

Clinical Article



Efficacy of 3D-Printed Titanium Mesh-Type Patient-Specific Implant for Cranioplasty

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ABSTRACT

Objective: Autologous bone grafting for cranioplasty is associated with a high infection rate and bone absorption. Synthetic implant materials for cranioplasty have been developed. In this study, we evaluated the efficacy of titanium mesh-type patient-specific implants (PSIs) for patients with skull defects using the dice similarity coefficient (DSC), clinical outcomes, and artifacts caused by implants.

Methods: This retrospective study included 40 patients who underwent cranioplasty with a titanium mesh PSI at our institution. Based on preoperative and postoperative computed tomography scans, we calculated DSC and artifacts.

Results: The calculated DSC of 40 patients was 0.75, and the noise was 13.89% higher in the region of interest (ROI) near the implanted side (average, 7.64 Hounsfield unit [HU]±2.62) than in the normal bone (average, 6.72 HU±2.35). However, the image signal-to-noise ratio did not significantly differ between the ROI near the implanted side (4.77±1.78) and normal bone (4.97±1.88). The patients showed no significant perioperative complications that required a secondary operation.

Conclusion: Titanium mesh-type PSIs for cranioplasty have excellent DSC values with lower artifacts and complication rates.

Keywords: Titanium; Printing, three-dimensional; Artifact

INTRODUCTION

The purpose of cranioplasty is to restore the cosmetic outcome and function of the cranial vault after traumatic brain injury or intracranial hemorrhage leading to decompressive craniectomy, bone resorption, or epidural abscess.⁴⁾ Cranioplasty not only restores function, but also restores patients' appearance and also aids in their social and emotional well-being.^{2,4,6,8)}

Autologous bone grafting for cranioplasty is considered to be the gold standard, since it does not generate any immune response and does not require remolding for the exact match of skull defects; furthermore it is a low cost technique.⁴⁾ However, autologous cranioplasty is associated with a number of complications, such as bone resorption and postoperative infection.¹⁶⁾ In previous studies, the infection rate after cranioplasty has been reported to be as high as 33%.^{1,8,13,16)} Polymethyl methacrylate (PMMA) is often used to rebuild bone grafts

Conflict of Interest

The authors have no financial conflicts of interest.

as an alternative choice for patients with autologous bone grafts. However, it has a high postoperative infection rate. The postoperative infection rate for autologous bone and PMMA bone grafts was reported to be 6.8% and 14.4% within 3 months, respectively, and the bone resorption rate for autologous bone grafts was reported to be 26%.¹⁶⁾ To overcome these problems, synthetic materials, such as titanium or poly etheretherketone (PEEK) have been introduced for cranioplasty implants.

In case of metal implants, titanium is the only material still in use because of its biologically compatible character and low infection rate.⁴⁾ In contrast to autologous bone grafts, titanium grafts do not cause shrinkage and do not lead to implant failure because of bone resorption and have a low reoperation rate.¹⁶⁾ In addition, its high density enables manufacture of thinner implants than that with other artificial materials. Its strength enables the implants to be lighter than other materials, for example, PEEK.

Patient specific implants (PSIs) that are designed based on preoperative computed tomography (CT) scans have the advantage of symmetry when compared to other PMMA implants or intraoperatively trimmed titanium mesh. Yeap et al.¹⁶⁾ reported that intraoperatively made titanium mesh is associated with complications of skin erosion or bone flap exposure up to 17.0%. Higher symmetry of implanted material compared to that of normal bone leads to lower tensile strength of the skin flap. In this study, we calculated the dice similarity coefficient (DSC) index to measure the similarity between a manufactured implant and the mirror image of normal bone.

Radiologic examinations of patients who underwent cranioplasty with synthetic materials are difficult to evaluate because of the artifacts generated by the foreign material. In this study, we evaluated the artifacts generated by titanium mesh-type PSIs.

The purpose of this study was to evaluate the efficacy of titanium PSIs by measuring the volumetric symmetry evaluated using the DSC, and the diagnostic advantage of the lower number of artifacts of titanium mesh-type PSIs compared to other solid-type PSIs for patients with skull defects.

MATERIALS AND METHODS

This retrospective study included 40 patients who underwent cranioplasty with a titanium mesh type PSI at in our institution from 2018 to 2020. Forty patients who underwent cranioplasty with titanium mesh-type PSIs were subjected to the same protocol for scheduled cranioplasty.

