



# Bone Flap Resorption Following Cranioplasty with Autologous Bone : Quantitative Measurement of Bone Flap Resorption and Predictive Factors

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**Objective :** To quantitatively measure the degree of bone flap resorption (BFR) following autologous bone cranioplasty and to investigate factors associated with BFR.

**Methods :** We retrospectively reviewed 29 patients who underwent decompressive craniectomy and subsequent autologous bone cranioplasty between April 2005 and October 2014. BFR was defined as : 1) decrement ratio ([the ratio of initial BF size/craniectomy size]–[the ratio of last BF/craniectomy size]) >0.1; and 2) bone flap thinning or geometrical irregularity of bone flap shape on computed tomographic scan or skull plain X-ray. The minimal interval between craniectomy and cranioplasty was one month and the minimal follow-up period was one year. Clinical factors were compared between the BFR and no-BFR groups.

**Results :** The time interval between craniectomy and cranioplasty was  $175.7 \pm 258.2$  days and the mean period of follow up was  $1364 \pm 886.8$  days. Among the 29 patients (mean age 48.1 years, male : female ratio 20 : 9), BFR occurred in 8 patients (27.6%). In one patient, removal of the bone flap was carried out due to severe BFR. The overall rate of BFR was  $0.10 \pm 0.11$  over 3.7 years. Following univariate analysis, younger age ( $30.5 \pm 23.2$  vs.  $54.9 \pm 13.4$ ) and longer follow-up period ( $2204.5 \pm 897.3$  vs.  $1044.1 \pm 655.1$ ) were significantly associated with BFR ( $p=0.008$  and  $0.003$ , respectively).

**Conclusion :** The degree of BFR following autologous bone cranioplasty was 2.7%/year and was associated with younger age and longer follow-up period.

**Key Words :** Autografts · Bone resorption.

## INTRODUCTION

Cranioplasty is usually performed for brain protection and cosmetic problem following decompressive craniectomy. Furthermore, previous studies have reported that cranioplasty improves neurological function<sup>11,12</sup>. In recent years, synthetic materials have been developed and occasionally used to re-

place autologous bone. However, autologous bone is still the preferred material because it has many advantages including low cost, lack of immunological response, and anatomical fit.

Cranioplasty is a relatively straightforward procedure. However, complications related to procedure including infection, wound dehiscence, postoperative hematoma or fluid collection, implant dislodgement, and bone flap resorption (BFR)

• Received : March 8, 2017 • Revised : June 29, 2017 • Accepted : August 2, 2017

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have been reported in many studies<sup>1,3,4,9,13,21,22</sup>. In particular, BFR remains a long-term concern after autologous bone cranioplasty and is considered a crucial factor for reoperation. Within the literature, the rate of BFR is reported to vary greatly from 2.7% to 51%<sup>3,6,7,12,18,21</sup>. To date, only few studies have attempted to identify the risk factors related to BFR<sup>2,3,7,18</sup>.

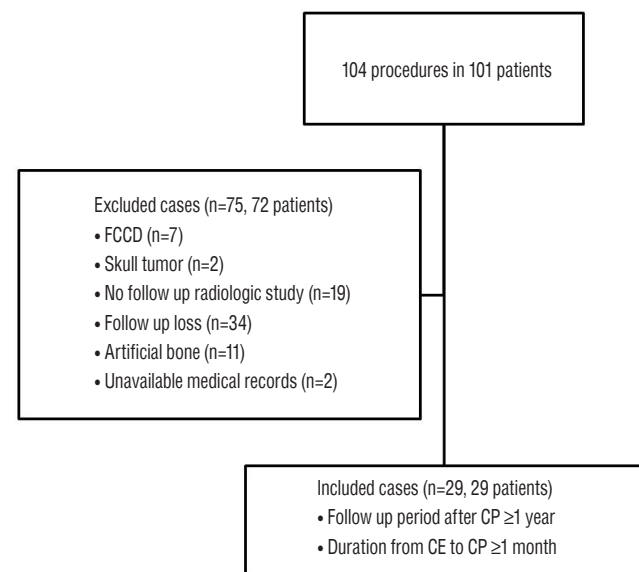
The aim of this study was to investigate the degree and related factors of BFR following autologous bone cranioplasty.

