The feasibility of producing patient-specific acrylic cranioplasty implants with a low-cost 3D printer

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OBJECTIVE Commercially available, preformed patient-specific cranioplasty implants are anatomically accurate but costly. Acrylic bone cement is a commonly used alternative. However, the manual shaping of the bone cement is difficult and may not lead to a satisfactory implant in some cases. The object of this study was to determine the feasibility of fabricating molds using a commercial low-cost 3D printer for the purpose of producing patient-specific acrylic cranioplasty implants.

METHODS Using data from a high-resolution brain CT scan of a patient with a calvarial defect posthemispherectomy, a skull phantom and a mold were generated with computer software and fabricated with the 3D printer using the fused deposition modeling method. The mold was used as a template to shape the acrylic implant, which was formed via a polymerization reaction. The resulting implant was fitted to the skull phantom and the cranial index of symmetry was determined.

RESULTS The skull phantom and mold were successfully fabricated with the 3D printer. The application of acrylic bone cement to the mold was simple and straightforward. The resulting implant did not require further adjustment or drilling prior to being fitted to the skull phantom. The cranial index of symmetry was 96.2% (the cranial index of symmetry is 100% for a perfectly symmetrical skull).

CONCLUSIONS This study showed that it is feasible to produce patient-specific acrylic cranioplasty implants with a low-cost 3D printer. Further studies are required to determine applicability in the clinical setting. This promising technique has the potential to bring personalized medicine to more patients around the world.

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KEY WORDS 3D printing; acrylic bone cement; additive manufacturing; cranioplasty; mold

THE reconstruction of a skull vault defect, termed cranioplasty, has a rich and fascinating history. For at least 5 millennia, surgeons have patched cranial defects with an immensely diverse range of materials ranging from fruit shells to sheep scapulae and man-made plastics.⁴² Even today, the pursuit of the perfect cranioplasty material and technique continues.

Skull defects are often the direct result of surgical decompressive craniectomy performed for acute neurosurgical emergencies.²³ The use of a patient's original bone flap for cranioplasty is theoretically sound and avoids the problems related to the use of bone from other sources, such

as human cadavers (allografts) or animals (xenografts), or the use of synthetic materials. In practice, however, cranioplasty using these bone flaps, which have been stored for a period of time either in a surgically created subcutaneous pocket or in a medical freezer, is plagued with a not insignificant risk of infections and bony resorption.^{8,11,22} With unnatural storage, the nature and content of these bone flaps are changed permanently, hindering successful reincorporation as part of the skull vault. Loss of osteogenesis probably plays a role; studies on human calvarial bone flaps have shown a diminution of osteoblasts after both subcutaneous⁴⁴ and low-temperature⁷ storage. Using

ABBREVIATION PEEK = polyetheretherketone.

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autografts from other parts of the body, such as the contralateral skull vault or the ribs, is feasible but incurs the cost of additional donor site morbidity.^{37,51}

Many synthetic materials have been used successfully in cranioplasty.^{20,42,43} Today, commonly used synthetic materials include acrylic, hydroxyapatite, titanium, ceramics, and polyetheretherketone (PEEK).⁴³ Although all of these materials may be used to produce prefabricated patient-specific implants, acrylic and hydroxyapatite are available in cement form that can be shaped intraoperatively. Commercially available prefabricated implants are designed to approximate the patient's calvarial shape but can be costly. The use of acrylic bone cement, also known as polymethylmethacrylate, is appealing due to a number of desirable properties, which include biocompatibility, malleability, strength, and a long history of use as an implant.⁴² It is also widely available due to its role in many orthopedic operations.³⁵ The mixing of the liquid and powder components of acrylic bone cement initiates an exothermic polymerization reaction, culminating in a soft and malleable putty which hardens in less than 20 minutes from the time of mixing. Similar to a craftsman, the surgeon must manually sculpt the putty into the approximate size, shape, and fit of the missing bone flap within the time window imposed by the polymerization process. This requires considerable skill and is a major obstacle to the optimal application of acrylic bone cement in cranioplasty. Despite the development of special techniques to aid manual shaping,^{29,46,53} the ability to consistently achieve a satisfactory result remains a challenge. This is particularly so when dealing with large defects.