All patients visited the outpatient clinic 2 to 6 weeks prior to cranioplasty for informed consent, medical history, laboratory tests, vital signs, preoperative CT scans, and Glasgow Coma Scale (GCS) scores. On the day of cranioplasty, all patients underwent postoperative CT scans, laboratory tests, vital signs, and GCS scores. On postoperative day 3, additional CT scans were taken, and laboratory tests were performed. Four weeks and 24 weeks after cranioplasty, the patients underwent laboratory tests and their GCS scores were also evaluated. Follow-up magnetic resonance imaging (MRI) was performed 24 weeks after cranioplasty.

The DSC index, which represents the similarity between the implanted image and the ideal image (mirror image) for skull defect reconstruction, was evaluated. CT datasets taken 3

days before and after cranioplasty were converted into 3-dimensional (3D) bone models and mirror images based on the normal site of the skull. The skull defect volume was measured in the same views after image registration. The burr hole site was excluded from the volume calculation. 3D Slicer (extension slicer RT, ver.4.11, open source) was used to create 3D bone model file (STL format) and to analysis the similarity between implanted model and the ideal model. Meshmixer (ver.3.5, Autodesk) was used to create mirrored model and edit the surface model created by 3D slicer. Microsoft Exel was also used for data manipulations and simple curve fitting.

This study was approved by the Institutional Review Board of the Hanyang University Medical Center (HYUH 2019-08-020). Owing to the retrospective nature of the study, the need for informed consent was waived.

RESULTS

Forty patients underwent cranioplasty with titanium mesh-type PSI from 2018 to 2020. Of these, 22 were males (55%) and 18 were females (45%). The mean age was 51.43 years. Indications for craniectomy were trauma (n=19, 47.5%), cerebro-vascular disease (n=17, 42.5%), and infection (n=4, 10%). Indications for cranioplasty were skull defects (n=34, 85%), prior cranioplasty infection (n=4, 10%), and bone resorption (n=2, 5%). The average estimated blood loss and operation time were 462.5 mL and 152.5 minutes, respectively (**TABLE 1, SUPPLEMENTARY TABLE 1**).

There were no significant complications, such as infection or hematoma, that required reoperation. We evaluated the GCS scores on the day of cranioplasty, 1 month postoperatively, and 6months postoperatively after cranioplasty. Cosmetic outcomes were also evaluated 1 month and 6months postoperatively. Cosmetic outcomes were evaluated on a scale of 1 to 10, with scores 8–10 indicating “very satisfactory,” 5–7 “partially satisfactory,” and 1–4 “unsatisfactory” outcomes by asking patients or care givers to answer the questionnaire (**TABLE 2**). There were no significant differences between the preoperative and postoperative GCS scores. The muscle reconstruction method had no significant influence on the GCS score. Seventy five percent of patients reported “very satisfactory” cosmetic outcomes 6 months after cranioplas surgery. **FIGURE 1** shows one of the patient's preoperative and postoperative axial CT scans.

TABLE 1. Characteristics of the study patients

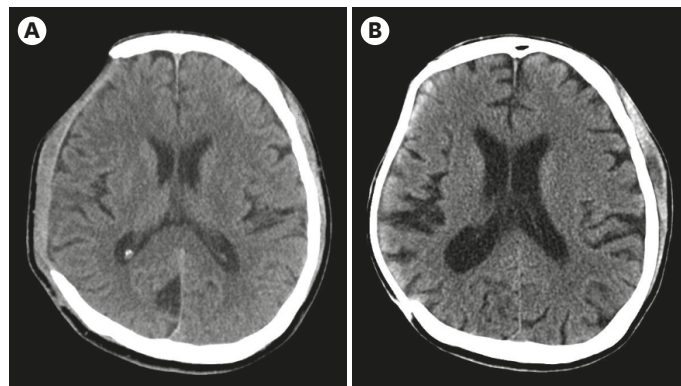
Characteristics	Total (n=40)
Sex (female)	18 (45.0)
Age (years)	51.4±18.1
Indications for craniectomy	
Trauma	19 (47.5)
Cerebrovascular disease	17 (42.5)
Infection	4 (10.0)
Indications for cranioplasty	
Skull defect	34 (85.0)
Bone resorption	2 (5.0)
Infection	4 (10.0)
Operation time (minutes)	152.5±51.7
Estimated blood loss (mL)	462.5±276.6

Data are shown as mean±standard deviation or number (%).