## MATERIALS AND METHODS

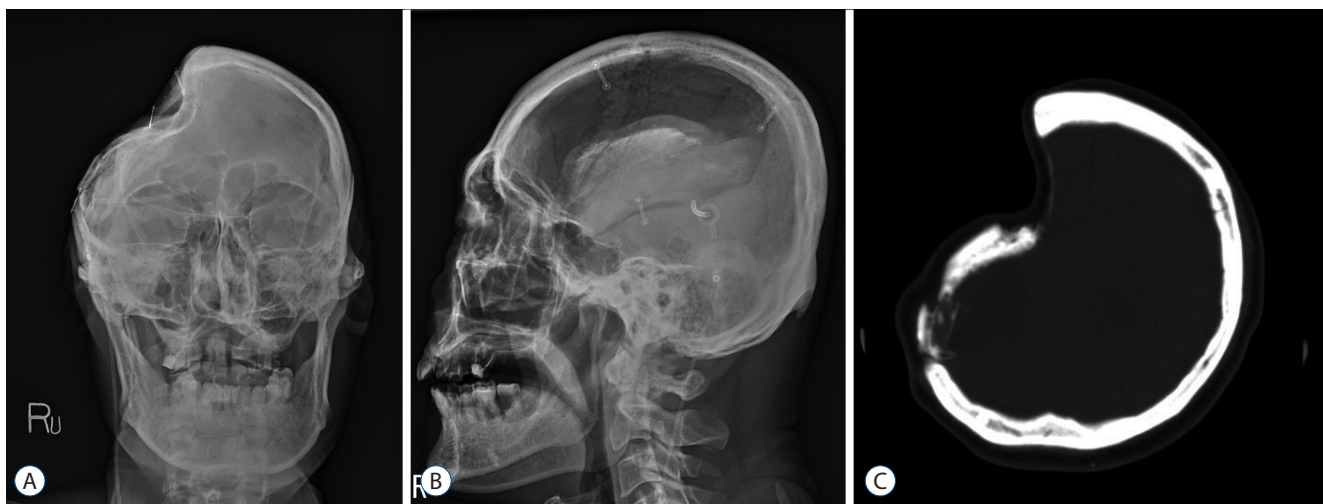
This study was designed as a single center retrospective cohort study. From April 2005 to October 2014, 101 patients who underwent cranioplasty following decompressive craniotomy for traumatic brain injury, subarachnoid hemorrhage, intracranial hemorrhage, brain tumor, and ischemic stroke were included. After excluding patients for exclusion criteria including follow-up loss, use of artificial bone, comminuted skull fracture, and skull tumor, 29 patients were included in the study (Fig. 1). Medical records were reviewed to determine initial diagnosis of craniectomy, age at cranioplasty, sex, past medical history, linear skull fracture, shunt-dependent hydrocephalus, duration from craniectomy to cranioplasty, operative time, infection, incidence of postoperative hematoma, and follow-up duration after cranioplasty.

BFR was defined as the followings : 1) decrement ratio ([the ratio of initial BF/craniectomy size]–[ratio of last BF/craniec-

tomy size]) >0.1; and 2) bone flap thinning or geometrical irregularity of bone flap shape on computed tomographic scan or skull plain X-ray (Fig. 2). The two-dimensional area was calculated on the computed tomographic scan or plain skull X-ray using the region of interest (ROI) parameter (free draw) in accordance to our institution's order communication system program, Maroview (version 5.409; INFINITT, Seoul, Korea) (Fig. 3). The minimal interval between craniectomy and cranioplasty was one month and the minimal follow-up



**Fig. 1.** Flow chart showing inclusion and exclusion criteria. FCCD : fracture compound comminuted depressed, CP : cranioplasty, CE : craniectomy.



**Fig. 2.** Plain skull x-ray anteroposterior (A), lateral view (B), and computed tomographic scan (C) demonstrating severe bone flap resorption 8 years after cranioplasty.

period was one year. BFR was determined based on the last follow up image.

We compared demographic and radiological factors between BFR and no-BFR groups. All continuous variables were presented as means±standard deviation. The Kruskal-Wallis test was used for continuous variables and Fisher's exact test for categorical variables. Results with two-tailed values less than  $p=0.05$  were considered statistically significant. All statistical analyses were performed using SPSS ver. 20.0 for Windows (IBM Corp., Armonk, NY, USA).

## RESULTS

The mean age of the 29 patients was  $48.1\pm19.7$  years (male : female ratio 20 : 9). Interval time between craniectomy and cranioplasty was  $175.7\pm258.2$  days and the mean follow-up period was  $1364\pm886.8$  days. A summary of the study population is described in Table 1.