By using molds that are cast based on the original bone flaps,^{3,10,57} the surgeon is able to easily create an implant in the likeness of the original bone flap. Obviously, this is not possible in cases where the bone flap has been discarded, destroyed, or is simply missing. Three-dimensional printing technology, also known as additive manufacturing, allows the rapid production of customized objects⁶ and has immense potential in the medical field, particularly for surgical planning and implant production.⁴⁰ With computer 3D modeling software and the patient's neuroimaging data, a mold can be designed, fabricated with this technology, and used to shape acrylic bone cement into an implant with good results.^{27,36} Although promising, this method has not been widely adopted, at least in part due to limited access to expensive commercial and industrial 3D printers. The proliferation of low-cost desktop 3D printers has the potential to change this. We conducted a preclinical study on the feasibility of producing patient-specific cranioplasty implants with a low-cost desktop 3D printer and acrylic bone cement.

Methods

High-resolution CT data from a patient who previously underwent a unilateral frontotemporoparietal decompressive craniectomy was obtained via a volumetric spiral CT scan of the head performed with a 320-slice commercial CT scanner (Aquilion ONE 320; Toshiba America Medical Systems, Inc.). The data, in DICOM format, was transferred to a computer workstation for manipulation.

With computer software (3D Slicer 4.3.1; Surgical Planning Laboratory), image segmentation was performed using the threshold method, taking advantage of the large difference in CT density between the bony skull and the soft tissue (Fig. 1A and B). Segmentation enabled the generation of 3D models of a skull (Fig. 1C) and a mold (Fig. 1E). For the skull model, a digital 3D model of the entire skull was generated based on the segmentation and exported in the stereolithography file format.

For the mold, a more complicated process was required. First, 2 digital 3D models were generated. The first model (the "normal" model) was generated based on the segmentation as performed above. The second model (the "dilated" model) was generated after dilating the segmentation by 1 mm. When the acrylic implant is subsequently produced, this dilation translates into a 1-mm gap between the implant and the patient's skull defect, avoiding an excessively tight fit. These 2 models were then exported in the stereolithography file format.

Next, using 3D modeling software (MeshMixer 2.4; Autodesk, Inc.), a mirror image of the normal model was created, resized, and overlapped onto the dilated model. The skull defect on the dilated model was then matched to the corresponding intact skull on the mirror image model; thus, when the acrylic implant is subsequently formed, it derives its contour from the patient's own intact contralateral skull. The mold design deliberately excluded parts of the squamous temporal bone, which, in a patient undergoing cranioplasty, would be covered by the temporalis muscle and not contribute to the shape of the head. Finally, portions of the skull not immediately adjacent to the craniectomy defect were removed to reduce the overall size of the mold.

The 3D models of both the skull and the mold were "sliced" with computer software (MakerWare 2.4.1.35; MakerBot Industries) with the following settings: infill, 20%; shells, 2; layer height, 0.1 mm; extrusion temperature, 230°C; speed while extruding, 90 mm/second; speed while traveling, 150 mm/second; and the addition of both raft and supports. The aptly named slicing process digitally cuts a 3D model into a contiguous series of thin slices, and then converts these slices into movement instructions for the extruder of the 3D printer. These instructions were exported to a file in x3g format and sent to the desktop 3D printer (MakerBot Replicator 2; MakerBot Industries), which fabricated the skull (Fig. 1D) and the mold (Fig. 1F) models in polylactic acid using the fused deposition modeling method.

This 3D printing technique²⁴ works by first heating a thermoplastic beyond its melting point, thereby liquefying it. The liquefied material is then pushed through an extruder mounted on a movable gantry. The extruder moves according to the instructions generated by the slicing process. The extruded material rapidly cools, bonding to either the build platform (for the first layer) or the previous layer (for subsequent layers). By laying down layer after layer in a precise manner based on the shape and dimensions of the digital 3D model, the digital model is thus converted into a physical object.

