



# Simultaneous Closure of Bilateral Cranial Defects Using Custom-Made 3D Titanium Implants- A Single Institution Series

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## ABSTRACT

**AIM:** To investigate the outcomes of the simultaneous closure of bilateral cranial defects using custom-made three-dimensional (3D) titanium implants.

**MATERIAL and METHODS:** Demographic data of 26 patients with bilateral cranial defects who underwent cranioplasty using the 3D custom-made titanium implants in our clinic between 2017 and 2022 were retrospectively reviewed. Data on the area of cranium defect, the time interval between last cranial surgery and cranioplasty, postoperative complications, etiology of the cranium defect, and hospitalization of the patient were statistically evaluated.

**RESULTS:** The incidence of bilateral cranioplasty was 19.11%. The gender distribution of patients was 4 (15.4%) female and 22 (84.6%) male, with a mean age of  $29.08 \pm 14.65$  years. The mean defect area was  $35.0 \pm 19.03$  and  $29.24 \pm 22.51$  cm<sup>2</sup> on the right and left sides, respectively. The etiology of the cranium defect was gunshot wounds in 12 patients, and 14 patients had a history of trauma-related injuries such as falls and vehicle accidents. Eight patients had a history of failed cranioplasty with autologous bone. Postoperative complications were wound dehiscence in two patients and diffuse cerebral edema in one patient. No mortality was recorded.

**CONCLUSION:** The custom-made cranioplasty is feasible for simultaneous closure of bilateral cranial defects. Many complications can be prevented by careful preoperative evaluation before surgery and an appropriate implant selection for the patient.

**KEYWORDS:** Bilateral cranial defect, Case series, Cranioplasty, Custom-made Implant, Titanium

**ABBREVIATIONS:** **3D:** Three-dimensional, **CSF:** Cerebrospinal fluid, **CT:** Computerized tomography, **HA:** Hydroxyapatite, **PEEK:** Polyetheretherketone, **PMMA:** Polymethylmethacrylate

## INTRODUCTION

Decompressive craniectomy is inferior to head traumas, brain tumors, displaced bone fractures, cranial bone tumors, infections, or brain edema after cerebral in-

farctions (29,34). Cranioplasty is a common surgical procedure to close the cranial bone defect that occurs after craniectomy (25). It is performed to provide mechanical protection of the brain parenchyma from external impacts to regulate the cerebrospinal fluid (CSF) dynamics and brain perfusion by

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stabilizing intracranial pressure and to solve the patient's aesthetic challenges (1,5,28,30). The cranial defect may be unilateral or bilateral depending on the etiology of craniectomy and usually closed by autologous bones. Synthetic materials, such as titanium, hydroxyapatite (HA), polymethylmethacrylate (PMMA), polyetheretherketone (PEEK), carbon fiber-reinforced epoxy resin, and bioactive glass are used in small or inappropriate bone grafts and cranioplasty for a long time (1,8,12,25,28,30,34). Various materials and techniques have advantages and disadvantages (34). Therefore, in the selection of suitable materials and techniques, particular criteria should be determined, such as biocompatibility (not initiating an allergic reaction against the patient and integrated with the cranium), not forming a medium for microorganisms that may cause infections, providing sufficient mechanical protection for the brain, not disrupting skin perfusion, not resorbing over time, not conducting heat, and being economically easily available (1,26,30-32).

In this study, patients who had bilateral cranial defects and underwent cranioplasty surgery with custom-made titanium implants produced with three-dimensional (3D) printers were clinically evaluated. We compared our results with the literature.

