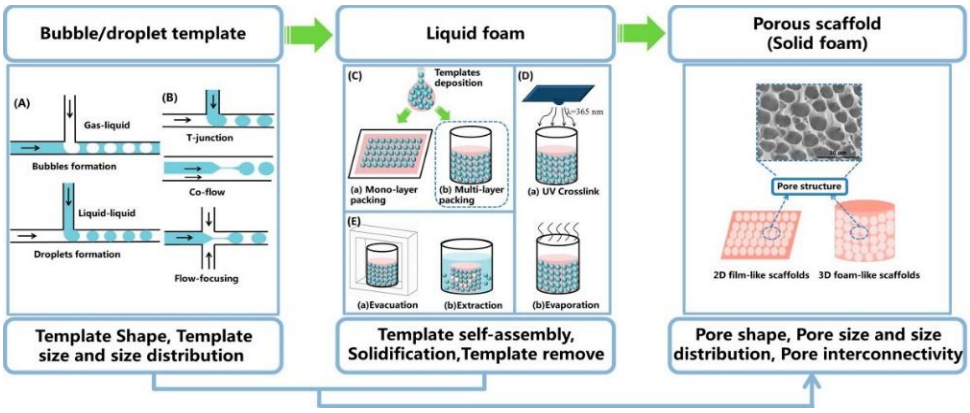


Fig. 5. Process flow of the microfluidic technology when fabricating solid polymeric scaffolds [39].

The distribution of pores, their shape, and their interconnectivities can be easily realized in microfluidics by the accurate control of the size and volume fraction of the bubble or droplet templates to fabricate porous structures. The overall external geometry and shape of the porous structures is controlled by the collector plate or container. In contrast to electrospinning, microfluidic technologies can be used to produce porous structures with good and reasonably controlled pore sizes and shapes as well as interconnectivities [38, 39].

The main challenge with microfluidic technologies is associated with the solidification process which may result in the loss of the initial formation and morphology of porous structures because of the instabilities associated with structures in liquid form [38].

Microfluidic technologies also use collector containers to fabricate 3D porous structures and these containers limits the control of the process over the overall external geometries and shape of 3D structures.

5.3 Additive Manufacturing

Additive Manufacturing (AM) technologies have demonstrated the ability to fabricate customized and patient-specific medical implants [22]. In AM technologies, 3D solid objects are built "layer-by-layer" in a sequential manner [22, 48-50]. Since the development of the first AM process in the 1980s, AM has evolved in its application and the materials that can be processed. At this stage, AM technologies are classified into seven main categories according to their manufacturing technique, namely, vat photopolymerization, material jetting, sheet lamination, material extrusion, powder bed fusion, binder jetting, and direct energy deposition [51-53].

The manufacturing principle of layer-by-layer material addition is generally the same for all AM categories. In material extrusion, for example, a polymer filament is fed into an extruder which melts the polymer and then extrudes it as molten material which is deposited layer-by-layer to fabricate 3D objects. Some of the specific AM processes that belong to material extrusion category is fused deposition modelling (FDM) and gel or paste extrusion [20, 22, 52]. Polymers such as PMMA, PEEK, HDPE, silicone rubber, and ePTFE have been processed in extrusion-based AM technologies [25, 41, 54-57]. In powder bed fusion (commonly referred to as laser sintering) process, powder particles of polymeric materials are deposited in a thin layer and fused together by a laser beam. Another layer of powdered particles is deposited on top of the previous one and the process continues to produce 3D objects [20, 22, 52]. Materials which have been used in powder bed fusion include PMMA, PEEK and HDPE as powder materials [4, 25, 35, 58, 59]. Lastly, in vat photopolymerization, light is used to cure and harden photo-sensitive resin materials to build 3D objects layer-by-layer. Specific examples of AM technologies which belong to this category include stereolithography, and digital light processing (DLP) [20, 22, 52]. Vat photopolymerization has been used to process polymeric materials such as silicone rubber and ePTFE [60, 61].

The layer-upon-layer fabrication technique of AM has enabled the use of these technologies in tissue engineering to fabricate complex internal implant geometry designs as well as accurately fine-tuning the internal porosity of porous implant structures to improve implant performance during facial augmentation [20, 36]. As mentioned before, the internal geometry design of porous structures can be complex (e.g., open internal pores) and these designs may be difficult or impossible to manufacture using conventional manufacturing methods [4, 36, 54]. The general process parameters that can influence the mechanical properties of 3D objects that needs to be fabricated with AM includes layer thickness, build orientation, build speed, different manufacturing temperatures, and the fill pattern and air gap between adjacent material powder particles, droplets, and extruded lines [54, 62]. The viscoelastic and thermal behaviour of the build material also plays a crucial role on the quality of implants manufactured with AM technologies [54]. Medical implants may be directly or indirectly manufactured with AM [29]. For producing customised and patient-specific facial polymeric implants directly through AM, the patient's geometrical information of the face and the head regions from Computed Tomography (CT) scans is required and the process unfolds as depicted in Figure 4 [22, 50, 53, 54]. The accuracy of parts manufactured with AM depends largely on the overall quality and resolution of CT scan images. Direct application of AM technologies also allows the incorporation of finite element analysis methods to be performed on the implant at the design stage to improve its design and optimize its performance before being translated into a real object [54].