The powder and liquid components of acrylic bone cement (Surgical Simplex P Radioopaque bone cement;

FIG. 1. Images demonstrating the threshold method of segmentation, showing the before (A) and after (B) results. The fused deposition modeling method accurately transforms computer-generated 3D models (skull [C] and mold [E]) into physical models (skull [D] and mold [F]). The support structures in the 3D printed skull phantom (D) allow the fabrication of the overhanging portions. A, B, C, and E are computer screen captures; D and F are photographs.

Stryker Corporation) were mixed in a plastic bowl to initiate the polymerization reaction. The mixture was stirred with a plastic spatula until it no longer adhered to the surgeon's glove. At that point, it was ready to be shaped. The bone cement putty was first stretched out like a disk to a uniform thickness and applied to the 3D printed mold, ensuring that the edges of the bone cement abutted the corresponding edges on the mold (Fig. 2A). The bone cement was allowed to harden and then was removed from the mold. With this method, the mold design and bone cement application process act in synergy to ensure that the outer contour of the newly formed acrylic cranioplasty implant approximates the contour of the missing bone flap. This is achieved in the following way. The middle portion of the mold that shapes the bone cement is based on the contour of the intact contralateral skull. By applying bone cement of uniform thickness to the mold, the contour of the mold is translated into the contour of the external surface of the formed implant. In its clinical application, the implant is anchored to the skull by plating its external surface to the skull surface, thus negating the effect of any difference in thickness between the implant and the patient's skull.

FIG. 2. Photographs showing application of bone cement to the mold for generation of the implant (A). The implant had a good fit to the skull phantom and approximated the contour of the contralateral skull, as demonstrated by views from the front (B), side (C), and top (D). Note that on the side view, the implant does not extend into the inferior temporal portion of the skull.

The 3D printed skull was used as a phantom onto which the newly generated acrylic implant was fitted (Fig. 2B–D). A digital photograph was taken of the skull phantom fitted with the implant to determine the cranial index of symmetry⁵⁸ using image analysis software (ImageJ 1.48v; National Institutes of Health). To determine the cranial index of symmetry, we first measured the total area of the skull. Next, the midline was identified and the skull divided into 2 halves. One half was reversed right to left and overlapped onto the other half. The area of overlap between the 2 halves was calculated and doubled (to account for the 2 halves of the skull). The cranial index of symmetry is the proportion (expressed as a percentage) of the overlapping skull area to the total skull area. For a perfectly symmetrical skull with complete overlap between its 2 halves, the cranial index of symmetry is 100%. Although originally conceived as an assessment for the severity of plagiocephaly in children,⁵⁸ this simple but intuitive method has been applied to evaluate the symmetry of cranial reconstructions in adult patients with skull defects.²⁸

Results

Both the skull phantom and the mold were designed and fabricated successfully. The generation and design of the digital models were completed in 60 minutes. The 3D models of the skull and the mold were fabricated in approximately 6 hours and 40 minutes and 33 hours and 20 minutes, respectively. The layer height setting was 0.1 mm. Printing with thicker layer heights, such as 0.2 or 0.3

mm, is possible and results in a shorter printing time but a coarser model.

To form the acrylic cranioplasty implant, 2 units of the bone cement were used; the first attempt using 1 unit resulted in a thin and uneven implant. Application of the bone cement in its putty form to the 3D printed mold was simple and straightforward. Fitting the implant to the 3D printed skull phantom did not require any further drilling or modification. The calculated cranial index of symmetry was 96.2%.

Discussion

Personalized medicine is poised to revolutionize the modern practice of medicine. In the treatment of cancer, the recognition of the differences in carcinogenesis among individuals has led, in some instances, to targeted molecular therapies with remarkable efficacy.⁴ Similarly, the refinement of imaging technology, coupled with the capability to produce patient-specific implants, has given rise to a proliferation of alternatives to traditional off-the-shelf implants. Progress in cranioplasty has not lagged. In the past 20 years or so, much has been achieved through research on the techniques to produce customized cranioplasty implants.^{13,14,19,21,27,34,36,48,49,54,56} Nevertheless, these impressive techniques have generally remained in the respective laboratories and universities in which they were developed. This is because they require technical expertise as well as expensive, sophisticated software and machinery that are beyond the means of most surgeons and hospitals. As a result, the majority of patients requiring cranioplasty have not benefitted from the advances in the field. There are commercial companies that provide these services outside of academia; the problem is that they typically do so for a hefty fee.

