On-Demand Intraoperative 3-Dimensional Printing of Custom Cranioplastic Prostheses

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Portions of this work were presented at the proceedings of the 84th Annual Scientific Meeting of the American Association of Neurological Surgeons in Chicago, Illinois, in May 2016, at the 13th Annual American Medical Association Research Symposium in Atlanta, Georgia, in November 2015, and at the 2015 Annual Meeting of the Congress of Neurological Surgeons in New Orleans, Louisiana in September 2015.

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Received, July 7, 2017.

Accepted, December 5, 2017.

Published Online, January 13, 2018.

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BACKGROUND: Currently, implantation of patient-specific cranial prostheses requires reoperation after a period for design and formulation by a third-party manufacturer. Recently, 3-dimensional (3D) printing via fused deposition modeling has demonstrated increased ease of use, rapid production time, and significantly reduced costs, enabling expanded potential for surgical application. Three-dimensional printing may allow neurosurgeons to remove bone, perform a rapid intraoperative scan of the opening, and 3D print custom cranioplastic prostheses during the remainder of the procedure.

OBJECTIVE: To evaluate the feasibility of using a commercially available 3D printer to develop and produce on-demand intraoperative patient-specific cranioplastic prostheses in real time and assess the associated costs, fabrication time, and technical difficulty.

METHODS: Five different craniectomies were each fashioned on 3 cadaveric specimens (6 sides) to sample regions with varying topography, size, thickness, curvature, and complexity. Computed tomography-based cranioplastic implants were designed, formulated, and implanted. Accuracy of development and fabrication, as well as implantation ability and fit, integration with existing fixation devices, and incorporation of integrated seamless fixation plates were qualitatively evaluated.

RESULTS: All cranioprostheses were successfully designed and printed. Average time for design, from importation of scan data to initiation of printing, was 14.6 min and average print time for all cranioprostheses was 108.6 min.

CONCLUSION: On-demand 3D printing of cranial prostheses is a simple, feasible, inexpensive, and rapid solution that may help improve cosmetic outcomes; significantly reduce production time and cost—expanding availability; eliminate the need for reoperation in select cases, reducing morbidity; and has the potential to decrease perioperative complications including infection and resorption.

KEY WORDS: 3D printing, Rapid prototyping, Cranioplasty, Prosthesis, Implant, Patient specific, Reconstruction

Operative Neurosurgery 15:341–349, 2018

DOI: 10.1093/ons/oxp280

Cranioplasty has long been performed using a variety of materials and techniques for the purpose of restoring cosmetic appearance and protecting underlying brain tissue.¹ Traditional aesthetic reconstruction techniques have focused on the use of autologous bone due to low rates of

infection, immunotolerance, and low cost of preservation.^{2–4} However, there is potential for postoperative complications surrounding the donor site, as well as the risk of infection and bone resorption.^{5–7} In addition, autologous grafts are inadequate for repairing large or intricate cranial defects.^{7,8} On the other hand, xenografts, and especially synthetic xenografts, have proven to be effective in a clinical setting.⁹ Novel cranioplastic approaches have been explored using synthetic alloplastic material in order to create customized craniofacial implants that have been shown to provide a more precise fit within the cranial defect, decrease operative time, and decrease perioperative complications including infection and resorption.^{9–11}

ABBREVIATIONS: 3D, 3-dimensional; CT, computed tomography; FDA, Food and Drug Administration; FDM, fused deposition modeling; PMMA, polymethyl methacrylate; STL, standard triangle language.

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Currently, the manufacturing of patient-specific cranial implants is typically outsourced to third party manufacturers, who create the implant after receiving computed tomography (CT) scan data. This procedure can take approximately 18 business days to complete and can cost an average of \$12 500 USD.¹²⁻¹⁵ Recently, the process of fused deposition modeling (FDM), an additive manufacturing process in which layers of material are built upon each other by a 3-dimensional (3D) printer controlled by a computer-aided manufacturing software program, has demonstrated increased ease of use, fast production time, and significantly reduced costs compared to existing development and manufacturing modalities.¹⁶⁻¹⁸

The increasing availability and affordability of high-resolution 3D printers has significantly expanded their potential for surgical application.^{9,19,20} As such, we evaluate the feasibility of using a commercially available 3D printer to develop and produce on-demand intraoperative patient-specific FDM printed cranioplastic prostheses in real time and assess the associated costs, fabrication time, and technical difficulty.

