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The Recent Revolution in the Design and Manufacture of Cranial Implants: Modern Advancements and Future Directions

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Abstract

Large format (*i.e.*, > 25 cm^2) cranioplasty is a challenging procedure not only from a cosmesis standpoint, but also in terms of ensuring that the patient's brain will be well-protected from direct trauma. Until recently, when a patient's own cranial flap was unavailable, these goals were unattainable. Recent advances in implant Computer Aided Design and 3-D printing are leveraging other advances in regenerative medicine. It is now possible to 3-D-print patient-specific implants from a variety of polymer, ceramic, or metal components. A skull template may be used to design the external shape of an implant that will become well integrated in the skull, while also providing beneficial distribution of mechanical force distribution in the event of trauma. Furthermore, an internal pore geometry can be utilized to facilitate the seeding of banked allograft cells. Implants may be cultured in a bioreactor along with recombinant growth factors to produce implants coated with bone progenitor cells and extracellular matrix that appear to the body as a graft, albeit a tissue-engineered graft. The growth factors would be left behind in the bioreactor and the graft would resorb as new host bone invades the space and is remodeled into strong bone. As we describe in this review, such advancements will lead to optimal replacement of cranial defects that are both patient-specific and regenerative.

Keywords

Cranioplasty; 3-D printing; Additive Manufacturing; Computer Aided Design (CAD); Cranial Implant; Regenerative Medicine; Tissue Engineering

I Introduction

The neurosurgical reconstruction of cranial defects has witnessed a tremendous evolution over recorded history. In discussing this evolution, it is important to elaborate upon the

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following: cranial defect size (*i.e.*, critical and non-critical size defects); implant material choice (*e.g.*, autologous or alloplastic grafts); and the use of tissue engineering strategies (*i.e.*, resorbable implants alone or the addition of cells and/or growth factors to facilitate regeneration). Other than cell-based therapy, these aspects of the surgical approach to cranioplasty are reported in Sanan and Haines' 1997 signature report[1]. Significant progress in the field since their landmark paper has prompted us to provide an updated review of the surgical approach to cranioplasty. We review recent advancements in: a) bone substitute materials (Section II); b) cranial implant fabrication through Computer Aided Design (CAD) and Computer Aided Manufacture (CAM) (Section III); c) Tissue Engineering therapies for the regeneration of critical size or larger bone defects (Section IV); and, d) advances in the neurosurgical approach to cranioplasty (Section V). We conclude with expected future improvements to cranial defect treatment options.

II Advances in Alloplastic Bone Substitutes for Cranial Repair

The Role of the Cranial Vault as a Skeletal Element

The skull is a unique boney element with structural and functional idiosyncrasies. Unlike other bones, the skull does not transmit weight or bear loads during ambulation or manipulation of the environment. The skull shields the brain from both trauma and infection. Current treatment options for large cranial defects are less effective at protecting the underlying brain than the unmodified adult skull. The implant-bearing skull may suffer abnormal strain concentrations that threaten its protective capability and an increased susceptibility to fatal head trauma[2]. The gap between the skull and an alloplastic implant may serve as a route for infection[3].

Critical Size Defect

The surgical demands of procedures involving trauma, vascular disease, infection, cancer, or congenital deformity often require neurological surgeons to osteotomize large areas of the cranium. Skull resection and entry sites of greater than 25 cm^2 are common in adults[4], and defects of 100 cm^2 are the average size seen by manufacturers of cranial prosthetic plates[5]. In an adult, 100 cm^2 is roughly a quarter of the total cranial surface area. A “critical size” defect is any that is too large for the patient to heal unaided[6]. If revascularization fails or is incomplete following bone flap engraftment, then resorption, necrosis, and/or infection commonly follows[7]. Furthermore, post-surgical healing of large bone flaps requires osteogenic activity that may tax the patient's regenerative abilities which are known to decline with age[8]. Re-incorporation of a large bone flap depends on the local healing response and vascular supply. The blood supply for cranial bone comes primarily from the underlying middle meningeal artery with a much smaller contribution from the overlying scalp[9].

Cranial defect repair following cranioplasty in children is of a different nature than in adults. Although there is a higher risk of resorption when flap replacement must be delayed[10], and there is a significant risk of inflammation or infection from delayed cranioplasty in the pediatric patient[11], the greater regenerative abilities and variety of sources of autologous

bone in children increases the likelihood of healthy regeneration of the cranial vault, when compared to adults[12].

Autografts and Allografts

First, patients commonly receive bone grafts from elsewhere in their body (*i.e.*, autograft tibia, rib, scapula, sternum, ilium, fibula, or cranium). Autograft therapy of cranial defects is the standard to which all other strategies are compared.[13] However, there are several limitations to its use: the supply of graft material is limited by donor site size; autograft harvesting risks long-term donor site pain and adjacent bone morbidity[14]; and the grafted bone may fail to vascularize[15]. Complex autografts require advanced technical abilities of the surgeon. For example, fibular or iliac bone may be difficult to shape for the complex geometry of some cranial regions. As a whole, this process is time-consuming, cumbersome, and may result in long-term pain at the donor site[1]. If graft integration is insufficient or fails, the resulting necrotic bone is at high risk for non-union, mal-union, or infection. Another outcome for necrotic cranial bone is resorption. Insufficiently vascularized regions of a cranial flap may also shield antibiotics and mute immune response. On rare occasions, extra-dural infection occurs.

A second option for large cranial defect repair, cadaver or live bone donation (*i.e.*, allograft), is often equally difficult to shape and carries risk of immunological rejection and pathogen transmission[16]. The use of bone and cartilage tissue from cadavers was an extension of the success of autograft transplantation that was popularized during WWI[7]. Allografts provide beneficial properties of structural integrity and facilitate remodelling[7] without the complications of donor site morbidity. However, significant risk of disease transmission, infection, and immunologic reactivity has impeded the use of allografts. Of note, advances in gene sequencing, sterilization, and graft harvesting and storage have minimized these risks to a significant extent.

