Cranioplasty with three-dimensional customised mould for polymethylmethacrylate implant: a series of 11 consecutive patients with cost-effectiveness consideration

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Technical Note

Keywords: 3D printing, cranioplasty, customised implant, polymethylmethacrylate, reconstructive surgery, three-dimensional template

DOI: https://doi.org/10.21203/rs.3.rs-97624/v1

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Abstract

Background

Different methods of cranioplasty for the reconstruction of bony skull defects exist. In the absence of the autologous bone flap, a customised manufactured implant may be the optimal choice, but this implant has several limitations regarding its technical standardisation and better cost-effectiveness.

Methods

This study presents a series of 11 consecutive patients who had undergone cranioplasty with customised three-dimensional (3D) template moulds for polymethylmethacrylate (PMMA) implants manufactured after 3D modelling on a specific workstation. The virtual images were transformed into a two-piece physical model using a 3D printer for the biomaterials. PMMA implant was produced intraoperatively with the custom mould. Cosmetic results were analysed by comparing pre- and postoperative 3D computed tomography (CT) images and asking if the patient was satisfied with the result.

Results

The average total time for planning and production of customised mould was 10 days. The 11 patients were satisfied with the result, and CT images presented harmonious symmetry when comparing pre- and postoperative scans. Cases of postoperative infection, bleeding, or reoperation in this series were not observed.

Conclusion

Cranioplasty with high-technology customised 3D moulds for PMMA implants can allow for an aesthetic reconstruction with a fast and cost-effective manufacturing process and possibly with low complication rates.

Introduction

Cranioplasty is a reconstructive surgery that has attracted the attention of doctors and researchers for a long time and is still one of the most commonly performed neurosurgical procedures worldwide. For over 5,000 years, surgeons have been trying to determine a suitable material for the proper repair of cranial defects. A notable example is the cranioplasty of a Peruvian skull from 2000 BC; the skull was found to have a left frontal defect covered with a 1-mm-thick gold plate. At that time, the material used for the repair directly reflected the patient's social level. This incessant search for a perfect material that provides a good functional and aesthetic result is observed even today [29].
Extensive cranial defects can occur owing to traumatic injuries, infections, congenital or neoplastic diseases, and decompressive craniectomy. Cranioplasty restores the cosmetic form of the cranium to avoid post-craniectomy complications such as seizures, syndrome of the trephined, and brain herniation through the defect [12, 16].

Several techniques are available for cranioplasty. The first is the use of autogenous bone flap removed from the patient and kept in the subcutaneous abdominal pocket or preserved using the deep freezer, but the risks of infection, absorption, and reduced strength in these cases should be considered [23, 1]. The utilisation of bone grafts from cadavers (allograft) or other types of animals (xenograft) has high complication rates and is considered obsolete [29].

Alloplastic reconstruction utilising biocompatible materials has been proven to be a reliable method when an autologous bone is not available. This material should be resistant to infection, inert, noncarcinogenic, malleable, strong, easily handled, and cost-effective [30]. Different biomaterials are used for cranioplasties, often based on the routine of the institution or on the personal experience of the surgeon. Polymethylmethacrylate (PMMA), hydroxyapatite, titanium, bioactive glass ceramics, and polyetheretherketone are the most available options, each with their respective advantages and disadvantages [29,30,22,35].

PMMA was first introduced after World War II, and it is biocompatible, malleable, and heat resistant with good strength; also known as acrylic, it has been widely used in cranioplasties for decades. Implant moulding occurs intraoperatively and is performed freehand by the neurosurgeon; it requires significant clinical skill and three-dimensional (3D) orientation to obtain a reasonable aesthetic result [6, 7].

In the last two decades [35,25,5,33], custom implant production based on 3D computed tomography (CT) with computer-aided design/computer-aided manufacturing (CAD/CAM) has been constantly refined, aiming for a precise and aesthetic fit over the cranial defect. The ideal implant biomaterial continues to be extensively researched, and several options have been used with similar results [13, 20, 21, 32]. The current article describes the confection of a high-technology two-piece mould with acceptable costs customised according to the patient's bone defect to perform intraoperative PMMA modelling.