METHODS

The feasibility of designing, producing, and implanting on-demand intraoperative 3D printed cranioplastic prostheses was evaluated using a cadaveric model. Retrosigmoid, supraorbital, occipital, interhemispheric, and orbitozygomatic craniectomies were fashioned on 3 adult cadaveric specimens (6 sides) using a high-speed surgical drill (Anspach eMAX 2 Plus, The Anspach Effort Inc, Palm Beach Gardens, Florida) in order to sample and assess a number of different regions with varying topography, size, thickness, curvature, and complexity.²¹⁻²⁴ CT-based cranioplastic implants were designed, formulated, and implanted into the cadaveric specimens. The accuracy of development and fabrication, as well as implantation ability and fit, integration with existing fixation devices, and incorporation of integrated seamless fixation plates were qualitatively evaluated. Additionally, time required for fabrication was analyzed and compared with existing methodologies.

Computed Tomography

Following craniotomy placement, all specimens underwent half-millimeter spiral CT (Biograph TruePoint PET•CT, Siemens AG, Munich, Germany). The obtained data, in Digital Imaging and Communications in Medicine file format, was then transferred to Materialise Mimics[®] software (Materialise NV, Leuven, Belgium) for conversion to standard triangle language (STL) file format.

Prosthesis Design

Based on manufacturer guidelines, the STL files were imported into Materialise 3-matic[®] (Materialise NV) software and the prostheses models for each craniotomy opening were created using a superimposition technique, wherein a model was created to fill a defined area around the surgical opening and the curvature of its surface was matched to that of the surface of the intact contralateral bone.²⁵ This process was chosen in order to simulate an on-demand process that could include patients with existing deformities or traumatic injury and who do not have preoperative CTs that would allow for the modeling of normal bone.

To perform design using the 3-matic[®] software, a free forming curve was created and superimposed onto the bone surrounding the defect. The area within the curve was then exported onto a 2D plane, and the contralateral surface was mirrored and superimposed in order to create the correct curvature for the prosthesis. The software's prosthesis function was then used to create a 3D master implant to exact thickness specifications that adequately filled the skull defect. Following creation of the digital design, the model was refined using variable thickness and Boolean subtraction to achieve continuity with the surrounding bone. Any obstructing material on the undersurface was removed and the edges were smoothed and chamfered (Figure 1).

Additionally, 3 interhemispheric and retrosigmoid prostheses were each designed with integrated fixation strips to assess the feasibility of providing seamless fixation (Figure 1). To accomplish this, adherence points were designed on a 2D plane, projected onto the prostheses, and fused using a unionizing function. These adherence, or fixation, plates were then given a thickness of 1.0 mm with 0.5 mm rounded edges. Prefabricated holes were designed into the plates to allow for titanium screw placement. Additionally, these integrated fixation plates were projected onto the surface of the skull so that they would contour and become flush with the natural curvature of the bone.

Design of Polymethyl Methacrylate Injection Molds

3D printed injection molds were also developed and assessed as an alternative method for fabricating cranioprostheses via the injection of polymethyl methacrylate (PMMA) into the printed mold.⁸ Box molds were constructed using a subtraction method from a previously generated zygomatic cranioprosthesis. Once the box molds were 3D printed, they were injected with PMMA (HydroSet[™], Stryker Corporation, Kalamazoo, Michigan) and allowed to dry for 15 min (Figure 2).

3D Printing of Cranial Prostheses

All cranioprostheses and box molds were created using a FDM 3D printer (Fortus 250mc, Stratasys Ltd, Eden Prairie, Minnesota) with a production grade acrylonitrile butadiene-styrene thermoplastic (ABSplus[™], Stratasys; not approved for clinical use) material, in place of the comparable and biocompatible polyetherketoneketone, calcium phosphate, or PMMA—used in many Food and Drug Administration (FDA) approved custom implants.^{8,13-15,26-29}

Prosthetic Cranial Flap Placement, Fixation, and Assessment

Each printed prosthesis was implanted into its corresponding cranial opening using the standard surgical technique. The fit of the 3D printed prostheses within the opening was assessed using a surgical microscope (Zeiss OPMI Neuro/NC 4 System, Carl Zeiss Meditec AG, Jena, Germany) for approximation of the defect, including any minute defects, and titanium plates and screws (Universal Neuro III, Stryker) were assessed for fixation to the skull. Cranioprostheses printed with integrated fixation plates were fixed to the skull with titanium screws and pressure was applied to assess fixation strength.

RESULTS

All cranioprostheses were successfully designed using the superimposition technique and were printed and detached from the

FIGURE 1. A to F, Design of 3D printable prostheses with integrated fixation strips. Computer generated models of 3D prostheses, both with and without integrated fixation strips, are illustrated integrated with the surrounding bone.

support material without difficulty (Figure 3; see **Supplemental Digital Content**, a 3D STL model of an orbitozygomatic prosthesis). Support material could be either dissolved away in an agitated detergent bath or simply broken away without damaging the prosthesis. The average time for design, from importation of CT data to initiation of printing, was 14.6 min.