Alloplastic (Synthetic) Bone Substitutes: Metal

If a patient loses their own cranial bone flap to trauma, infection, or cancer resection, there are primarily three classes of artificial augmentation materials: metal, polymer, and ceramic. The use of metallic bone substitutes (*i.e.*, alloplastic materials) has a long history. The most common material still in use is grade 5 surgical titanium (*i.e.*, Ti-6Al-4V), usually referred to as “titanium” or Ti-6-4[17]. Titanium is used in the cranium for fixation devices (*e.g.*, plates and screws), mesh, or solid plates (Figure 1), or in combination with other materials such as inert plastic or ceramic components.[4] It is generally accepted that titanium is corrosion-resistant, although there is evidence that trace minerals are released over time,[18] perhaps eliciting a subtle immunologic response.[19] Insufficient perfusion of the overlying scalp flap and mechanical irritation from underlying alloplastic materials or fixation devices (*e.g.*, Ti micro-plating and screws), may lead to inflammation, seroma, infection, or implant fenestration through the scalp.[20]

The skull has elastic properties that are similar to the cortical bone found in long bones.[21] Ti-6Al-4V has an elastic modulus that ranges from 14.5-38.5 GPa[22] (Giga-Pascal) for porous implants to 110 GPa[23] for bulk specimens. This compares to an elastic modulus of

approximately 10.4-19.6 GPa, depending on the location and quality of bone (e.g., radionecrosis or osteoporosis can reduce bone quality), in the adult skull. [21] While titanium implants are less likely to fail during traumatic loading than other alloplastic materials, they may potentially break the surrounding bone or suffer a fixation screw pull-out, especially in regions where strain is concentrated (e.g., microplate fixation).[24] An alternative strategy would be to use an overlapping margin to maximize contact between the implant and the patient's skull.[25] With abutting, overlapping, or both types of margins it is unlikely that the implant-bearing skull would dissipate strain as effectively (*i.e.*, without failure) as a normal unaffected skull.[26] Finally, it is important to note that surface-textured or bioactively functionalized[28] titanium implants can strongly incorporate soft tissue such as dura and periosteum; this can make revision difficult.[27]

Synthetic Bone Substitutes: Polymers

Poly(methyl methacrylate) (PMMA) is perhaps the most frequently used cranial bone graft substitute (Figure 2). It is often provided as a powder and liquid (*e.g.*, Cranioplastic™, DePuy Synthes, Raynham, MA), which are combined to form a malleable paste that is shaped intra-operatively to fit the contours of the patient's cranial defect during surgery. PMMA offers the advantages of a protective, defect-filling replacement that lacks post-operative inflammation. However, PMMA is not without its disadvantages. The polymerization process is significantly exothermic and generates large amounts of heat energy (78-120 °C)[29] during the period when it can be manually molded into place. Inadequate cooling of the material can thus damage surrounding brain tissue or dura. PMMA is associated with significant post-placement shrinkage. Other complications of PMMA cranioplasty include infection[30] and pulmonary embolism (due to PMMA extravasation into venous circulation).[31] Most importantly, PMMA lacks the osseointegrative and osteoinductive properties that would provide complete regeneration of reliable bone in a large cranial defect. However, the lower elastic modulus of PMMA (approximately 3 GPa) compared to surgical titanium (approximately 110 GPa) conveys a lesser discontinuity at the implant-host interface, and may result in less stress-shielding and less loosening of fixation devices over time. Nonetheless, a discontinuity remains. Therefore, traumatic injury directly to a PMMA plate can force it through the adherent screws and drive it directly into the brain, grossly endangering the patient.[32] The safety of one particular product line, Hard Tissue Replacement by Lorenz Surgical, Inc. (BIOMET, Warsaw, IN), has been called into question for patients undergoing decompressive craniectomy.[33]

Another polymer, polyethylene, has long been in use as a material for cranial implants. It is also known to carry a risk of infection.[34] The leading vendor has been MEDPOR® (Figure 3), now a subsidiary of Stryker (Kalamazoo, MI), which provides a highly porous form of this material that is flexible, can be easily cut with a scissors, and has recently been combined with titanium mesh in a new product.[35]

Several other polymers have been investigated for large format cranial implants: PEEK (poly-ether-ether ketone),[36] Polypropylene Polyester Knitwear,[37] and PEKK (Poly-ether-ketone ketone) (Figure 4).[38] There is also an FDA-approved PEKK custom cranial implant

product (Oxford Performance Materials, South Windsor, CT). These materials have been used for the prefabrication of cranial implants (see Section IV). Vendors of these polymeric materials claim that they are more similar in their material properties to the surrounding bone, especially in regard to elastic modulus. Oxford Performance Materials also claims that PEKK is osteoconductive.[38]

Synthetic Bone Substitutes: Ceramics

Calcium phosphate (CaP) has received mixed reviews as a bone substitute. Some consider CaP a tissue engineering scaffold and have observed limited resorption and/or support of new cranial bone growth and remodeling, perhaps in children;[39] others, however, have seen no such resorption.[4] In either case, these malleable ceramic alloplastic materials are extremely brittle and are largely used to fill minor gaps in the skull. Stryker's CaP product, Bone Source™, for example, is FDA-approved for repair of cranial fracture gaps of less than 5 mm.[40] CaP paste hydrolyzes into solid HA (hydroxyapatite) inside the body. Bone grows epitaxially onto solid HA or into the margins of adequately porous HA.[41, 42] HA, hydrolyzed *in situ*, is approximately one order of magnitude more brittle than calvarial bone[43] and exhibits approximately 60% of the compressive strength of PMMA (much less than 60% under tension or bending).[44-46] Self-setting CaP paste is commonly troweled into large cranial defects over a titanium mesh to provide additional stiffness[1, 4] or pre-operatively prepared via the use of skull models.[47] The fragility of HA, however, precludes its isolated use for large deficits.