BFR occurred in 8 patients (27.6%). There were no significant differences in the presence of skull fracture and shunt-dependent hydrocephalus between the BFR and no-BFR groups (Table 2). Furthermore, there were no significant dif-

ferences in operative time and duration of bone flap storage between the two groups (Table 3). The overall rate of BFR was  $0.10\pm0.11$  over 3.7 years and the degree of BFR was 2.7%/year. In other words, when BFR occurs, bone flap can be estimated to be resorbed at about 2.7% per year. Following univariate analysis, younger age ( $30.5\pm23.2$  vs.  $54.9\pm13.4$ ) and longer follow-up period ( $2204.5\pm897.3$  vs.  $1044.1\pm655.1$ ) were significantly associated with BFR ( $p=0.008$  and  $0.003$ , respectively) (Fig. 4). In one patient, removal of the bone flap was carried out due to severe BFR.

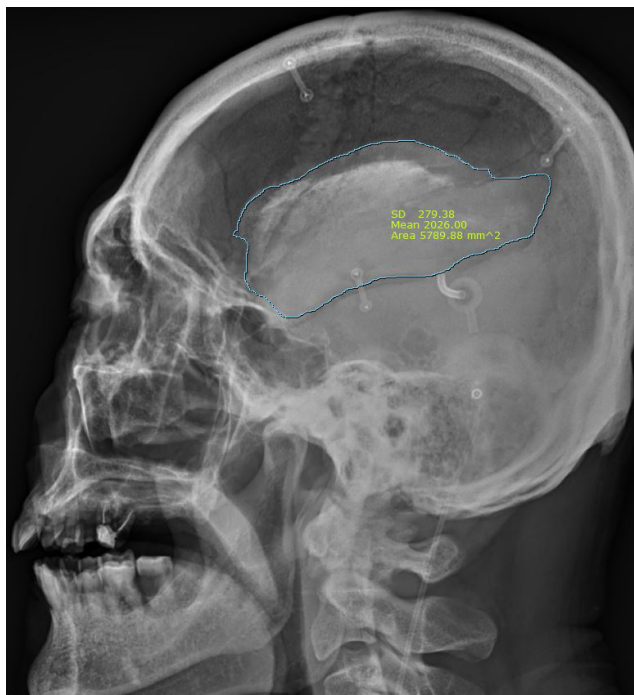
## DISCUSSION

This study showed that the degree of BFR following autologous bone cranioplasty was associated with younger age and longer follow-up period. Furthermore, the incidence and degree of BFR were found to be 27.6% and 2.7%/year after cranioplasty, respectively.

As previously mentioned, the incidence of BFR varies from study to study. These variations in BFR may be attributed to different BFR definitions and follow-up durations. Dünisch et al.<sup>7)</sup> measured defect size using the formula  $A=\pi/4\times B\times b$  (with B and b being the longest diameters of an elliptical area) and classified the degree of BFR as either type I necrosis (a thinning of the bone flap and/or a beginning resorption along the rims of the flap) or type II necrosis (as a circumscribed, complete lysis of the bone within the flap, including inner and outer table). Another investigator calculated defect size as an ellipse with  $\pi\times a\times b$  (longest axis being 2a and the 90° short axis being 2b)<sup>18)</sup>. Because these methods are semi-quantitative and BFR has an irregular margin, we quantitatively measured the decrement ratio of the bone flap size using the ROI curve. This method is quantitative and superior in calculating the BFR rate after cranioplasty.

Previous studies suggest younger age, bone flap fragmentation, shunt-dependent hydrocephalus, large bone defect, and time interval from craniectomy to cranioplasty are the risk factors of BFR<sup>3,6,19)</sup>. Younger age was also indicated as a risk factor of BFR in our study. Although the exact mechanism relating to this remains unknown, a thinner skull and faster bone turn-over may be associated with BFR in the younger population<sup>2,7,12,16,17,19)</sup>.