TABLE 2. Clinical and cosmetic outcomes

Clinical outcomes	One piece (n=13)	Two piece (n=27)	Total (n=40)	p-value
GCS score				
Operation day				
11	1 (7.7)	3 (11.1)	4 (10.0)	0.710
12	2 (15.4)	2 (7.4)	4 (10.0)	
15	10 (76.9)	22 (81.5)	32 (80.0)	
One month after operation				
11	0 (0.0)	2 (7.4)	2 (5.0)	0.252
12	3 (23.1)	2 (7.4)	5 (12.5)	
15	10 (76.9)	23 (85.2)	33 (82.5)	
Six month after operation				
12	2 (15.4)	3 (11.1)	5 (12.5)	1.000
15	11 (84.6)	24 (88.9)	35 (87.5)	
Cosmetic satisfaction				
One month after operation				
6	1 (7.7)	2 (7.4)	3 (7.5)	0.985
7	2 (15.4)	5 (18.5)	7 (17.5)	
8	4 (30.8)	9 (33.3)	13 (32.5)	
9	4 (30.8)	6 (22.2)	10 (25.0)	
10	2 (15.4)	5 (18.5)	7 (17.5)	
Six months after operation				
6	1 (7.7)	4 (14.8)	5 (12.5)	0.965
7	2 (15.4)	3 (11.1)	5 (12.5)	
8	2 (15.4)	4 (14.8)	6 (15.0)	
9	5 (38.5)	9 (33.3)	14 (35.0)	
10	3 (23.1)	7 (25.9)	10 (25.0)	

Values are presented as number (%).
GCS: Glasgow Coma Scale.

**FIGURE 1.** Axial computed tomography scans of patient (A) preoperative, (B) 6 months after cranioplasty.

The mean volume of flap was 596.03 cm³ (standard deviation [SD], 108.69 cm³); the minimum size was 361.2 cm³ (DSC, 0.92) and maximum was 842.1 cm³ (DSC, 0.86). The mean value of the DSC was 0.75, which indicates high similarity between the implanted model and the ideal model (**SUPPLEMENTARY TABLE 2**). In 2 patients who underwent bilateral reconstruction, it was not feasible to compare the results because of the small sample size and the lack of an ideal image. Stieglitz et al.¹²⁾ showed that the average intraoperatively fabricated DSC of PMMA was 0.66 (SD, 0.12). The DSC value in our study showed higher volumetric symmetry than that of the PMMA PSIs in their study. DSC was calculated as follows:

$$DSC = \frac{2 \times (A \cap B)}{A + B} \quad (1)$$

(A, reference, mirror model based on the normal site; B, post explanation of implant)

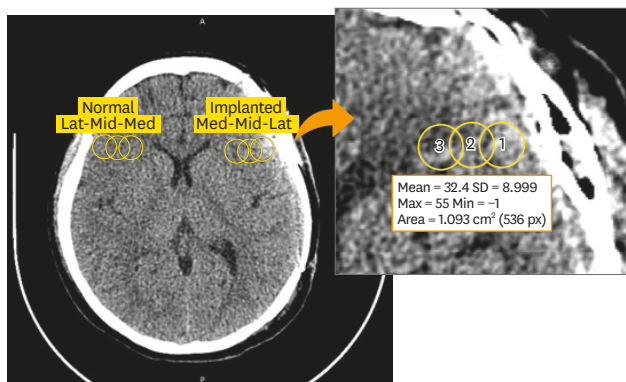


FIGURE 2. Placing region of interest area (medial, middle, and lateral) from the normal bone or implant.

Artifacts generated by titanium implants were evaluated using the signal-to-noise ratio (SNR) and noise. The SNR and noise, which represent mean attenuation and SD in Hounsfield units, were measured at 6 regions of interest (ROIs) near the normal bone and implanted site, respectively. We obtained mean CT attenuation values in Hounsfield units for bilateral muscle and tissue areas near the implant by manually placing ROIs over an area of 1.0 cm². The SNR was calculated as the value of the ROI divided by the image noise (SD of ROI). Image noise was determined by measuring the SD of the CT numbers in the target ROIs (FIGURE 2).

$$SNR = \mu / \sigma \quad (2)$$

(μ , mean gray value of ROI; σ , SD of the ROI's gray value)

The noise was 13.89% higher in the ROI near the implant site (average, 7.64 hounsfield unit \pm 2.62) than in that near the normal bone (average, 6.72 \pm 2.35). However, the image SNR did not significantly differ between the ROI near the implant site (4.77 \pm 1.78) and that near the normal bone (4.97 \pm 1.88) (FIGURE 3).