In this study, we show that it is feasible to produce a patient-specific cranioplasty implant by using a low-cost desktop 3D printer coupled with cheap and widely available acrylic bone cement. All of the software that we used is free and downloadable via the internet. The authors, despite being surgeons with no specialized training in either computer 3D modeling or engineering, were able to design and fabricate the mold, and then use the mold to produce a customized cranioplasty implant. The implant had a good fit to the skull phantom and resulted in a cranial index of symmetry of 96.2%. To put this into perspective, in the original study on plagiocephaly, the mean cranial index of symmetry of normal children was 96.3%, whereas that of children with plagiocephaly was 81.9%.⁵⁸ In a study with adult patients, which calculated the cranial index of symmetry of skull defects that were reconstructed digitally, researchers reported an astounding mean score of 99.2%; however, this result must be viewed in light of the fact that they examined only digital models, which tend to be closer to perfect and more idealized.

The process of mold and implant fabrication should be as simple as possible while being applicable in a wide variety of cases. Mold fabrication techniques that require an intact bone flap^{3,10,57} cannot be used when the original bone flap is not available. The method of mold production by direct casting of the defect on the patient's head^{2,25,50}

is inaccurate due to the presence of soft tissue and the absence of the normal calvarial curvature. These factors explain our choice to design the mold based on the patient's intact contralateral skull by the use of computer 3D modeling techniques based on high-resolution CT scan data. Most published techniques for producing molds using computer 3D modeling and 3D printing^{12,17,31} require fabrication via 3D printing of both the skull defect and a preliminary implant. This is followed by alteration of the implant by hand to fit the defect and then casting of the implant to create a mold.

We have condensed these steps by directly designing the mold digitally for fabrication using 3D printing. Our technique is similar to that used by Kim and colleagues,²⁷ albeit with one difference. To create their implant, Kim et al. compressed bone cement between the 2 parts of their mold, whereas we applied bone cement to the surface of our 1-part mold. We feel that our mold design is simpler and yet able to create a sufficiently accurate implant. Finally, in contrast to mold techniques that produce the acrylic implant preoperatively,^{2,12,25,31,50} we prefer to sterilize the mold for the intraoperative fabrication of the acrylic cranioplasty implant. Intraoperative implant fabrication not only deviates less from the recommended usage of the bone cement but also allows for the immediate reproduction of another implant should the need arise.

To translate our results to the clinical setting and produce implants for use in patients, more research is needed. Here, 2 considerations are paramount: the accuracy of the 3D printing process and the material used to fabricate the mold. To our knowledge, there are no published peer-reviewed studies on the accuracy of the particular 3D printer used in this study. Our own tests, in which geometrical objects (e.g., cubes) of known dimensions are 3D printed, consistently show that measured dimensions of the 3D printed objects do not deviate from the original digital dimensions by more than 0.5 mm (unpublished data). From the literature, a generalization may be inferred by analyzing published studies that examined the accuracy of 3D printers using the same method of 3D printing, i.e., the fused deposition modeling method. In one such study,¹⁵ researchers measured bone thickness at different sites as well as distances between anatomical landmarks on 3D printed skulls and mandibles. Comparisons were made between the measurements on the 3D printed models and those on their corresponding digital models. For skulls, they found a mean difference (error) of just 0.1 mm. In another study,⁴⁵ researchers imaged cadaver shoulder and hip joints with CT scans. With the resulting imaging data, 3D models were computer generated and then fabricated using fused deposition modeling. Next, by laser scanning of both the original cadaveric joints and the 3D printed models, they generated pairs of digital 3D models for comparison. Here, they also found a low overall error of 0.3 mm. Although these 2 studies used different methodologies and studied different parts of the human body, they arrived at remarkably similar results (0.1 mm in one study and 0.3 mm in the other). Taken together, this submillimeter accuracy attests to the high degree of precision achievable by the fused deposition modeling method of 3D printing.