## ■ MATERIAL and METHODS

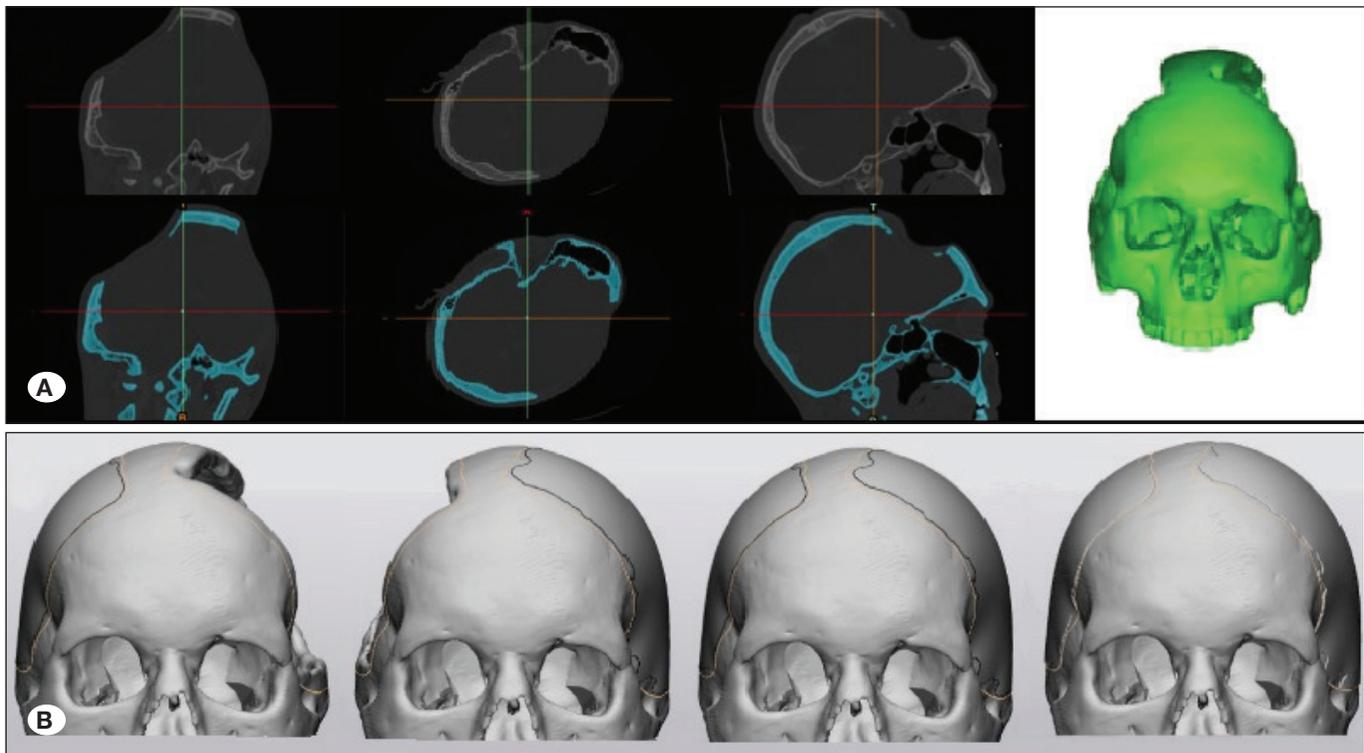
Local ethics committee approval was obtained for our study (071/14/2020/318). Because of the retrospective nature of the study, patient consent was not required.

## Study Design, Inclusion Criteria

We retrospectively evaluated the patients who underwent bilateral cranioplasty surgery with personalized titanium material produced with 3D printers between 2017 and 2022 in our clinic. We included patients who had bone defects on both sides of their cranium and were covered with personalized titanium material produced with 3D printers in the same surgery. Patients with unilateral or bilateral cranium defects who underwent cranioplasty at different times were excluded. In our study, demographic data such as gender and age of the patient, etiology of the cranium defect, area of cranium defect, the time interval between last cranial surgery and cranioplasty, history of cranioplasty surgery, cranioplasty material used in previous cranioplasty surgery, the reason for repeat cranioplasty, duration of hospitalization, postoperative follow-up time, postoperative complications, and postoperative complication surgery were evaluated.