Prosthetic Cranial Flap Placement and Fixation

All prostheses seamlessly approximated the outer bone table of the skull defect and were flush with the skull when inserted. Each cranioprosthesis was fixed to the skull using 3 to 4 points of fixation. The use of titanium plates and screws allowed for uncomplicated fixation and the screws were advanced into the printed material without difficulty (Figures 4 and 5).

Due to the nature of the ABS^{plus}™ (Stratasys) material used, integrated fixation strips would not reliably stay attached to the implant if fabricated at less than 1 mm in thickness. So, 1 mm thick fixation strips were incorporated into several printed models. These strips achieved sturdy fixation with the surrounding bone, did not break or loosen when pried with significant force, and, as they were designed to conform to the contour of the skull, did not require additional bending or shaping. However, these strips were notably thicker than standard titanium plates, which are 0.5 mm and were not completely flush with the outer surface.

3D Printed PMMA Injection Molds

Detailed injection molds were easily created using the 3-matic® software (Materialise NV) and PMMA was injected into the box mold without difficulty (Figure 2). To facilitate removal of the dried PMMA from the mold, the mold was covered with plastic wrap prior to injection of PMMA.⁸ After removing the dried PMMA, any uneven edges were easily smoothed using the surgical drill. The mold consistently created a prosthesis that provided an exact fit within the skull defect and sat flush with the surrounding bone.

Assessment of Print Time

The average print time for all cranioprostheses was 108.6 min (Table). Print time was also assessed for different resolutions, where high resolution correlated to 0.178 mm layer thickness, medium resolution to 0.254 mm, and low resolution to 0.330 mm. At medium resolution, all cranioprostheses were printed in less than 3 h. The addition of integrated fixation strips increased average print time by 16 min in the retrosigmoid approach and 62 min in the interhemispheric approach.

DISCUSSION

As 3D printing technology continues to advance, new materials including those approved by the FDA for prosthetic devices and reconstruction, including PMMA, are becoming available for use with commercially available printers. Oxford Performance

FIGURE 2. PMMA cranioplasty injection molds. 3D printed box mold of an orbitozygomatic impression and PMMA in powder form. The PMMA, after being processed into cement, was subsequently poured into and encased in the closed box mold in order to generate the prosthesis.

TABLE. 3D Printing Time Versus Resolution

Cranioplasty site	High resolution (0.17 mm)	Medium resolution (0.254 mm)	Lowest resolution (0.33 mm)	Average print time
Retrosigmoid	82	55	41	59
Retrosigmoid with fixation plates	92	58	42	64
Interhemispheric	92	54	96	80
Interhemispheric with fixation plates	195	126	106	142
Occipital	293	169	132	198

Materials (South Windsor, Connecticut) recently developed a proprietary OXPEKK[®] polymer, marketed as OsteoFab[®], that meets FDA and European Union requirements for use in long-term human implantable devices and is currently used in cranioplastic implants produced by their partner Zimmer Biomet (Warsaw, Indiana) using a laser sintering process.^{13,15,28} The newfound commercial availability of implantable materials, inexpensive printers, and user-friendly design software is allowing for the rapid and inexpensive development and fabrication of patient-specific implants.^{8-11,14,15,17,19,20,30,31} In conjunction with rapid print times, these factors have created the possibility for development of intraoperative 3D cranioprostheses which, in select cases, could eliminate the need for reoperation for cranioplasty.

Currently, it takes an average of 18 d to procure a custom craniofacial prosthesis from a third-party supplier necessitating

reoperation for implantation (Figure 6A).¹³ Using the processes described herein, we were able to perform a rapid CT of the skull and design a digital prosthesis model in under 20 min, all with minimal specialized or technical training, and without the need to outsource any tasks. Once the design was exported to the 3D printer, the average print time for each model was 125 min (range: 36-384 min)—a time frame that could theoretically allow for intraoperative fabrication (Figure 6B). As print time is a function of individual printer capability, these times may not be reflective of all 3D printers and print time could be significantly reduced with the use of alternative current or future generation printers, allowing for a wider range of clinical application. All prostheses evaluated seamlessly approximated the bony opening, followed the curvature of the skull, were flush with the skull when inserted and were seamlessly fixed to the skull using conventional titanium plates and screws. Although

FIGURE 3. 3D printed cranial prostheses. The cranial bone flaps removed from cadaveric specimens served as the templates for 3D printed prostheses using CT scan data. Each of the 6 different prostheses is depicted positioned beside their corresponding bone flaps.

unnecessary herein, the printed material could be easily drilled down or sculpted using the surgical drill if needed. Additionally, the evaluated injection molds demonstrated to be a feasible alternative to directly 3D printed prostheses, although required additional steps for fabrication and additional sculpting before fixation (Figure 2).