In our study, we used polylactic acid to fabricate both the skull phantom and the mold. Polylactic acid is a biodegrad-

able and biocompatible thermoplastic with widespread applications in both medical and nonmedical fields.^{26,30} It has been used for implantation in the human body for functions ranging from soft tissue fillers^{5,52} to fracture fixing screws.¹ With a glass transition temperature of 55°C,¹⁶ it is unsuitable for the autoclave. Hydrogen peroxide plasma and ethylene oxide both sterilize at compatible temperatures and have been used to sterilize objects constructed with polylactic acid without causing any significant changes to their biomechanical properties.³⁹ With material biocompatibility as well as sterilization addressed, one unresolved issue remains, which is the potential effect that the temperature elevation during bone cement polymerization may have on a polylactic acid mold. In one laboratory experiment,¹⁸ the surface temperature of the bone cement reached an average of 63.5°C during polymerization. Whether this could adversely affect the mold remains uncertain. While conducting our study, we did not detect any appreciable physical changes in the mold after application of the bone cement. Nonetheless, further study is required on the effects that the bone cement polymerization process may have on 3D printing materials.

The 3D printer used in this study costs approximately US \$2000, which is far less than the costs of commercial and industrial 3D printers. The economic consideration of any health care intervention is important. Today, health care is consuming an ever-increasing share of the total output generated by human endeavors; in 2011 alone, the world spent a staggering US \$6.9 trillion on health care.⁵⁵ The enormous health care expenditure has been ascribed to, among other reasons, the high and rising costs of technological advancements in the diagnosis and treatment of diseases.⁹

One such advancement is the advent of prefabricated patient-specific implants in the field of cranioplasty. Prefabricated implants, such as those made of hydroxyapatite, PEEK, and titanium, are commercially available and have been used with good results.^{33,38,41,47} As we alluded to, commercial products are expensive, having been developed and marketed with the primary intention of generating profits. This is supported by the published literature. In an American study,³⁸ the average cost of PEEK implants was approximately US \$10,450, while in a Dutch study³³ on 10 titanium implants and 7 PEEK implants, the average cost was US \$11,200 (€10,000; €1 = US \$1.12). The average cost of hydroxyapatite implants was US \$7840 (€7000) in an Italian study⁴⁷ and US \$8960 (€8000) in a French study.³²

In contrast, an acrylic implant made using our technique costs, in terms of manpower (a neurosurgical resident's wages for 1 day = SG [Singapore] \$400) and consumables (cost of 3D printing material = SG \$10; cost of 2 units of bone cement = SG \$150; cost of 1 cycle of hydrogen peroxide plasma sterilization = SG \$30), approximately US \$430 (SG \$590; SG \$1 = US \$0.73), an order of magnitude less than the cost of commercial prefabricated implants.

That these commercial implants can contribute as much as 64% to the total cost of cranioplasty (including the costs of the implant, anesthesiology, surgery, and the entire hospital stay), according to one study,³³ is astounding. The high cost renders them plainly unaffordable to many patients. Our local experience is no different; despite living

in a relatively affluent country, Singaporean patients not uncommonly decide against the PEEK implant due to financial constraints and opt instead for the cheaper option of surgeon-shaped acrylic implant. Thus, it is imperative that we develop alternatives that benefit not only the rich and the fortunate.

Conclusions

In this study, we showed that it is feasible to produce patient-specific acrylic cranioplasty implants with a low-cost desktop 3D printer. Further studies are planned to bring this technique from the proverbial bench to the patient's bedside. One can only hope that our work, together with that of others, may finally allow personalized medicine to reach its full potential and bring about the next revolution in health care.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Supplemental Information

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Author Contributions

Conception and design: all authors. Acquisition of data: Tan, Ling. Analysis and interpretation of data: all authors. Drafting the article: Tan. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Tan. Administrative/technical/material support: Tan. Study supervision: Dinesh.

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