**Methods**

This observational non-experimental cohort study was conducted as a retrospective analysis of a prospective collected data in four parts: the Neurosurgery Department of the Instituto de Neurologia de Curitiba, a Brazilian health technology start-up, a postgraduate team in Biotechnology at the Universidade Positivo, and a Brazilian International Organization of Standardization 13485 certified surgical products company.

Eleven (6, female; 5, male) patients with large cranial defects were selected at the Instituto de Neurologia de Curitiba between May 2018 and March 2020. Indications for customised cranioplasty were decompressive craniectomy in eight patients, infection of a polyetheretherketone implant in one patient, and tumour infiltration in two patients. All surgeries were performed a minimum of 2 months after the initial craniotomy.
This study complied with ethical standards, and patients or members of their families provided informed consent for inclusion in the study.

**Preoperative care**

Every patient underwent a high-resolution CT scan (1.25-mm slice thickness). The bone window was selected to visualise bone details. These images were shared by cloud from the Radiology Department at the Instituto de Neurologia de Curitiba to the engineering/design team.

**CAD/CAM treatment** CT images were exported in Digital Imaging and Communications in Medicine (DICOM) files. Subsequently, 3D reconstruction software was used to render the images (Fig. 1), reproducing the patient’s bone skull three-dimensionally. The software used for converting DICOM files to stereolithography (STL) file images was InVesalius 3.1 open-source software for the reconstruction of CT and magnetic resonance images (https://invesalius.github.io/), free of charge, developed by Brazilian Paulo Amorim in partnership with the Renato Archer Information Technology Center.

With generated rendering, a 3D parametric modelling software was used to treat the cranial defect. This software is parametric and classified as a “middle engineer” and has several tools for modelling 3D geometries. Skull defects were isolated and edited with surface treatment tools for detailing and refinement aesthetically and geometrically compatible with the real skull defect (Fig. 2).

The prosthesis was modelled based on an isolated defect. The defect was geometrically filled through the modelling tools, generating a 3D model of the intended prosthesis (Fig. 3). Planning approval by the neurosurgical team was required before triggering the CAM process.

In two patients (patients 9 and 11), a special frame template was created to determine the area of bone tumour infiltration. This frame served as a window to allow the precise removal of the custom cranioplasty.

**Mould and test implant printing**

After completion and approval of virtual treatment, the STL extension file was sent to a 3D printer slicing application to enable production. A craniectomy defect model, test implant, and two-piece mould templates were printed with Stratasys, Ltd. fused deposition modelling technology (Fig. 4). A nonstick layer was applied over the modelling surface of the two-piece mould to prevent the implant from sticking. Each printed piece was properly identified. Full production, from CAD/CAM to delivery, took 10–13 days.

**Intraoperative management**

A two-piece mould, craniectomy defect model, and test implant underwent sterilisation 24 to 48 hours prior to surgery. Patient care (anaesthesia induction, positioning) was performed as routine. Skin incision was created using a previous surgical scar in all patients. Craniectomy borders were exposed entirely (Fig. 5). The test implant was placed over the defect to check fitting quality, confirming no evidence of unevenness or gap between the bone and prosthesis (Fig. 6). After verification, the PMMA was prepared in a two-piece mould (Fig. 7). Once hardened after the thermo-reaction, the implant was compared with the test implant. Several
small holes were drilled in the implant for assimilation with the tissues. Finally, it was placed over the defect and fixed in the skull with mini titanium plates (Fig. 8).

**Post-operative care**

A high-resolution CT scan was performed to visualise the aesthetic result and symmetry. The patients were discharged 24 hours after surgery.

**Patient’s perception of the final result of cranioplasty**

To assess the cosmetic results, all patients were asked if they were satisfied with the result 2 months after surgery, responding objectively with YES or NO. One patient was unable to respond owing to her neurological condition, and her family members’ response was considered.