III Advances in Pre-operative Cranial Implant Fabrication

Pre-fabrication of a well-fitting implant saves operating room procedure time, may render the procedure less invasive, and reduces cost and the risk of infection. Until recently, preoperative fabrication was achieved manually, using topographical information lacking precision.[48, 49] Although infection remains the most cited reason for implant revision or removal,[46, 47] poor fit nonetheless represents a crucial area for improvement. Fortunately, the recent revolution in 3-D printing has made its way to cranioplasty graft design, thereby vastly improving the “fit” of premade cranial grafts. Barnatt[50] discusses the various types of 3-D printing technologies, now preferably referred to as Additive Manufacturing (AM)[51] (formerly known as Rapid Prototyping or Solid Free-Form) that have been utilized to produce both inert implants for patients and tissue-engineered implants for preclinical tissue engineering research. In regard to cranial implants, one of the first AM technologies, stereolithography, utilized models of the skull obtained from CTscans to manually design cranial implants that were then recast in implantable materials.

There are not many non-toxic, resorbable materials that can be used in these printers at this time. All AM technologies build an implant layer by layer from a Computer Aided Design (CAD) file. Table 1 presents the three basic mechanisms by which current 3-D printers render implants. The first method is light-based polymerization, *i.e.*, photocrosslinking, of liquid polymer resin. Two types of devices use this first method, photocrosslinking; they are stereolithography[52, 53] and continuous Digital Light Processing.[54] A second method for 3-D printing implants use liquid or heat to bind particles. One of the earliest technologies to do so, referred to as 3-D Printing (3DP™, Therics Inc., Princeton, NJ), involves the injection of

a liquid binder (which may contain cells and/or growth factors) into powder[55]. Selective Laser Sintering (SLS) uses a laser to bind powder, layer by layer (3D Systems, Valencia, CA). The third AM modality, Fused Deposition Modeling (Stratasys Inc., Eden Prairie, MN), uses an inkjet to extrude material that is heated just above melting temperature.[56] A variation on this method prints an implant in wax (Sanders Prototype, Milton, NH) for later replacement with resorptive materials.[57]

Cranial Implant CAD Software

Computer aided design of cranial implants can involve the use of templates, such as that of an average skull image or of a right-left mirrored image of the patient (only useful if the defect does not cross the midline).[58-60] The template is then appropriately warped to the region of the skull defect. The defect-filling portion of the template is then “cookie-cut” so that thickness can be added to create a tapered edge that abuts and/or overlaps the surrounding skull (Figure 5). During this process of ensuring a good fit, it is also important to: (1) ensure there is no intersection of the adjacent dural sac and brain, and (2) ensure there is sufficient scalp to cover the implant or that galeal scoring and/or tissue expansion may be necessary prior to placement of the implant..[5, 59, 62, 63]

One area that deserves special attention with either autologous or alloplastic repair is the upper orbital rim and brow, also referred to as the orbital bandeau. Where there is risk to the frontal sinus mucous membranes it is often obliterated; these risks include either (1) a lack of containment, risking mucocoele, or (2) adjacency to alloplastic materials, risking deterioration and erosion due to poor integration which may then be followed by infection. While congenital malformation repair may require orbital advancement, care must be taken not to encroach the orbital roof, apex, or medial wall. Encroachment in these areas can lead to neurovascular compromise, especially compromising visual acuity or causing external ophthalmoplegia. It is also important in these cases that revision around the nasion or glabellar regions not cause problems with nasal angulation or asymmetry.[61]

Additive Manufacture: Metallic Cranial Implants

Carr *et al.* (1997) and Eufinger *et al.* (1995)[64] have demonstrated a system for milling of titanium (inert) prosthetic cranial plates. These techniques continue to be in practice today.[65] While new Ti alloys are being developed, the most commonly used material continues to be Ti-6Al-4V, which can be rendered via SLS,[66] Selective Laser Melting (SLM),[67] Electron Beam Melting.[68, 69] These technologies may be able to create porous spaces in the 150-1000 μm range that are mostly likely to promote adjacent bone ingrowth.[67, 69] It remains to be shown whether surface ingrowth will create a stress-strain gradient that can successfully translate strain during a traumatic impact. One group[70] has noted CAD/CAM-rendered ceramic-implants to be more expensive than PMMA- or Ti-implants prepared in the same manner. Further, they find Ti-implants are the least likely to be removed and that they are a useful alternative when PMMA-implants need to be removed.

Additive Manufacture: Polymeric Cranial Implants

The utilization of synthetic polymers for additive manufacturing (AM) of cranial implants is currently the most widely utilized methodology. Given the difficulties of working with

PMMA, most of the companies that offer AM of patient-specific polymer implants do so with PEEK via SLS. The design of these implants can be modified to match the material properties to those of the surrounding skull.[71] Lethaus *et al.*[36] concluded that the material properties of PEEK cranial implants are preferable to those of titanium cranial implants. Jaekel *et al.* report that PEEK material properties are sensitive to the crystallinity of the material that is used.[72] Carbon-fiber reinforcement of PEEK, which can be rendered by stereolithography,[73] has been offered as a means of increasing the material's fatigue resistance in areas of the skeleton that carry a constant load.[74]

Additive Manufacture: Ceramic Cranial Implants

Ceramics have been demonstrated to be a good bone scaffolding material in sub-critical size defects, although their material properties preclude their use for larger deficits (see section 2.4). Attention has recently turned to stereolithography to render large format ceramic cranial implants.[42] A French group, led by Moreau, has generated ceramic graft implants via an AM technique in which polymer is used as a binder during 3-D printing and then sintered away. Their results indicated the potential to use ceramics for large scale defect filling. Also under investigation is a new composite material composed of 50% Beta-tricalcium phosphate (B-TCP) and 50% poly(D, L)-lactide (PDLLA) that is synthesized via SLM.[75]

IV Tissue Engineering

Tissue engineering involves the use of resorbable scaffolds, growth factors, cells, and sometimes bioreactors. There are thus no FDA-approved standard of care approaches to tissue engineered repair of large (> 25 cm^2)[4] cranial defects. We limit discussion here to tissue engineering cranial deficit therapies that are in the clinic or clinical trials.