## Surgical Preparation and Technique

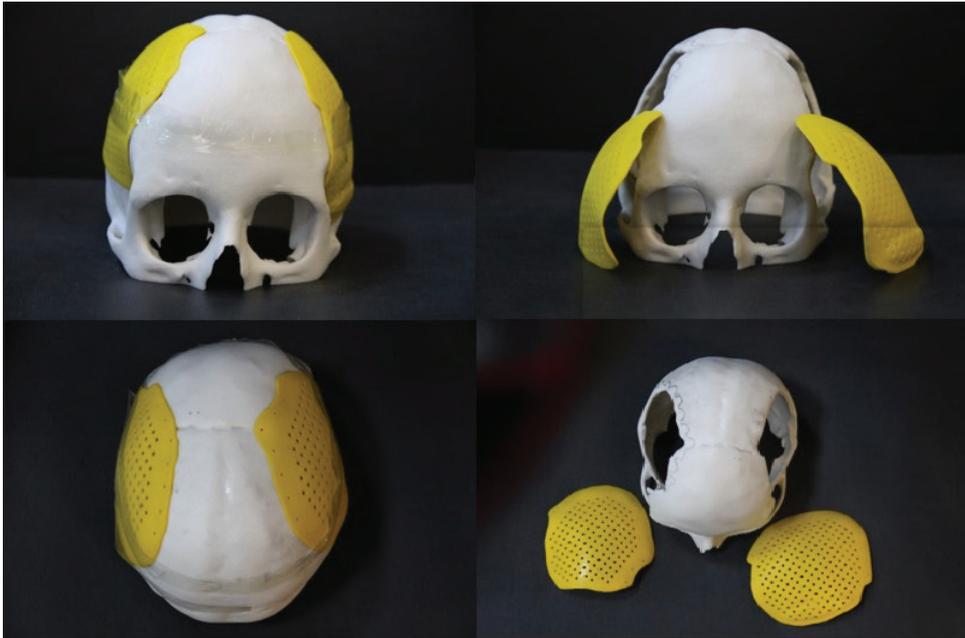
Planning and designing processes were made in Gülhane Medical Design and Manufacturing Center. Using the DICOM data of the cranial computerized tomography (CT) (Figure 1), a 1/1 scale plastic model of the patient's cranium and the cranial implant to close the cranium defect was designed and developed using the special designing software programs (Mimics and 3-matics, Materialize Mimics Innovation Suite, Belgium). Features such as the suitability of the skin and brain tissue are taken into consideration by the designing engineers. The plastic models were manufactured using a



**Figure 1:** **A)** Three-dimensional (3D) images of cranium defects were created in the virtual environment. **B)** Three-dimensional (3D) image of implants that cover the cranium defects were created in the virtual environment.

3D plastic printer (ZCorp, Zprinter 650). The cranial implant was manufactured using a metal 3D printer that uses selective laser melting technology (M2 Cusing, Concept Laser GmbH Lichtenfels, Germany) and medical Ti-alloy Rematitan (Ti6Al4V, Grade 23 [ELI]). The 3D image of the patient's cranium and the plan of the implant to close the cranium defect were created in a virtual environment (Figure 1). The titanium implant with 2.4-mm diameter holes was produced following the 3D model

(Figure 2). A preoperative skin evaluation of the patient was performed (Figure 3). After the antiseptic procedures, the patient was given a position that would provide access to the defect area on both sides or access to the area on the side of the large defect. The previous skin incisions were used to reach the defect area. The incision was enlarged when necessary. When the titanium implant was fully inserted into the defect area, the dura was suspended with 5.0 silk sutures



**Figure 2:** Plastic models were produced according to the three-dimensional (3D) images in the virtual environment.



**Figure 3: A)** Before surgery, photographs of the patient showing the cranium defects were taken from all angles. **B)** After surgery, photographs of the patient showing the cranium defects were taken from all angles. (The patient consented to the publication of his image.)

to prevent epidural hematoma. In patients with defects in the temporal region, the temporal muscle was suspended to the implant with 2.0 vicryl sutures. The titanium implant was fixed to the cranium with titanium mini-screws (Figure 4). A positive pressure subgaleal drain was placed to prevent epidural hematoma.