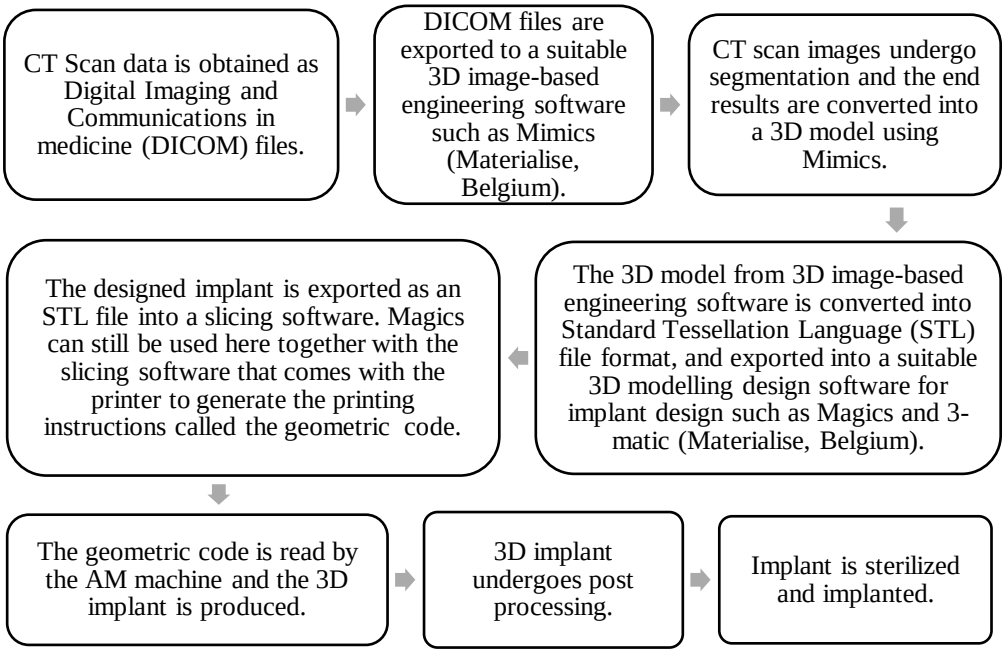


Fig. 6. Flow diagram of a typical AM process to produce a medical implant [63].

AM technologies can also be indirectly used to manufacture implants and supplement conventional manufacturing methods as well as electrospinning in the production of moulds for patient-specific implant geometries and porous implant structures [22, 26, 46]. Cast cranial plates which are used to augment large bone defects in the skull region may for example be fabricated using negative mould halves produced through AM. The 3D cast model to be manufactured is designed using the patient's skull information from CT scan data [26]. In electrospinning, AM can be used to fabricate the collector which can be used for manufacturing 3D porous implant geometries [46].

In comparison to electrospinning technology and the microfluidic technologies, AM technologies have complete control over both the external and internal geometries of 3D printed objects.

6 Processability of polymeric materials in additive manufacturing to enable the direct fabrication of polymeric facial implants

Currently, different polymeric materials are being investigated for processability in AM technologies to enable their clinical use in cranio-maxillofacial augmentation surgery. This reality is precedented by the diversity of AM technologies which can process many polymeric materials [35]. PMMA is available as medical-grade powders and filaments and they have been successfully used in powder bed fusion and material extrusion respectively [35, 41]. Espalin *et al.* [41] were able to successfully use extrusion-based AM technology to demonstrate the feasibility of the direct manufacturing of customized PMMA parts in AM using information from CT scan data. It was found that the mechanical properties and porosities of PMMA parts were consistent with commercially available PMMA craniofacial implants [41]. Velu and Singamneni [35] investigated the processability of PMMA powder as a medical-grade material to enable the fabrication of PMMA implants through powder bed

fusion. From the study, single layer specimens were successfully manufactured using optimised process conditions. The success of the experiment largely depended on a compromise between laser power and scanning speed in the powder bed fusion process [35].