Scaffolds

In addition to the previously noted use of ostensibly resorbable ceramics, patients in several studies involving large resorbable Poly(α-hydroxy ester)-based prosthetics have encountered problems of excess lactic acid due to normal implant degradation. While solid PLGA has shown osteoconductive properties in humans,[76-79] large PLGA prosthetics undergoing mechanical strain have been observed to develop a rapid decrease in molecular weight, and loss of strength followed by bulk degradation, releasing dangerous levels of lactic acid (Bos *et al.*, 1991).[80] These polymer chains are soluble in the extracellular fluid when their molecular weight falls below 7,000 Daltons,[81] at which point the polymer has little strength and begins to fragment due to local mechanical stresses. When particles are approximately 20 μm they can be phagocytosed by multinucleated cells or macrophages. Those particles that are not phagocytosed continue to degrade and decrease in size. As lactic and glycolic acid are released, there is danger of a local drop in pH, regardless of peri-implant vascularity.[82, 83] Many workers concur that these byproducts prevent bone ingrowth beyond a few millimeters and suggest that PLGA or PLA suture, meshes, solid plates, and screws are best for narrow gap repair of 5 mm or less in bone and/or overlying membranes.[84-87]

Polycaprolactone (PCL) can be 3-D printed via Fused Deposition Modeling. It has been used in a number of preclinical bone tissue engineering studies. Probst *et al.*[88] report the

implantation of a 3-D printed PCL and tricalcium phosphate cranial scaffold. They note observing CT-based evidence of bone consolidation as well as good integration of the implant after 6 months. In a previous study, they concluded that the *in vivo* resorption of these scaffolds would be due to molecular weight, crystallinity, hydrophilicity, and design.[89]

Growth Factors

Bone tissue engineering became a large scale clinical reality with Medtronic's (Minneapolis, MN) Infuse® (collagen sponge, BMP-2, and titanium cage) for intervertebral fusion. Despite concern about the safety and efficacy of this approach,[90, 91] off-label use has extended to osteonecrotic mandible[92] and upper[93] and lower alveolar repair[94] with mixed results. Questions about dose and release rate have led to studies of new implant release strategies.[95]

Cells

Research is underway to characterize[96] the potency and safety of using embryonic, postnatally induced pluripotent or isolated mesenchymal stem cells (MSCs) to seed a scaffold with bone progenitor cells for culture in a bioreactor[97, 98] or inside the body (Figure 6).[99] It is expected that allografted bone marrow-derived MSCs will not cause an immune response, and if quickly replaced by autologous bone progenitor cells they may provide a banked source of cells to produce osteoconductive and osteoinductive scaffolds.

V Neurosurgical techniques and clinical implications

Clinically, the nature of cranial repair is dictated largely by circumstance. Defect size, location, and laterality limit which material (or fabrication method) can be used. The cost and availability of resources, as well as the timing/emergent nature of the case, present similar constraints. Only in elective surgery can the full spectra of cranioplasty resources be considered (Figure 7).

Most frequently, as in the case of decompressive hemicraniectomy, the autologous flap remains available for use. In these instances, flaps may be frozen (typically at -80°C) or implanted subcutaneously in the abdominal wall for later implantation (weeks to months after the initial surgery, although the timing is controversial[100, 101]). As such, evidence maintains the superiority of the autograft. Importantly, however, autologous bone may be subject to aseptic necrosis, infection, and may not survive freezing.[102] The frequency and predictability of these scenarios is unclear. However, we recommend the use of autologous flaps when possible.

When autologous bone is unavailable or unsuitable for cranioplasty, the choice of specific allograft material is left to the discretion of the neurosurgeon. However, it is critical that a highly protective material like allograft or titanium be used in an area where brain herniation, infection, and/or CSF leak is present or imminent. Indeed, given the possibility that time may be needed for autologous bone grafts to incorporate, it may best to use inert material, such as titanium, for reliable protection where the risk is high.

At present, the evidence for adoption of a specific synthetic graft material is lacking.[103] Hospital resources and policy, cost, and technical experience tend to dictate which material

will be used, and clinical history seems to predict outcome more so than choice of material. In our experience, the availability and long-term success rate of titanium (i.e., surgical grade 5 titanium, Ti-6Al-4V), specifically with regard to its resistance to infection, has contributed to its dominance in recent decades. However, in a review of the literature Yadia *et al.* report the infection rate following cranioplasty averages 7.9% and that the difference in infection of autologous versus alloplastic grafts is not statistically significant.[104]

VI Future Directions in Cranioplasty

Since Sanan and Haines'[1] review of the historical and current approaches to cranioplasty, a revolution has occurred in fabrication technologies (*e.g.*, CAD software and 3-D printing) and regenerative medicine (*e.g.*, tissue engineering). Now the two fields are coming together. Regenerative medicine can solve the problems of good integration of implants and protection of the underlying brain from infection. Patient-specific fabrication of non-resorbable materials that serve specific local needs should be able to replicate, if not improve upon, the distribution of traumatic mechanical forces that might threaten the brain following cranioplasty.