**Postsurgical Follow-up**

A CT scan was performed after the 6<sup>th</sup> hour postoperatively to evaluate the position of the implant after surgery and to reveal any postoperative bleeding. Drains were removed within 48 hours unless otherwise noted. For infection prophylaxis, intravenous ceftriaxone treatment was continued in the first 72 hours postoperatively, three doses a day. At the next time interval, prophylaxis was carried on with oral amoxicillin-clavulanic acid preparations. Sutures were then removed at the end of the second postoperative week.

**Statistical Analysis**

The IBM SPSS Version 25.0 statistical package program (IBM Corp., Armonk, NY) was used for data analysis in our study.

**RESULTS**

A total of 136 patients underwent cranioplasty between 2017 and 2022, and 26 (19.11%) of them had bilateral cranium defects. Twenty-two (84.6%) patients were men, and four were women (Table I). The mean age was 29.08 ± 14.65 (9–64) years. The mean cranium defect area was 35.0 ± 19.03 (15.01–84.32) and (12.46–77.73) cm<sup>2</sup> on the right and left sides, respectively, with a total of 63.62 ± 39.41 (32.65–161.87) cm<sup>2</sup> on both sides (Table II). The etiology of the cranium defect was gunshot wounds in 12 patients. Fourteen patients had a history of trauma-related injuries such as falls and vehicle accidents. Eight patients (30.8%) had a history of failed cranioplasty with autologous bone. Postoperative complications developed in three (11.5%) patients. Wound dehiscence was observed in two patients. While one of the patients recovered with wound dressing follow-ups without surgery, the other patient underwent wound revision surgery. Diffuse cerebral edema was revealed in one patient at the 8th hour postoperatively. The patient’s implants were removed.

Regardless of the side of the cranium defect areas, there is no statistically significant difference among gender and age, etiology of the cranium defect, history of cranioplasty surgery, postoperative complications, and complication surgery.

There is a statistically significant relationship between the time interval between last cranial surgery and cranioplasty and the cause of the cranium defect. This period is longer in patients with gunshot wounds than the others (Table III).

**DISCUSSION**

Bilateral cranial defects are challenging for neurosurgeons and differ from unilateral defects, in which the area of the defect is larger, the atmospheric pressure on the brain is higher, and the presence of two different operating sites for cranioplasty increases the risk of infection. Cosmetic outcomes may not be as satisfactory as unilateral defects because the degree

**Table I:** Demographics and Operative Characteristics

Patients’ Groups	Frequency
<b>Sex</b>	
Male	22 (84,6%)
Female	4 (15,4%)
<b>Cause of Cranium Defect</b>	
Firegun Injury	12 (46,2%)
Traumatic Fracture	14 (53,8%)
<b>Postoperative Complications</b>	
None	23 (88,5%)
Opening The Incision Site	2 (7,7%)
Diffuse Brain Edema	1 (3,9%)
<b>Previous Cranioplasty Surgery</b>	
None	18 (69,2%)
Autological Bone Flap	8 (30,8%)
<b>Reason of Repeat Cranioplasty Surgery</b>	
None	18 (69,2%)
Osteomyelitis	4 (15,4%)
Bone Resorption	4 (15,4%)



**Figure 4:** The picture shows the condition of the implants after they are placed. (The patient consented to the publication of his image.)

**Table II:** Demographics and Operative Value

Patients' Groups	Value
Patient's age ( year)	29.08 ± 14.65 (9 - 64)
Area of cranium defect (cm <sup>2</sup> )	
Right	35.0 ± 19.03 (15.01 - 84.32)
Left	29.24 ± 22.51 (12.46 - 77.73)
Total	63.62 ± 39.41 (32.65 - 161.87)
Time from last cranial surgery to cranioplasty surgery (month)	17.0 ± 11.68 (3 - 43)
Duration of hospitalization (day)	8.77 ± 7.44 (3 - 30)
Postoperative follow-up time (month)	29.23 ± 14.47 (11 - 60)

**Table III:** Relationship Between Cause Cranium Defect and Time From Last Cranial Surgery to Cranioplasty Surgery

Cause of Cranium Defect	Time from last cranial surgery to cranioplasty surgery (month)
Traumatic Fracture	12.14 ± 5.2
Firegun Injury	16.33 ± 0.67

Data are expressed as mean ± standard deviation.  
Mann-Whitney U Test p=0.35

of skin contracture on bilateral cranial defects may be a challenge for closure of the skin after the insertion of implants. Classical reconstruction techniques such as mirror imaging of the healthy and unaffected cranial side are not suitable for bilateral defects with missing midsagittal planes (4,6,33). In our study, we used postcraniectomy cranial CT scans (5–10 mm slices) to generate 3D images of the implant for the bilateral cranial defects. Although there are a few cases of cranioplasty or case reports, there has been no clinical study in the literature evaluating the results of cranioplasty surgery for bilateral cranium defects.