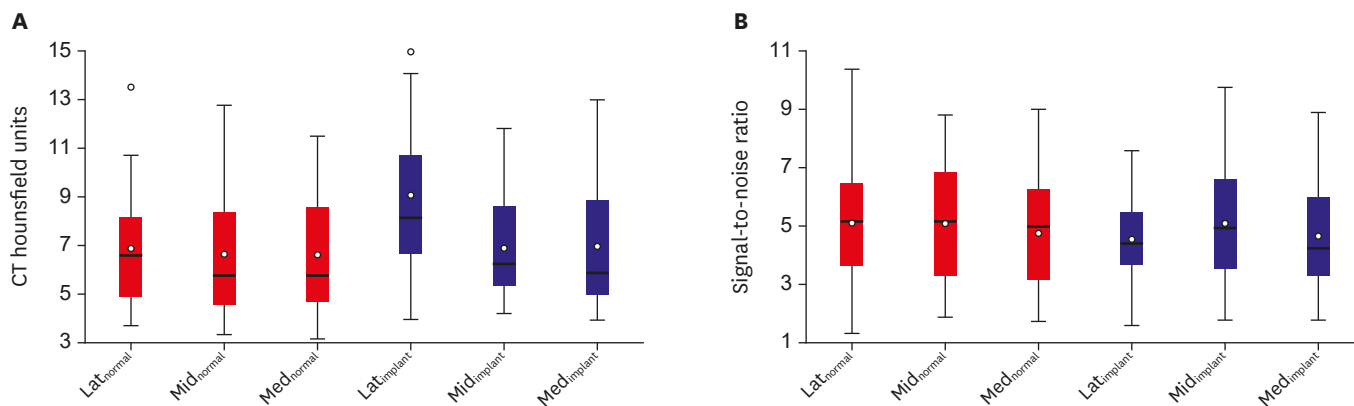


FIGURE 3. Boxplots compare the values between normal and implant side (A) CT value of ROI (hounsfield units), (B) signal-to-noise ratio of ROI. CT: computed tomography, ROI: region of interest.

DISCUSSION

Titanium is lighter and stronger than the human skull bone. Furthermore, when it is manufactured from PSIs and mesh types, it matches the edges of the skull defect more perfectly and shortens the operation duration than when intraoperatively trimmed titanium mesh is used. For example, intraoperatively trimmed titanium implants sometimes result in skin erosion because of the increased tensile stress of the mesh shape resulting in unmatched original contour.¹¹⁾ Yeap et al.¹⁶⁾ reported that intraoperatively made titanium mesh has a complication rate of 17%, including skin erosion or bone flap exposure.

Autologous bone grafts for cranioplasty are known to have a high risk of bone resorption and infection, which leads to secondary surgeries. As mentioned previously, the overall infection rate after cranioplasty is as high as 33%.^{1,8,13,16)} Regarding autologous bone grafts and PMMA, their infection rates are up to 6.8% and 14.4% within 3 months, respectively.^{5,14)} One of the advantages of cranioplasty with autologous bone or PMMA is its low cost. However, because of infection after cranioplasty, implant removal, use of long-term antibiotics, and additional cranioplasty with new artificial implants, it costs more than initial cranioplasty with titanium mesh type PSIs.⁶⁾ Furthermore, it adds to the social and economic burden of the patient.

Lethaus et al.⁶⁾ reported that the total cost for primary reconstruction of skull defects with PSIs and autogenous bone grafts is 15,532.08 and 10,849.91 EUR, respectively. However, when it comes to secondary reconstruction using PSIs because of irreversible complications, such as bone resorption or infection, the total cost for PSIs and autogenous bone grafts is 15,532.08 and 26,086.06 EUR, respectively, without considering the cost of surgical removal of autogenous bone and the emotional and social burden for the patient.⁶⁾ Since infection and bone resorption rates of autologous bone grafts are not thought to be low, we should consider PSIs for cranioplasty of skull defects, even if autologous bone grafts are usable. In the literature, the complication rates of titanium PSIs vary from 4.1% to 29%, with surgical removal rates ranging from 0% to 15.9%.^{4,10)}

In this study, there were no complications, such as postoperative infection, skin erosion, bone resorption, implant displacement, or fixation failure in the mean follow-up period of 0.87 years (range, 4 months to 1 year). The mean operation time and estimated blood loss were 152.5 minutes (70–305 minutes) and 462.5 mL (100–1,500 mL), respectively compared to of 131.81 minutes and 415.55 mL, respectively, reported in the previous literature. Therefore, it is acceptable that some of our patients not only underwent cranioplasty but also received ventriculo-peritoneal shunt for hydrocephalus.²⁾ However, it should be noted that there were limited number of patients in this study, and long-term follow-up is still needed.

In our study, 4 patients received titanium mesh-type 3D printed implants after infection with a previous autologous bone graft, requiring craniectomy. The time interval between craniectomy because of infection and titanium PSI cranioplasty was at least 6 months with adequate use of antibiotics. Their surgeries were successfully completed, and postoperative images showed no signs of infection. Titanium mesh-type PSI is not only an alternative choice for cranioplasty but also a treatment for these patients.