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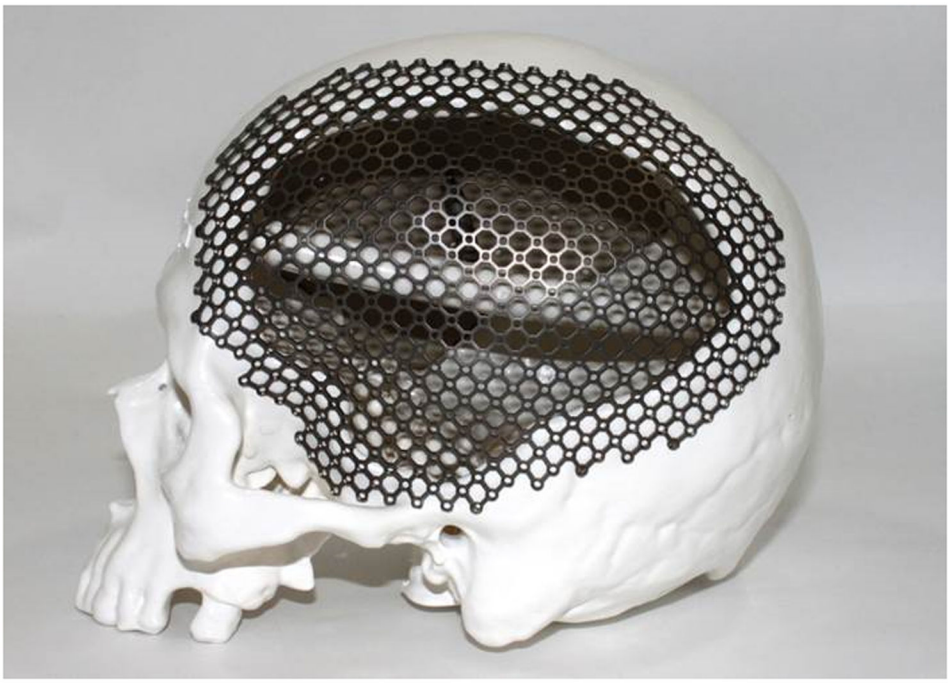


Figure 1.
Titanium mesh cranial implant (courtesy: Medtronic, Minneapolis, MN).

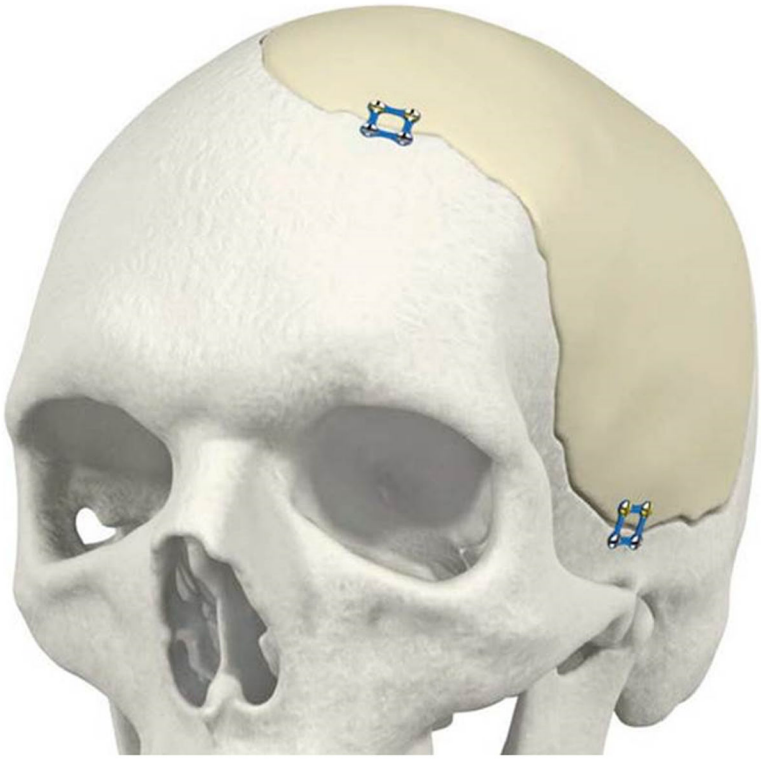


Figure 2.
PMMA implant (courtesy: Stryker, Kalamazoo, MI).