The commonly used materials in the repair of cranial bone defects are autologous bones, titanium, HA, PMMA, PEEK, and bioceramics (1,12,34). Autologous bones with bone flaps are preserved after craniectomy, rarely bones that shifted to the defect area or are obtained from different parts of the body. Although the biocompatibility of autologous bones is efficient, resorption of the bone flap due to the insufficient blood supply and infection problems because of storage conditions are frequently experienced. At present, the first option for cranioplasty is the bone flaps hidden after craniectomy (7,8,19,30,34). In our study, concealed bone flaps were used after craniectomy in eight patients, repeat cranioplasty due to osteomyelitis was applied to four patients, and bone resorption was done in four patients. Futile bone flaps of 18 patients were not stored after craniectomy.

Titanium, HA, PMMA, and PEEK can be used by shaping intraoperatively or producing preoperatively as custom-made in suitable 3D printers (7,19,20,29,34). Biocompatibility, responsiveness, durability, and heat insulation of the implants vary depending on the material used. Intraoperatively shaped implants are inexpensive and accessible; however, it often

fails to meet the patient's cosmetic expectations. Although patient-specific implants produced in 3D printers are more expensive and poorly accessible, patient satisfaction is very high after surgery (2,9,15,16,22,26).

The most common problem of surgeons in cranioplasty surgeries is the decrease in volume and quality of the skin covering the defect that occurs due to multiple cranial surgeries (17). The risk of this problem increases directly proportional to the size of the cranium defect area (14,17). Because our study is limited to bilateral cranium defects and skin reserve, we performed our preoperative skin evaluation very carefully.

Cranioplasty surgery can improve the patient's neurological functions and cognitive status by regulating cerebral blood flow and CSF circulation (3,5,23,24). We did not observe any changes in the neurological functions of our patients; however, in the patient evaluation questionnaires we conducted after surgery, we found an improvement in the cognitive status of the patients and a significant decrease in their aesthetic challenges. The effect of cranioplasty surgery on seizures is controversial. While there are opinions stating that seizures will decrease by regulating cerebral blood flow after cranioplasty surgery, there are also opinions stating that cranioplasty causes seizures like all other cranial interventions (3,18,23,24,27). In the long-term follow-up of our patients, we observed that the antiepileptic treatment was terminated or the amount of antiepileptic drug used was reduced.

There are different viewpoints on the timing of cranioplasty surgery (3,18). Morton et al. reported in their study that the risk of infection was highest in the first 2 weeks after craniectomy, the risk of hydrocephalus was highest in the first 3 months,

and the risk of seizures was highest after 3 months (18). De Cola et al. reported that neurological functions improved at the highest level in the first 3 months after craniectomy and cognitive status improved at the highest level after 3 months (3). We waited for at least 1 year since the last surgery of the patients who had a history of gunshot injury or whose bone flap was removed due to osteomyelitis. We determined other patients according to their risk of postoperative complications and their expectation of improvement in neurological functions and cognitive status. Except for one patient, we planned cranioplasty surgery at least 6 months after the last cranial surgery. We operated on one of our patients in the 3<sup>rd</sup> month to improve neurological functions.

All implants except HA-containing implants do not adapt to cranial enlargement, so cranioplasty surgery is controversial in age groups where cranial enlargement continues (2,7,16). Williams et al. reported a case of cranioplasty in which a 3D patient-specific titanium implant was used due to bilateral defects in one of 22 pediatric patients in their study (32). Two female patients in the pediatric age group were included in our study: one 15-year-old and one 9-year-old. The 15-year-old patient developed bilateral bone flap resorption, and the 9-year-old patient underwent cranioplasty in the 3<sup>rd</sup> month after the last craniectomy.