Treating the infection related to cranioplasty primarily requires additional readmission and surgical procedures for decompressive craniectomy and cranioplasty. Not only does it incur additional medical expenses, but it also burdens the patients emotionally. Considering the

risk of infection with autologous bone grafts, we should consider using synthetic materials for primary cranioplasty after craniectomy.⁶⁾

This study showed excellent DSC values because reconstruction was conducted based on a mirror image (normal side). The mean value of DSC in this study was 0.75, showing an excellent volume match with the ideal model, which was the mirror image of the normal skull bone. A previous study evaluating the intraoperatively fabricated PMMA PSI reported a DSC value of 0.66 (median, 0.69; SD, 0.12).¹²⁾ Compared to this value, the DSC of the preoperatively manufactured titanium mesh PSI in our study had better results.

However, from the patient's perspective, cosmetic outcome refers to the outer view, including soft tissues. Craniectomy leads to temporalis muscle injury and progressive atrophy.^{3,9)} Therefore, even if the DSC of the implanted PSI is near 1, it does not necessarily ensure similarity of the outer surface.

It is widely accepted that disturbance of the vascular and nervous networks to the temporalis muscle contributes to the occurrence of temporalis muscle hollowing.^{3,9)} For the 32 patients of our study, we considered the temporalis muscle contour reconstruction from the manufacturing stage of PSI. There were 2 types of temporalis muscle reconstructions. One had an additional temporal plate (**FIGURE 4A**) and the other had deviation and elevation of the temporal plate without an additional plate (**FIGURE 4B**). Park et al.¹⁰⁾ showed a similar method called “Modified cranioplasty” with elevation of the temporal plate of the titanium PSI to prevent temporalis muscle hollowing. Their study evaluated the distance from the midline to the skin margin on postoperative axial and coronal CT scans, which showed that the difference was 2.24% higher in conventional cranioplasty coronal CT scans (-2.17% vs. +0.07%).⁹⁾ In our study, 40 patients with muscle reconstruction with or without additional temporal plate, reported their cosmetic outcome on a scale of 1 to 10. With scores 8–10 indicating very satisfactory outcome, 30 patients reported their cosmetic outcome as “very satisfactory”. Muscle reconstruction with or without additional temporal plate did not significantly affect the cosmetic outcomes. However, since a small number of patients were evaluated, a larger study is required.

Artifacts of metal implants limit further diagnostic evaluation using CT or MRI. In addition to metallic implants for cranioplasty, endovascular coil mass or orthopedic screws generate artifacts, and efforts have been made to reduce artifacts.^{7,15)} In general, the artifacts of solid metallic implants are similar to those of bone or objects with high noise because of their rough surfaces. In our study, we used mesh-type titanium, and the value of SNR was not

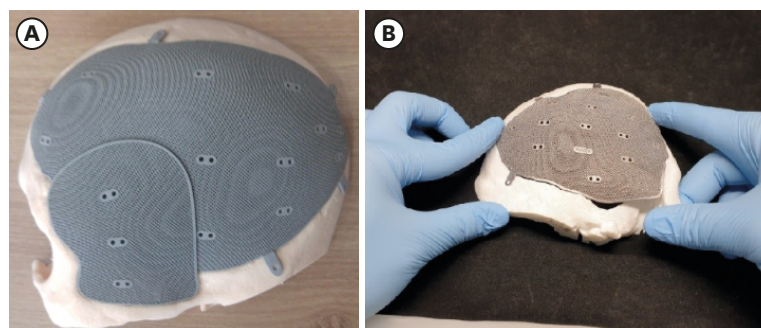


FIGURE 4. (A) Muscle reconstruction with additional temporal plate, (B) muscle reconstruction with deviation and elevation of the temporal plate without an additional plate.

very different from that of near-bone ROIs. By using titanium and fabricating the implant as mesh-type, we can obtain lower artifacts, which facilitates further radiologic examination of the patient.

CONCLUSION

Titanium mesh-type PSIs had superior clinical outcomes with respect to postoperative complications, patient satisfaction, and imaging artifacts. DSC evaluation showed a superior symmetry compared to that reported in other studies with different materials and manufacturing methods.

Further studies with larger patient groups and long-term follow-up periods with advanced materials and manufacturing techniques are warranted.

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SUPPLEMENTARY MATERIALS

SUPPLEMENTARY TABLE 1

Forty patients demographics

[Click here to view](#)

SUPPLEMENTARY TABLE 2

DSC values of 40 patients

[Click here to view](#)

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