Bone flap fragmentation has also been suggested as a risk



**Fig. 3.** Quantitative measurement of two-dimensional bone flap size using a region of interest free draw curve.

**Table 1.** Summary of study population

Variable	Study population (n=29) (percentage or ratio)
Sex (male : female)	20 : 9 (2.2)
Age	48.1±19.7 (5–71)
Hypertension	
Yes	10 (34.5)
No	19 (65.5)
Diabetes mellitus	
Yes	10 (34.5)
No	19 (65.5)
Initial diagnosis	
Traumatic brain lesions	14 (48.3)
Cerebral infarction	3 (10.3)
Spontaneous ICH or SAH	10 (34.5)
Tumor	2 (6.9)
Skull fracture	
Yes	8 (27.6)
No	21 (72.4)
Operative time	152.1±54.8 (70–280)
Initial ratio of BF size/CE size	0.90±0.03 (0.82–0.96)
Last ratio of BF size/CE size	0.80±0.11 (0.45–0.92)
Delta ratio	0.10±0.11 (0.01–0.43)
Ventriculoperitoneal shunt	
Yes	8 (27.6)
No	21 (72.4)
Infection after CP	
Yes	4 (13.8)
No	25 (86.2)
Revised CP	
Yes	1 (3.4)
No	28 (96.6)
Epidural event after CP	
Yes	5 (17.2)
No	24 (82.8)
Duration of BF storage	175.7±258.2 (32–1245)
Duration of follow up after CP	1364.2±886.8 (377–3138)

Values are presented as mean±standard deviation (range) or number (%) unless otherwise indicated. ICH : intracerebral hemorrhage, SAH : subarachnoid hemorrhage, BF : bone flap, CE : craniectomy, CP : cranioplasty

factor for BFR<sup>2,3,19)</sup> and could potentially result in severe disruption of the blood circulation, disturbing angiogenesis, and leading to nutritional deficit of the bone flap<sup>2,3,8,19)</sup>. In 2013, Bowers et al.<sup>2)</sup> showed that comminuted skull fracture was a risk factors for BFR in pediatric patients following cranioplasty. On the contrary, there was no correlation between bone flap fragmentation and BFR in a study of younger patients <19 years of age<sup>10)</sup>. We assumed that comminuted fracture

**Table 2.** Univariate analysis of categorical variables between BFR and no-BFR groups

	BFR group (n=8)	No-BFR group (n=21)	p-value
Sex (M : F)	6 : 2	14 : 7	1.000
Hypertension			0.201
Yes	1	9	
No	7	12	
Diabetes mellitus			0.201
Yes	1	9	
No	7	12	
Diagnosis			0.916
Trauma	5	9	
Infarction	1	2	
ICH or SAH	2	8	
Tumor	0	2	
Skull fracture			1.000
Yes	2	5	
No	6	16	
VP shunt			1.000
Yes	2	6	
No	6	15	
Infection after CP			0.552
Yes	0	4	
No	8	17	
Revised CP			0.276
Yes	1	0	
No	7	21	
Epidural event after CP			1.000
Yes	1	4	
No	7	17	

BFR : bone flap resorption, M : male, F : female, ICH : intracerebral hemorrhage, SAH : subarachnoid hemorrhage, VP : ventriculoperitoneal, CP : cranioplasty

may hinder the bone remodeling process and our study population included only four patients <19 years, therefore we did not investigate correlation between comminuted fracture and BFR. Instead, we investigated the association between linear skull fracture and BFR and found no statistically significant difference.

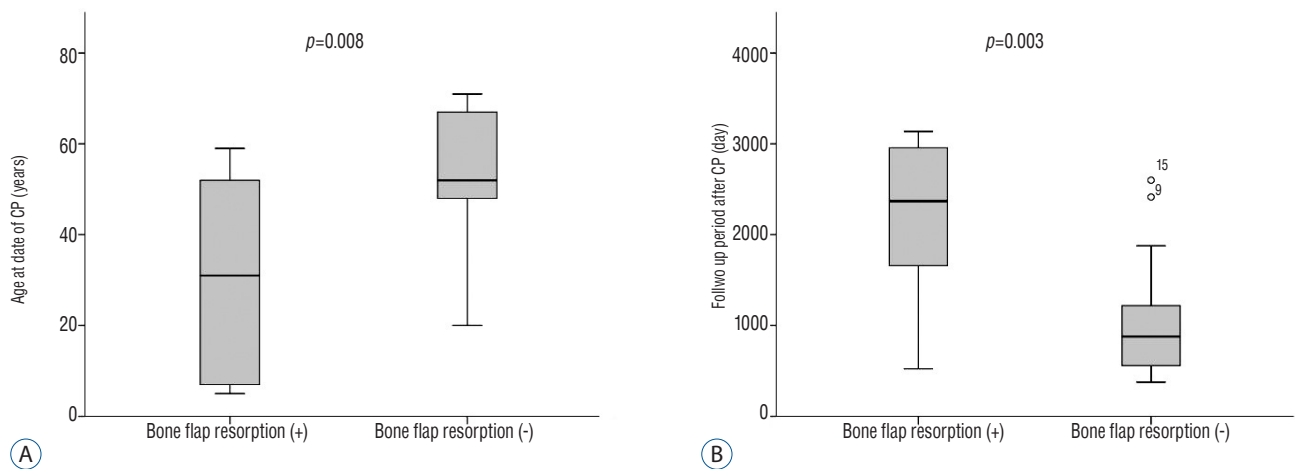
Shunt-dependent hydrocephalus as a risk factor for BFR is controversial. Some studies suggest that shunt placement reduces adherence of the dura mater to the bone flap and negatively influences skull growth, thus contributing to BFR<sup>2,7,10,15,19)</sup>. However, in agreement with our finding, Brommeland et al.<sup>3)</sup> failed to demonstrate correlation between shunt-dependent hydrocephalus and BFR.