Postoperative complications, such as infection, graft rejection, skin problems, intracerebral/subdural/epidural hematomas, seizures, and hydrocephalus are common after cranioplasty surgery, while complications such as diffuse brain edema can be rarely observed (3,18,21,27). Infection is a major complication that requires implant removal. We used titanium-containing implants with holes in the cases of our study. We think that the fact that titanium does not form a nutrient medium for microorganisms compared with other materials, and that it cannot form a biofilm layer due to the holes it contains, prevents the colonization of microorganisms. The implant promotes immunity in the local area because the holes contained in the implant do not prevent diffusion between the tissues in the epidural area and under the skin. In performing bilateral surgery, we started surgery on the other side after the closure of the skin on one side has been completed. The implant was kept in water containing antibiotics to prevent infection during surgery, and the duration of antibiotic use for prophylaxis was extended. Because of all these conditions, we did not experience any postsurgical infection and implant reaction due to the responsive nature of the used material. Other common problems after cranioplasty surgery are loss of skin quality, deterioration of skin blood supply, and opening in the incision line due to scar tissue formation in the incision area (14,17). Two of our patients requested postsurgery with the complaint of opening the incision line in which one patient had dressing follow-ups, and the other patient required surgery for wound revision. Intracranial hemorrhages are another important problem experienced after cranioplasty surgery (3,11,18,31). The potential space that occurs in the epidural region after surgery plays a vital role in the formation of epidural and subdural hemorrhages. In addition, interventions made during the dissection of the dura from the subgaleal space may cause intracerebral and subdural

hemorrhages. Insufficient bleeding control in the temporal muscle in surgeries involving the temporal region may cause epidural bleeding (11,29,31). We kept skin elevation limited to avoid subdural and intracerebral hemorrhage while performing surgery. To avoid epidural bleeding, we suspended the dura on the implant using the holes of the implant in several places. Another advantage of the perforated implant used in the cases of our study is that it prevents hematoma formation in the epidural area with a drain in the subgaleal area. Diffuse brain edema that occurs in the early period after cranioplasty is rare but has a high mortality rate (35). Pathophysiologies such as intracranial hypotension, brain parenchyma reperfusion damage, hypoxia, autoregulation failure, cerebral ischemia, and loss of CSF due to negative pressure drainage play an important role in the development of the complications (10,13). In one of our patients, who was operated in the 3<sup>rd</sup> month for the recovery of his neurological functions, diffuse cerebral edema occurred in the 8<sup>th</sup> hour after the surgery. The implants were removed, and medical treatment was given for the edema.

The major limitation of this study is the limited number of patients. But technical features of the cases make this study more valid and reliable.

## ■ CONCLUSION

Simultaneous closure of the bilateral cranial defects is challenging and poses many technical difficulties with several complications. These complications can be overwhelmed by careful preoperative evaluation of the patient and selection of appropriate implant. Using the 3D printers in the closure of bilateral defects, the most suitable implant for the patient's defect can be produced before surgery. These implants prevent repeat surgeries, ensuring that the patient is operated on in a single session. Therefore, it reduces the risk of complications due to repetitive surgeries such as postsurgical infection, intracranial hemorrhage, and wound problems.

### AUTHORSHIP CONTRIBUTION

Study conception and design: OT, SK, DE, YI, MK

Data collection: SK, DE

Analysis and interpretation of results: SK, YI, MK

Draft manuscript preparation: OT, SK, DE

Critical revision of the article: YI, MK

Other (study supervision, fundings, materials, etc...): IB, SA

All authors (OT, SK, DE, YI, MK, IB, SA) reviewed the results and approved the final version of the manuscript.