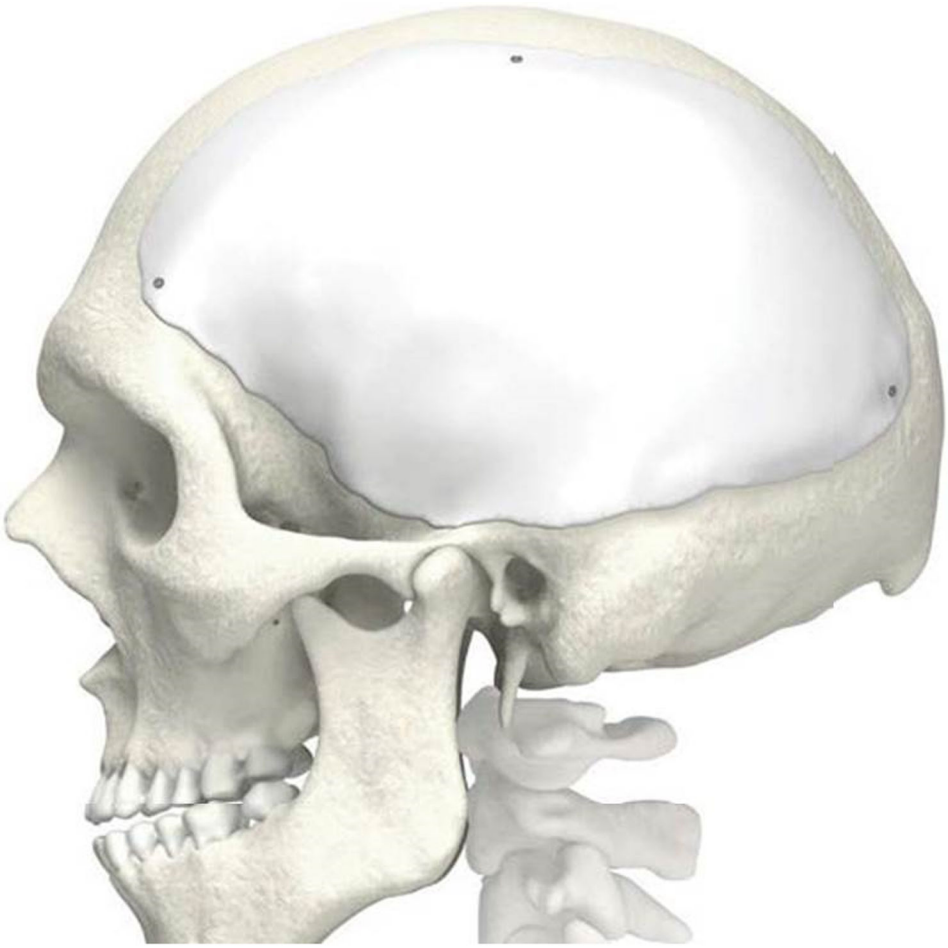
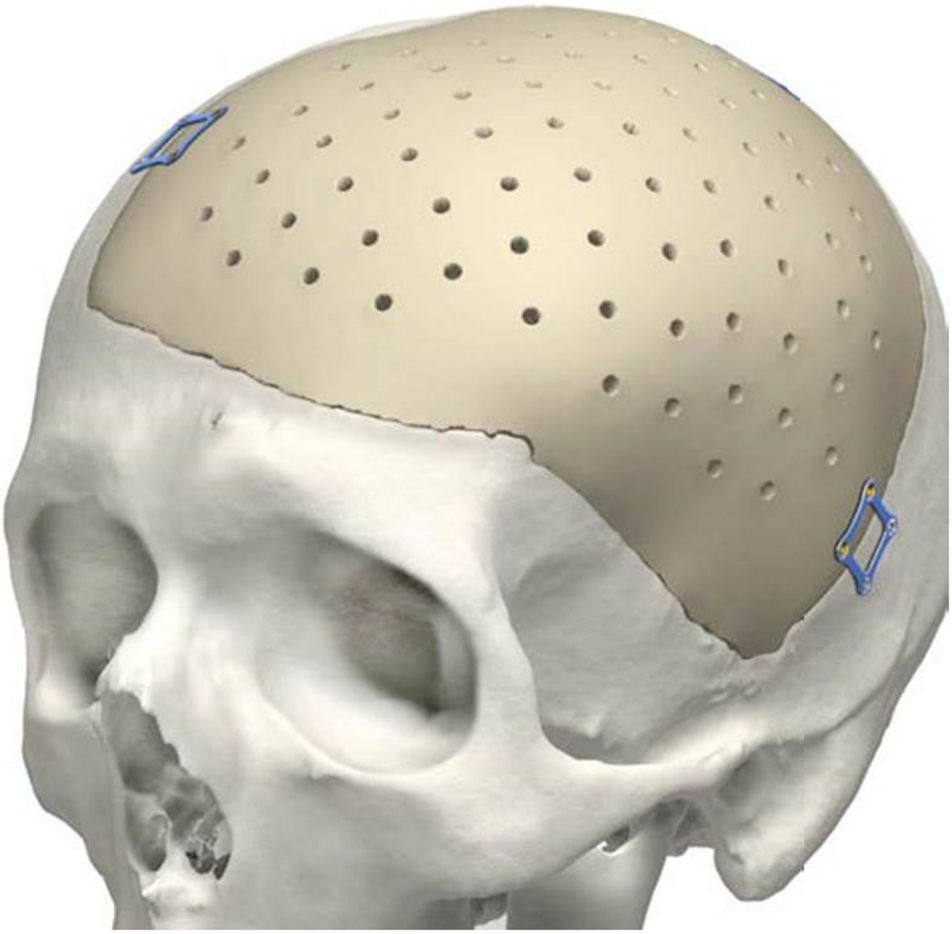


Figure 3.
MEDPOR® implant (courtesy: Stryker).