Another controversy is the effect of time interval to cranio-

**Table 3.** Univariate analysis of continuous variables between BFR and no-BFR groups

Variable	BFR group (n=8)	No-BFR group (n=21)	p-value
Age (years)	30.5±23.2	54.9±13.4	0.008
Operative time (min)	181.8±50.9	140.8±53.0	0.067
Initial BF size (mm <sup>2</sup> )	9823.1±3763.6	7840.7±3257.6	0.324
Initial ratio of BF/CE size	0.92±0.02	0.89±0.03	0.093
Last ratio of BF/CE size	0.68±0.15	0.84±0.05	0.001
Delta ratio (initial ratio-last ratio)	0.24±0.14	0.04±0.03	0.000
Duration of BF storage (days)	125.6±46.1	194.9±302.0	0.279
Duration of FU after CP	2204.5±897.3	1044.1±655.1	0.003

Values are presented as mean±standard deviation. BFR : bone flap resorption, BF : bone flap, CE : craniectomy, FU : follow-up



**Fig. 4.** Box plot showing bone flap resorption related to the age at the date of CP (A) and bone flap resorption related to follow up period after CP (B). CP : cranioplasty.

plasty. Many investigators recommend cranioplasty be performed after 3 months from craniectomy if the neurological status and medical conditions are stabilized<sup>4,7)</sup>. Conversely, delayed cranioplasty can result in complications such as sunken scalp, decreased brain perfusion, and abnormal cerebrospinal fluid dynamics. In a retrospective study of 77 patients with autologous bone flap, longer duration between craniectomy and cranioplasty was associated with BFR<sup>3)</sup>. However, in agreement with our findings, a recent study failed to demonstrate any association between the timing of cranioplasty and BFR<sup>7)</sup>. This discrepancy may be attributed to the heterogeneous and retrospective design of each study.

Recent research has indicated an association between bone flap storage method and BFR<sup>5,14)</sup>. A retrospective study of 290 patients showed that the incidence of BFR was higher in the cryopreservation group compared with the subcutaneous pocket group<sup>5)</sup>. The authors hypothesized that cryopreserva-

tion of the bone flap might lead to increased osteoclast activity and bone resorption<sup>5)</sup>. Interestingly, bone flap storage in the abdominal subcutaneous fat is reported to lead to osteolysis by macrophages, which may result in enhanced BFR<sup>20)</sup>. Cryo-preserved autologous bone grafts were used in the current study, therefore we could not compare the incidence of BFR according to storage methods.

This study has some limitations. First, this single center study is limited by its small size and retrospective design. Second, two-dimensional measurement of stereoscopic bone flaps may be problematic in determining the exact area. When considering the curvature of skull vault, the degree of BFR can be underestimated at the near the vertex of skull. Third, although the longer the duration of follow-up, the risk of BFR increased, we could not estimate whether every bone flap might undergo resorption or there might be time window for osteoconduction of re-inserted bone flap. Further research



will be needed. Nonetheless, we minimized measurement error by calculating the area difference using a program that enabled the ROI free draw method.

## CONCLUSION

The risk of BFR following autologous bone cranioplasty is associated with younger age and longer follow up period. Thus, radiological long-term follow up is recommended in the younger population.

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