**Results**

Table 1 shows each patient’s sex, age, cause of defect, defect location, size of the defect, total time for production, and implant thickness. A comparison between pre- and postoperative 3D CT scans of all patients is shown in Fig. 9. CAD/CAM treatment was performed in 5 to 6 days and 3D printing in approximately 20 h, plus 4–5 days for template cleaning, sterilisation, and delivery. No complications were observed during each planning. Costs per implant were approximately 6300 dollars (37000 reais).
Table 1
Patients’ descriptions

| Patient # | Sex | Age (years) | Cause of defect                                      | Defect location                  | Size of the defect | Total time for production | Implant thickness |
|-----------|-----|-------------|------------------------------------------------------|----------------------------------|--------------------|---------------------------|------------------|
| 1         | F   | 67          | Decompressive craniectomy for brain infarction       | Right frontotemporoparietal      | 10 × 13 × 3,5 cm   | 11 days                   | 0,2 cm           |
| 2         | F   | 15          | Decompressive craniectomy for intracranial hemorrhage| Left frontotemporoparietal       | 9,5 × 10,2 × 4,8 cm | 11 days                   | 0,2 cm           |
| 3         | M   | 35          | Decompressive craniectomy for brain edema            | Right frontotemporoparietal      | 10,25 × 12,3 × 3 cm | 10 days                   | 0,2 cm           |
| 4         | M   | 19          | Osseous dysplasia and local infection                 | Bifrontal                        | 12,7 × 12,3 × 6,2 cm | 11 days                   | 2,8 cm           |
| 5         | F   | 42          | Decompressive craniectomy for brain edema            | Left frontotemporoparietal       | 13,5 × 11,7 × 3,3 cm | 10 days                   | 0,2 cm           |
| 6         | F   | 42          | Decompressive craniectomy for brain edema            | Right frontal                     | 9,3 × 8,7 × 2,2 cm  | 9 days                    | 0,2 cm           |
| 7         | M   | 32          | Decompressive craniectomy for trauma                 | Right frontotemporoparietal      | 11,5 × 14,6 × 2,9 cm | 11 days                   | 0,2 cm           |
| 8         | M   | 63          | Decompressive craniectomy for brain tumor            | Right parietal                    | 8 × 12 × 3,2 cm     | 9 days                    | 0,2 cm           |
| 9         | F   | 42          | Intraosseous meningioma                               | Left retrosigmoid                 | 6 × 5,9 × 1,2 cm    | 10 days                   | 0,4 cm           |
| 10        | F   | 51          | Decompressive craniectomy for brain infarction       | Right frontal                     | 7,5 × 9,2 × 2,4 cm  | 9 days                    | 0,2 cm           |
| 11        | M   | 19          | Fibrous dysplasia                                    | Right sphenoidal                  | 6 × 4,7 × 0,9 cm    | 9 days                    | 0,3 cm           |

In the first patient, it was necessary to reperform the implant due to early deformation. This occurred because the plate was removed before being completely hardened. Minor adjustments with drill were
necessary to improve aesthetics only in the first two patients. Post-operative infection, bleeding, or necessity for reoperation was not observed. All 11 patients answered YES regarding satisfaction with the implant.

**Discussion**

With the current paradigms of personalised medicine, various methods have surged to improve the aesthetic results of cranioplasties [22,35,6,25,5,33,13,20,21,32,19]. This revolution in modern practice occurs due to the 3D printing of biomaterials and its disruptive applications in the twenty-first century medicine. Correction of cranial defects is a perfect example of this technological application: a closed, rigid, and immovable compartment with a defect that can be corrected by overlapping a simple prosthesis.

Although autogenous bone flaps are still the best option for defect correction, they are frequently unavailable for several reasons [12, 23, 1, 22, 27, 28]. Various studies have shown the advantages and disadvantages of every material used for cranioplasty [29, 22]. Infection rates may vary among patients receiving custom implants, and infection is still the most common complication in cranioplasty surgery with variable incidence rates. Regardless of the selected method, the timing of cranioplasty, patient’s performance, choice of the material, and surgical running time affect the risk of complications [12, 16, 23, 1, 30, 22, 9]. PMMA often exhibits low complication rates in cranioplasty [16, 6, 7, 33, 15, 8, 26, 3]. Infections or complications in the 11 patients from this study were not observed.