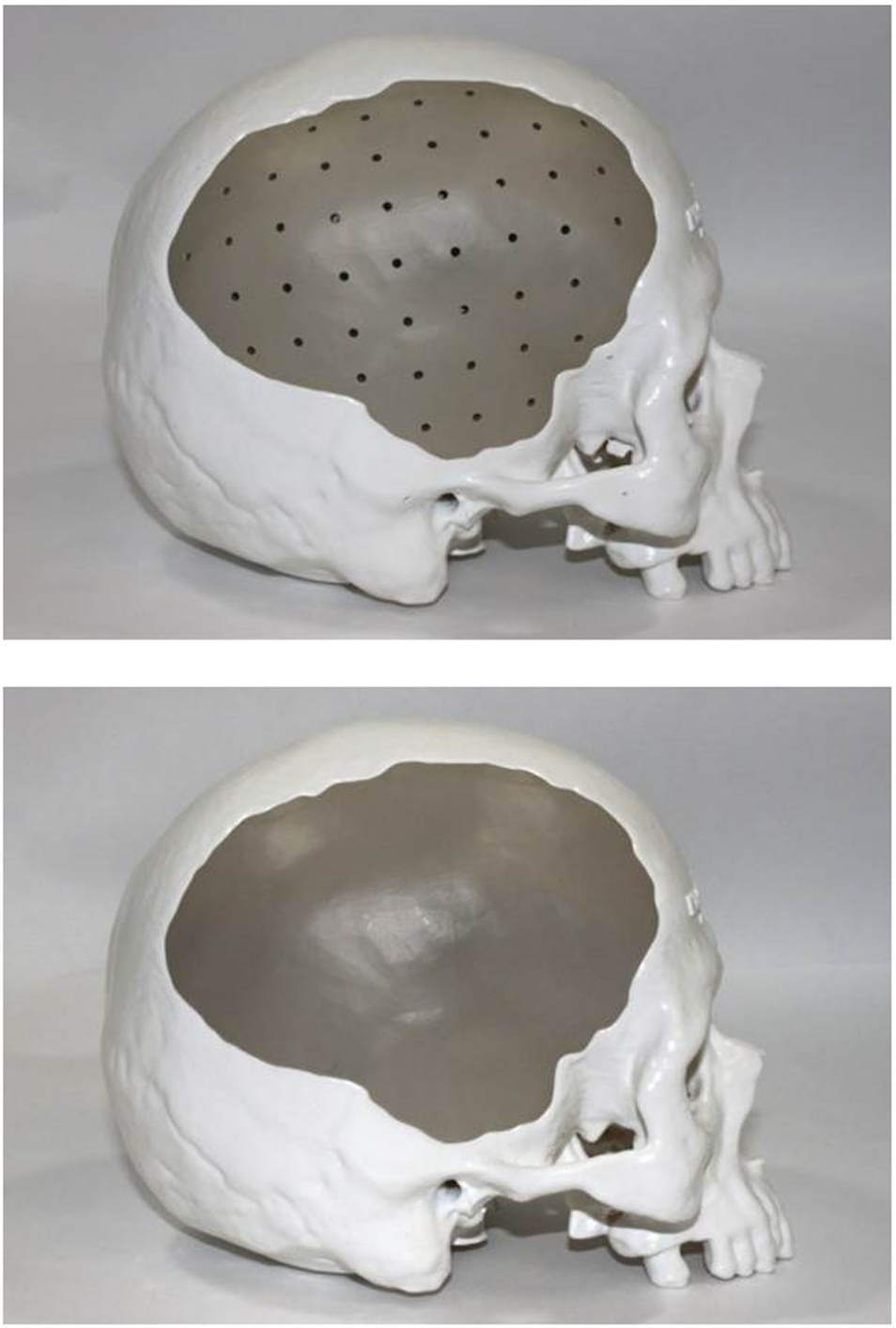


Figure 4.
PEEK implant (courtesy: A: Stryker; B: KLS Martin, (City, St of HQ); C: KLS Martin).

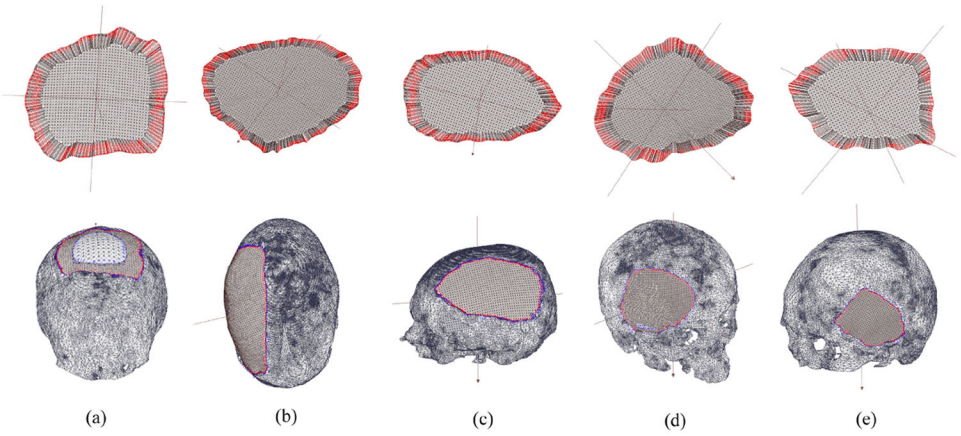


Figure 5.

Cranial template used to design five (a-e) patient-specific implants, all with tapered edge fit. Red surface on taper is in contact with surrounding skull (Figure 4 from: Kyoung-june Min and David Dean. Highly Accurate CAD Tools for Cranial Implants. In (R.E. Ellis and T.M. Peters, Eds.): MICCAI 2003, LNCS 2878, pp. 99-107, 2003. © Springer-Verlag Berlin Heidelberg 2003).