While the durability of clinically approved materials has been established and meets or exceeds regulatory standards,¹³⁻¹⁵ material strength and durability should be considered during design and computational analyses should be incorporated in order to avoid potential structural weaknesses or extreme stresses during assembly—as recently described in detail by Ridwan-Pramana and colleagues.³²

Integration of fixation strips directly into the design of the prostheses was also evaluated and resulted in an increase in print time of 16 min for the retrosigmoid prostheses and as much as 62 min for the interhemispheric prostheses. This substantial increase in the interhemispheric design was due in part to the additional support material required to stabilize the implant during printing—something that could be controlled for in future designs. However, as titanium plates and screws integrated easily with the printed material, this large increase in print time for the integration of adherence strips may not be justified with currently available technologies.

A major concern when producing clinically viable 3D printed prostheses is the ability to sterilize the implant. The process of 3D printing thermoplastics using FDM extrudes the liquid plastic

from the printing jet at temperatures of 190°C to 240°C, above the recommended temperatures for both steam and dry heat sterilization.^{33,34} A 2014 study by Rankin and colleagues³¹ found that samples collected immediately upon extrusion in an FDM printer were completely sterile and free of all remnant DNA as determined by negative PCR testing. They additionally concluded that if printed onto a sterile surface in a clean environment, such as an operating room, that the device would be ready for surgical application as soon as printing was complete.³¹ Additionally, a previous study by Kondor et al³⁴ showed that 92% of 3D printed surgical instruments were sterile and ready for use immediately after printing. So, while future generation printers could be designed to ease sterilization or incorporate additional sterilization measures, prostheses printed using approved materials could still undergo sterilization using conventional methods, although this may contribute to increased preparation time.¹⁵

Commercially produced patient-specific craniofacial implants can incur significant costs of around \$12 500 USD per unit.¹² In contrast, the methodology proposed herein using FDM would be significantly cheaper even when considering printer and raw material costs.³⁰ Due to the extreme variability in printer and raw material cost and capabilities, it was not possible to perform a true comprehensive cost analysis; however, each of our printed prostheses would cost less than \$1 USD to manufacture using PMMA and if designed by clinical personnel. This could additionally lower associated costs and create a new profit center for hospitals and practices that could provide both clinicians and

patients with a much more cost effective option, and potentially allow for increased availability of patient-specific prostheses including in developing nations.

Limitations

Although this study demonstrates that on-demand intraoperative printing is feasible, it is limited by its use of non-FDA approved materials, the use of a single 3D printing modality, and its cadaveric nature. Currently, clinical application of this process would be limited to institutions that possess intraoperative CT or other comparable scanning capabilities.³⁵ Additional studies are necessary to compare the practicability and relative costs of FDM to other types of 3D printing, including stereolithography, liquid interface production, laser sintering, and multimaterial printers—including those that can directly incorporate titanium plates into the prostheses—and to assess the possibility of incorporating antibiotic and biomaterials, including stem cells, as well as intracranial pressure monitors, drug reservoirs, flexible materials for decompressive craniectomies, and self-fixation capabilities. Clinical studies are also necessary to determine the full applicability and practicality of these processes in a surgical setting.

CONCLUSION

On-demand 3D printing of cranial prostheses is a simple, feasible, inexpensive, and rapid solution with a number of

potential clinical benefits. The technical difficulty of developing these prostheses is minimal and implantation is technically comparable and potentially easier than current fixation techniques. Low fabrication times highlight the advancement of user-friendly rapid prototyping software and underscore the ability for rapid production of patient-specific prostheses. In the future, these concepts could be applied intraoperatively wherein a rapid CT or surface scan of the bone opening is performed and a custom cranioprosthesis is designed and 3D printed bedside during the remainder of the operation. On-demand printing of custom prostheses may help improve cosmetic outcomes; significantly reduce production time and cost—expanding availability of custom prostheses; eliminate the need for reoperation in select cases, reducing morbidity; and has the potential to decrease perioperative complications including infection and resorption.³⁶ Clinical studies are necessary to determine full practicability of this technique as well as to evaluate the potential for incorporation of antibiotic and biomaterials, including osteoblasts, and integration of intracranial pressure monitors and flexible materials for use in decompressive craniotomies, among others possibilities.