## ■ REFERENCES

1. Aydin S, Kucukyuruk B, Abuzayed B, Aydin S, Sanus GZ: Cranioplasty: Review of materials and techniques. *J Neurosci Rural Pract* 2(2):162-167, 2011
2. Bruno Z, Angelo N, Riccardo S, Nicola Z, Stefano P, Camillo PP, Federico N, Carlotta M: Custom-made hydroxyapatite cranioplasty: Radiological and histological evidence of bone-biomaterial osteointegration in five patients. *Asian J Neurosurg* 15(1):198-203, 2020

3. De Cola MC, Corallo F, Pria D, Lo Buono V, Calabrò RS: Timing for cranioplasty to improve neurological outcome: A systematic review. *Brain Behav* 8(11):e011106, 2018
4. Egger J, Gall M, Tax A, Ücal M, Zefferer U, Li X, von Campe G, Schäfer U, Schmalstieg D, Chen X: Interactive reconstructions of cranial 3D implants under MeVisLab as an alternative to commercial planning software. *PLoS One* 12(3):e0172694, 2017
5. Erdogan E, Duz B, Kocaoglu M, Izci Y, Sirin S, Timurkaynak E: The effect of cranioplasty on cerebral hemodynamics: Evaluation with transcranial Doppler sonography. *Neurol India* 51(4):479-481, 2003
6. Fuessinger MA, Schwarz S, Cornelius C-P, Metzger MC, Ellis E, Probst F, Semper-Hogg W, Gass M, Schlager S: Planning of skull reconstruction based on a statistical shape model combined with geometric morphometrics. *Int J Comput Assist Radiol Surg* 13(4):519-529, 2018
7. Goiato MC, Anchieta RB, Pita MS, dos Santos DM: Reconstruction of skull defects: Currently available materials. *J Craniofac Surg* 20(5):1512-1518, 2009
8. Hanasono MM, Goel N, DeMonte F: Calvarial reconstruction with polyetheretherketone implants. *Ann Plast Surg* 62(6):653-655, 2009
9. Harris DA, Fong AJ, Buchanan EP, Monson L, Khechoyan D, Lam S: History of synthetic materials in alloplastic cranioplasty. *Neurosurg Focus* 36(4):E20, 2014
10. Hassaneen W, Germanwala A, Tsimpas A: Malignant cerebral edema following cranioplasty. *J Clin Neurosci* 25:130-132, 2016
11. Hill CS, Luoma AMV, Wilson SR, Kitchen N: Titanium cranioplasty and the prediction of complications. *Br J Neurosurg* 26(6):832-837, 2012
12. Izci Y, Seçer HI, Ilica AT, Karacalioglu O, Onguru O, Timucin M, Korkusuz F: The efficacy of bioceramics for the closure of burr-holes in craniotomy: Case studies on 14 patients. *J Appl Biomater Funct Mater* 11(3):e187-196, 2013
13. Kaneshiro Y, Murata K, Yamauchi S, Urano Y: Fatal cerebral swelling immediately after cranioplasty: A case report. *Surg Neurol Int* 8:156, 2017
14. Kwiecien GJ, Sinclair N, Coombs DM, Djohan RS, Mihal D, Zins JE: Long-term effect of cranioplasty on overlying scalp atrophy. *Plast Reconstr Surg Glob Open* 8(8):e3031, 2020
15. Lethaus B, Safi Y, ter Laak-Poort M, Kloss-Brandstätter A, Banki F, Robbenmenke C, Steinseifer U, Kessler P: Cranioplasty with customized titanium and PEEK implants in a mechanical stress model. *J Neurotrauma* 29(6):1077-1083, 2012
16. Messina G, Dones I, Nataloni A, Franzini A: Histologically demonstrated skull bone integration in a hydroxyapatite prosthesis in a human. *Acta Neurochir (Wien)* 153(8):1717-1718, 2011
17. Mikami T, Suzuki H, Ukai R, Kimura Y, Miyata K, Akiyama Y, Wanibuchi M, Mikuni N: Flattening the curvature of synthetic materials to relieve scalp skin tension in cranioplasty. *J Clin Neurosci* 61:196-200, 2019