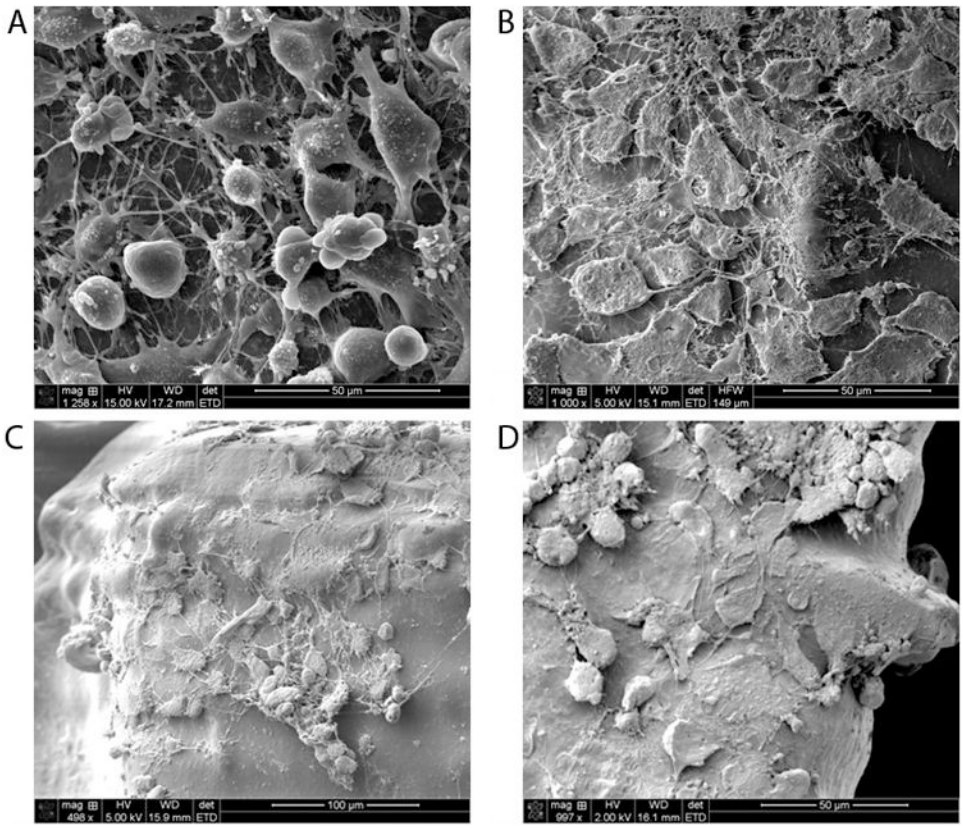


Figure 6.

3-D printed Poly(propylene fumarate) (resorbable polymer) scaffolds seeded with human mesenchymal stem cells at (A) 6 hours, (B) 18 hours, (C) 30 hours, and (D) 48 hours. (Figure 8 from: Wallace, Jonathan, Martha O. Wang, Paul Thompson, Mallory Busso, Vaijayantee Belle, Nicole Mammoser, Kyobum Kim, John P. Fisher, Ali Siblani, Yueshuo Xu, Jean F Welter, Donald P. Lennon, Jiayang Sun, Arnold I Caplan, and David Dean. "Validating continuous digital light processing (cDLP) additive manufacturing accuracy and tissue engineering utility of a dye-initiator package." Biofabrication 6, no. 1 (2014): 015003).

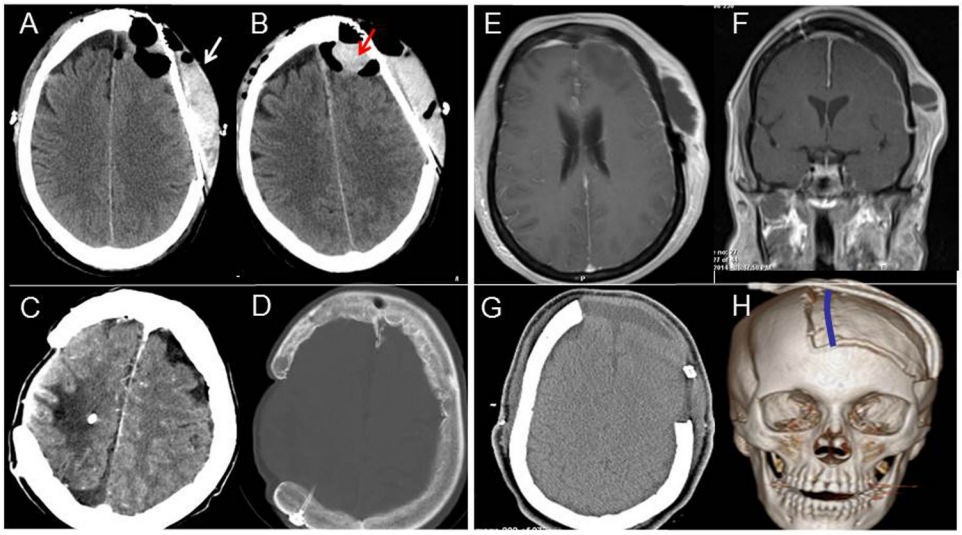


Figure 7.

(A) Mesh cranioplasty after removal of large infiltrative space-occupying intracranial lesions may lead to accumulation of subgaleal/epidural hematoma through the pores of the mesh graft (white arrow) – one disadvantage of using mesh-cranioplasty in such cases. (B) Trauma to the cranioplasty graft in such conditions can precipitate subdural hemorrhage (red arrow) as well as impact brain injury leading to parenchymal bleeds. (C, D) In patients with abnormally thick skulls or hyperostosis, a synthetic graft that matches the skull thickness can produce catastrophic intracranial injury upon subsequent direct impact over the graft. In such cases, a thicker plate with embedded re-engineered bone would be superior. (E, F) Post-operative cranial osteomyelitis involving a craniotomy flap across the superior sagittal sinus. (G) CT head non-contrast axial section following cranioplasty removal and wound wash-out. (H) 3-D reconstruction of cranial defect crossing superior sagittal sinus (indicated in blue) showing the extent of proposed customized delayed non-mesh cranioplasty.

Table 1

Three basic additive manufacturing technologies for binding materials together during a 3-D printing process and the materials which can be used. There are not many implantable materials that can be 3-D printed at this time. However, at a minimum, these technologies can be used to 3-D print a model of a shape designed on a computer. That part can then be the positive for a mold that is then used to cast an implantable material.

Modalities	Light-Based	Liquid or Heat-Based	Mesh/Coat
Stereolithography	Polymer, Ceramic		
DLP Projection (cDLP)	Polymer, Ceramic		
Inkjet/Cell	polymer, cells		
3D Printing		Polymer	
Extrusion		Polymer	
Laser Sintering & Selective Laser Melting, Electron Beam Deposition, Electron Beam Melting		Polymer, Metal	
Electrospinning			Polymer