PEEK is more difficult to process in extrusion-based AM systems than PMMA and often results in parts with unsatisfactory qualities such as defects which appear as weld lines between extruded lines and material degradation due to overheating [54, 64]. Honigmann *et al.* [64] were however able to overcome the challenges associated with processing PEEK through extrusion-based AM systems and were able to successfully produce implants. Medical-grade filaments are difficult to source and as a result, medically certified granules of PEEK were used to make PEEK filament for this study [64]. Hoskins *et al.* [59] successfully processed PEEK through laser sintering and found that the performance of parts produced was significantly higher than the performance of the polymers which were previously processed through LS. Li *et al.* [65] successfully used additively manufactured PEEK implants to reconstruct jawbone defects in six patients. Upon follow-up, no complications were reported for five of the patients and they were satisfied with the surgical results. A PEEK implant however had to be removed for one patient because of implant visibility under the skin at 10 months after surgery [65]. Silicone rubber material is also difficult to process through extrusion-based AM technologies. Problems include nozzle clogging because of material curing and accumulating in the nozzle and material deviation from the print path once extruded from the nozzle [29, 66]. Despite these challenges, Zuhlke *et al.* [67] were able to process medical-grade silicone filament in FDM extrusion-based AM system and used the samples for *in vivo* animal studies. After two weeks, it was found that silicone samples produced through FDM did not elicit inflammatory response and they induced good healing around them. The processing of silicone rubber through binder jetting proved promising as evidenced by a study conducted by Yang *et al*. [68]. From this study silicone rubber was used successfully to fabricate 3D porous structures using the technology [68]. In vat photopolymerization, Wagner *et al.* [60] successfully used silicone rubber in stereolithography to fabricate structures which can mimic the non-linear elasticity of soft tissues.

Similar to silicone rubber and PEEK, ePTFE is also hard to process through AM technologies and often require polytetrafluoroethylene to be combined with other materials to improve its viscous and shear-thinning properties to enable its processability. This also mean that medical-grade PTFE is yet to be tested in AM for processability to enable the direct manufacturing of ePTFE implants. In a study by Jiang *et al.* [57] PTFE combined with gellan gum (an additive normally used to stabilise and improve the binding ability of materials) was successfully used in extrusion-based AM. ePTFE porous structures made with pure polytetrafluoroethylene were obtained after the removal of gellan gum through thermal treatment [57]. Zhang *et al.* [61] adopted a different technique and used a composite made up of polytetrafluoroethylene particles and poly (ethylene glycol) diacrylate in a DLP vat photopolymerization process to fabricate 3D structures. They also obtained ePTFE made with pure polytetrafluoroethylene after the removal of poly (ethylene glycol) diacrylate [61].

HDPE has been processed through material extrusion and powder bed fusion AM techniques as filament and powder respectively [4, 56, 58]. Wampol [56], reported that extruded HDPE fail to properly adhere to the printing bed during laying down of the first layer in material extrusion AM. The part then separates from the bed due to material shrinkage and warpage during the print. Hoelzel [58] used HDPE in powder bed fusion AM and reported that parts produced in HDPE powder tends to curl on the powder bed because of the specific material properties such as semi-crystallinity, and high melting temperature. Despite this, Paxton [4] used medical-grade HDPE scaffolds produced through powder bed fusion for *in vitro* and *in vivo* studies. The performance of these scaffolds was compared with moulded StarPore® HDPE scaffolds and MEDPOR® HDPE scaffolds and after 8 weeks it

was found that scaffolds produced through powder bed fusion were more conducive to tissue ingrowth than both StarPore® and MEDPOR® scaffolds [4].

7 Conclusion

Synthetic polymeric implants can be effectively used for cosmetic reconstruction of parts of the face that are affected by facial abnormalities. These implantable medical devices have shown clinical outcomes that are comparable to bone transplants which are usually the gold-standard of treatment for facial defects. Conventional manufacturing methods can be used to fabricate polymeric implants but from literature, these manufacturing methods have shown limited control over the pore size, geometry, and interconnectivity which are essential for implant stability and successful facial reconstruction. These shortcomings can be overcome using AM technologies which have demonstrated the ability to fabricate customized and patient-specific facial polymeric implants with complex designs from CT data of the patient's facial features. Current challenges with processing polymeric materials in AM include material shrinkage, warpage, clogging, topology defects, and material degradation due to overheating. Despite all these challenges, the rapidly evolving field of AM offers many future opportunities for the direct manufacturing of porous polymeric cranio-maxillofacial augmentation implants.

8 Acknowledgements

The financial support from the South African Research Chairs Initiative of the Department of Science and Innovation and National Research Foundation of South Africa (Grant № 97994) and the Collaborative Program in Additive Manufacturing (Contract № CSIR-NLC-CPAM-18-MOA-CUT-01) is gratefully acknowledged. The centre for rapid prototyping and manufacturing is also acknowledged for allowing the authors to use its facilities for research.

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