18. Morton RP, Abecassis IJ, Hanson JF, Barber JK, Chen M, Kelly CM, Nerva JD, Emerson SN, Ene CI, Levitt MR, Chowdhary MM, Ko AL, Chesnut RM: Timing of cranioplasty: A 10.75-year single-center analysis of 754 patients. *J Neurosurg* 128(6):1648-1652, 2018
19. Neovius E, Engstrand T: Craniofacial reconstruction with bone and biomaterials: Review over the last 11 years. *J Plast Reconstr Aesthet Surg* 63(10):1615-1623, 2010
20. Prasad GL, Menon GR, Kongwad LI, Kumar V: Outcomes of cranioplasty from a tertiary hospital in a developing country. *Neurol India* 68(1):63-70, 2020
21. Robles LA, Cuevas-Solórzano A: Massive brain swelling and death after cranioplasty: A systematic review. *World Neurosurg* 111:99-108, 2018
22. Rosinski CL, Patel S, Geever B, Chiu RG, Chaker AN, Zakrzewski J, Rosenberg DM, Parola R, Shah K, Behbahani M, Mehta AI: A Retrospective comparative analysis of titanium mesh and custom implants for cranioplasty. *Neurosurgery* 86(1):E15-E22, 2020
23. Rynkowski CB, Robba C, Loreto M, Theisen ACW, Koliass AG, Finger G, Czosnyka M, Bianchin MM: Effects of cranioplasty after decompressive craniectomy on neurological function and cerebral hemodynamics in traumatic versus nontraumatic brain injury. *Acta Neurochir Suppl* 131:79-82, 2021
24. Rynkowski CB, Robba C, de Oliveira RV, Fabretti R, Rodrigues TM, Koliass AG, Finger G, Czosnyka M, Bianchin MM: A comparative study of the effects of early versus late cranioplasty on cognitive function. *Acta Neurochir Suppl* 131:75-78, 2021
25. Sanan A, Haines SJ: Repairing holes in the head: A history of cranioplasty. *Neurosurgery* 40(3):588-603, 1997
26. Shah AM, Jung H, Skirboll S: Materials used in cranioplasty: A history and analysis. *Neurosurg Focus* 36(4):E19, 2014
27. Shih FY, Lin CC, Wang HC, Ho JT, Lin CH, Lu YT, Chen WF, Tsai MH: Risk factors for seizures after cranioplasty. *Seizure* 66:15-21, 2019
28. Solmaz I, Onal B, Civelek E, Pusat S, Kircelli A, Secer HI, Izci Y, Gonul E: Experience in cranioplasty operations: Short review. *Turk Norosir Derg* 20(1):36-42, 2010
29. Tehli O, Dursun AM, Temiz C, Solmaz I, Kural C, Kutlay M, Kacar Y, Ezgu MC, Oguz E, Daneyemez MK, Izci Y: Computer-based surgical planning and custom-made titanium implants for cranial fibrous dysplasia. *Neurosurgery* 11 Suppl 2:213-219, 2015
30. Wiggins A, Austerberry R, Morrison D, Ho KM, Honeybul S: Cranioplasty with custom-made titanium plates--14 years experience. *Neurosurgery* 72(2):248-256; discussion 256, 2013
31. Williams LR, Fan KF, Bentley RP: Custom-made titanium cranioplasty: Early and late complications of 151 cranioplasties and review of the literature. *Int J Oral Maxillofac Surg* 44(5):599-608, 2015
32. Williams L, Fan K, Bentley R: Titanium cranioplasty in children and adolescents. *J Craniomaxillofac Surg* 44(7):789-794, 2016
33. Wittner C, Borowski M, Pirl L, Kastner J, Schrempf A, Schäfer U, Trieb K, Senck S: Thickness accuracy of virtually designed patient-specific implants for large neurocranial defects. *J Anat* 239(4):755-770, 2021
34. Zanotti B, Zingaretti N, Verlicchi A, Robiony M, Alfieri A, Parodi PC: Cranioplasty: Review of materials. *J Craniofac Surg* 27(8):2061-2072, 2016
35. Zhang X, Pan B, Ye Z, Li Z, Mo F, Wang X: Massive brain swelling after cranioplasty: A case report. *J Neurol Surg A Cent Eur Neurosurg* 80(6):498-502, 2019