Disclosures

This study was made possible by a grant from the Clinical and Translational Science Center at Weill Cornell Medical College, funded through the National Institutes of Health (NIH UL1RR024996). The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENTS

Authors report a cadaveric feasibility study on the use of an intraoperative 3D printing of custom cranioplastic prostheses. The proposed model appears easy to apply and the results realistic. Surely, this could be the future of cranioplasty operation, reducing costs and operative time, avoiding in selected cases the need for reoperation.

New technologies, software with user-friendly interface and certified materials will surely improve the technique leading it to widespread diffusion in most neurosurgical departments. This dissemination could ultimately even more reduce the related costs.

Prospective studies focusing on feasibility, patient outcome and cost-benefit analysis are warranted to confirm the validity of this technology.

Francesco Tomasello
Messina, Italy

The authors report their experience with “in-house” 3D printing of cranial reconstruction implants. Advantages include both time and financial savings as well as in house rapid modifications for patient specific implants. Some of these implants can even be produced and provided during the same day as the original surgery. Classically, the cranioplasty is a delayed, elective procedure, where the implant can be made available well in advance of the procedure. However, in some cases the implant may need to be modified based on anatomic changes, unexpected findings and a poor fitting implant. Soft-tissue may impede the fitting of the implant and make it difficult to find an ideal “fit” with out of house produced prosthetics. The ability to modify the implant design, rapidly produce the implant, and avoid significant delays and cost significantly improve the level of care available to patients. This study demonstrates those advantages. Tailoring implants for the orbitozygomatic, retrosigmoid, and interhemispheric defects is a great advantage. Given these instances having in-house capabilities are a tremendous asset.

Rocco A. Armonda
Washington, District of Columbia

The authors describe their use of 3D printing for creating customized cranioplasties for skull defects in the context of using these created prostheses for operative reconstruction in real time, thereby avoiding time delay and substantial cost. They demonstrated their concept with proof of principle on 3 cadaveric specimens with 5 different skull defects. The cosmetic results and fit of the prosthesis appeared excellent in this cadaveric model.

A few challenges need to be addressed before this technique can be widely incorporated for clinical practice. An FDA-approved material with appropriate material strength and durability must be identified for use. Costs of intraoperative fabrication are not insignificant, and include purchase and maintenance of a high-quality 3D printer capable of rapid printing, operating room and staff time when printing is being performed and nothing else is being done, and cost of materials. Ownership of the process will need to be defined - will the surgeon be responsible for

operating the printer, or will some other staff member need to be trained to do so. The authors used a Biograph TruePoint PET•CT (Siemens AG, Munich, Germany) for “preoperative” imaging in their study, which currently limits use to elective cases with preoperative imaging. The authors would need to determine if intraoperative imaging tools, such as the AIRO CT (Brainlab, Munich, Germany) has sufficient imaging quality too be used for prosthetic reconstruction to expand possibilities to cases in which the need for cranioplasty is defined at the time of surgery; And lastly, the time of fabrication in the operating room is a concern. Most cranioplasties can be performed with a pre-fabricated prosthesis in under 2 hours. In this study, 2 of the 5 prostheses took over 2.5 hours to fabricate, which adds additional time and costs to the procedure.

Once the above issues are addressed, a clinical study, which includes true cost analysis, with comparison to prefabricated costs and consideration of the number of cranioplasties which would need to be performed to recoup costs of new hardware, would be necessary. If the 3D printing technique, shown in this study to be feasible, is also shown to be clinically possible at improved cost, then clinical adoption of the technique could occur. I would expect such use would be most likely in hospitals in which a high volume of cranioplasties are performed.

N. Scott Litofsky
Columbia, Missouri

The authors have described their protocol for in-house rapid 3D printing of cranioplasty for cranial defects. The technique is relatively simple with available technology and can be adapted to the variety of cranial defects encountered in practice. This practice of in-house 3D printing has been used in the past to create physical models to allow preoperative planning. This paper, and others soon to come, take 3D printing into the realm of real time intraoperative use. All neurosurgeons are familiar with the slow-motion process of extraoperative cranioplasty creation, and those responsible for capital budgets are very well aware of their excessive costs. When costs exceed value, as is the current state in commercial cranioplasty, it is inevitable that innovative groups will invent around the status quo. The authors should be commended for their innovation.

The questions going forward are: who will assume responsibility for quality control, sterility, etc? Will institutions, medical systems, insurance companies create their own implants? Surely this will not be limited to cranioplasty. What other surgical implants will be created locally, bypassing industry?

Richard W. Byrne
Chicago, Illinois