The inflated costs for a high-quality custom template [20, 31, 24] may be directly associated with bureaucracy, health systems limitations, and the lack of specific certified manufacturing processes in Brazil. Several studies have demonstrated the feasibility of producing low-cost custom implants, offering significant potential for cost savings and improving aesthetic results and patients’ quality of life [25, 13, 32, 11, 33, 2, 17]. However, solutions that match the prominent level of medical technology available with optimised costs are still required.

Interdisciplinary collaboration between engineering and neurosurgery is an evident starting point. This concept, as previously described [13, 32, 19, 2, 17], favoured the creation of the mould. The use of 3D images facilitated the integration between medical staff and engineering. As observed in several articles [30, 6, 7, 25, 5, 33, 13, 20, 21, 32, 19], the various CAD/CAM techniques offer safe and satisfactory aesthetic results regardless of the implanted biomaterial, provided that an appropriate scientific methodology is followed. In our experience, the ideal algorithm for mould production was observed when the surgeon adequately expressed his/her need to the engineering team via a medical phantom.

Following technological development, there are complex and rigorous regulatory issues specific to a particular country. Accessibility and regulatory compliance for 3D custom implants still lacks proper validation in Brazil. This makes the use of modern biomaterials temporarily unfeasible, which are still pending approval by the Agência Nacional de Vigilância Sanitária. This is a bureaucratic step that involves long-term efforts and needs to be fulfilled.

While the regulation of some biomaterials does not occur, the confection of 3D printed moulds for customised PMMA implants has been described as an alternative solution [26, 11, 2, 14]. In the
manufacturing process, the cost of material to produce moulds is similar to that of the prosthesis. By automating the interdisciplinary design of implants during their manufacture under validated systems, the application of 3D printing could be routinely used in clinical practice while continuously overcoming the limitations [20, 21, 34]. Product production, whether mould or implant, is achievable in less than 14 days. For the present article, up to 7 days from image acquisition to sterilisation has been fully possible.

The fight against bureaucracy and overpricing has become the next challenge. In the current Brazilian model, there is often an intermediary responsible for supplying products, adding a significant increase in the final value. In early 2017, three possible suppliers for custom cranioplasty templates were listed at our institution. None had legal regulations consistent with the use of biomaterials or appropriate specifications regarding implant production. The final cost to the patient or to the health insurance ranged from 14,000 dollars (70,000 reais) to 44,000 dollars (220,000 reais). Even considering Brazilian taxes, such prices are 2 to 7 times more expensive than expected in other countries [4, 18, 10] and often evolve into judicialization, harming all parties involved, specifically the patient. In the proposed method, a cost of less than 8,000 dollars was achieved.

We advocate that a high-quality solution under the scientific method can be cost-effective. If intermediary supplier bias is excluded, the entire system can benefit from reduced costs. Therefore, such technology could continue to evolve, focusing on welfare.

**Conclusion**

Cranioplasty with high-technology customised 3D moulds for PMMA implants can achieve symmetric and aesthetic results, possibly with low complication rates. Systematisation of the entire manufacturing process leads to a fast and cost-effective process.

**Declarations**

**Ethical approval:** This study was granted exemption by the institutional research ethics committee – Comitê de Ética em Pesquisa em Seres Humanos do Instituto de Neurologia de Curitiba (CEPSH-INC) due to its observational non-experimental cohort design. For inclusion in this type of study formal informed consent was signed by patients or members of their families.

**Consent for publication:** Informed consent was obtained from all individual participants included in the study.

**Availability of data and materials:** The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

**Competing Interests:** The authors declare the following financial interests/personal relationships, which may be considered as potential competing interests: The authors Caetano Silva Lobo, Ana Flávia Oliveti, and Rafael Martinelli de Oliveira declare that they exercise technical and administrative functions in BMR
Medical, responsible for manufacturing implants. The authors Erasmo Barros da Silva Júnior and Marcelo de Paula Loureiro declare to be technical consultants of BMR Medical, receiving fees for this function.

**Funding:** No funding was received for this research.

**Authors' contributions:** RO, AF and CS conducted CAD/CAM treatment. EB, AH and RR performed all surgeries. MP analyzed and interpreted the images regarding reconstruction. All authors read and approved the final manuscript.

**Acknowledgements:** any.

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