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RESEARCH

# Volumetric changes in the bone flap at one year follow up in patients undergoing craniotomy

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**Abstract**

Although bone resorption has been extensively reported following craniectomy, bone resorption and fusion rates following craniotomy remains unexplored. The aim of the present study was to conduct a volumetric assessment of craniotomy resorption and fusion rates at one year following the index surgery. Adult patients who had a computed tomography scan immediately after craniotomy and at one year follow up were included in the study. Various baseline demographic variables and reason for craniotomy, method of fixation, and post-operative complications were recorded. 3D-Slicer was used to demarcate the bone flap segments – central flap, flap edge, kerf, burr-holes, and periphery and the volumes of both computed tomography scans were compared. 34 patients with a mean age of 59.29 ± 17.77 years were included in the study. Tumors were the most common indication of craniotomy. Four patients reported significant pain related to their hardware and one patient reported postoperative cerebrospinal fluid leakage. The mean follow-up period was 357.4 ± 62.67 days. An overall increase in the bone volume was observed in the kerf (+ 8.46%) and burr-hole regions (+ 12.92%) while the central flap (-1.55%), flap edge (-4.48%) and periphery (-3.5%) depicted bone resorption. The increase in volume in the kerf space represents at an average less than 10% bridging of the gap and is far from fusion. On multivariable regression, a negative correlation was observed between the change in peripheral bone volume and patient age and a positive correlation between male sex and flap edge volume change. Cranial flap bone loss in patients who underwent craniotomy was quantified in this study while an overall increase in bone volume was observed in the regions of the kerf and the burr-holes one-year postoperatively, less than 10% of the kerf space was bridged by bone.
Clinical Trial Number: Not Applicable.

**Keywords** Craniotomy · Bone Flap Remodeling · Trauma · Critical Care · Bone Resorption · Computed Tomography

## Introduction

Craniotomy is the cornerstone of contemporary neurosurgery [1, 2]. Although bone resorption is an established complication following craniectomy, analyses of bone resorption and bony fusion following craniotomy are scarce [3–5]. Recently, synthetic implants have been increasingly utilized as replacements for bone flaps; however, there is growing evidence indicating a heightened risk of complications, including bone flap resorption and surgical site infections in these cases [6–8]. A recent study examining complications associated with the use of plates for bone replacement reported infections in 39% of the cases, with discrepancies in implant brand and size observed in 30% of the cases [9]. Previous research has also highlighted the elevated risk of infections and the need for plate removal in instances involving titanium plates and screw fixation [10]. Cerebrospinal fluid (CSF) leakage, reported in 1–14% of cranial procedures, can further lead to complications such as meningitis, intracranial hypotension, and subdural hematoma if not promptly diagnosed [11]. While dural interventions play a critical role in postoperative CSF leakage, the absence of robust bone fusion may further exacerbate the risk of CSF leakage.

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Previous studies have sought to quantify the rates of bone fusion and resorption in patients undergoing cranial interventions. *Korhonen* et al. in their cohort of 45 patients, observed bone flap resorption in approximately 90% of cases at follow-up, with participants under 30 years of age exhibiting significantly reduced bone flap volumes [12]. Similarly, *Adaaquah* et al. reported solid and probable fusion in 60% and 15% of the study cohort, respectively. [1]. Another study reported an overall fusion rate of 76.6% among 276 patients who underwent craniotomy [4]. Although *Korhonen* et al. attempted to assess the volumetric changes in cranioplasty bone flaps, no comparable studies have employed volumetric assessment to evaluate bone flap changes in patients following craniotomy [1, 4, 12].

Our study seeks to address a notable gap in literature quantitatively evaluating the rates of bone flap resorption in craniotomy patients, an area less explored compared to bone fusion post cranioplasty. Specifically, we aim to investigate the extent of bone flap resorption by quantitatively analyzing computed tomographic (CT) scans obtained postoperatively and comparing them with scans taken at one-year follow-up, using a standardized volumetric segmentation protocol. Additionally, we aim to elucidate factors that may influence the rate of bone flap resorption.

## Methodology

### Study design

This was a retrospective study, enrolling patients who underwent a craniotomy between June 2006 – June 2020 at Massachusetts General Hospital and Brigham and Women's Hospital, Boston, MA. Patients were then included based on the established inclusion and exclusion criteria of the study. Patients who i) had a postoperative head CT as well as one at a one-year follow up, ii) underwent craniotomy for any indication, and iii) were above the age of 18 years, were included in the study. Patients who i) underwent a decompressive craniectomy, ii) did not have a follow up scan at 12 months post-operatively, iii) were below the age of 18 years, iv) died within the first year of follow up v) had a prior neurosurgical procedure of the cranium and vi) had a low-quality CT scan were excluded.

### Variables

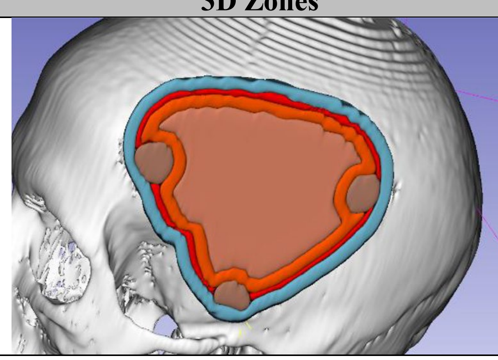
In this study, baseline demographics, including age at the time of surgery and sex, were recorded for all patients. Additional data related to craniotomy procedures were also documented, such as the date of craniotomy, the specific region(s) of the craniotomy, and the method of flap fixation. Information on the occurrence of flap migration and postoperative complications, including postoperative pain, surgical site infections, cerebrospinal fluid leakage, and any subsequent readmissions, was systematically collected.

### CT analysis

3D slicer is an open-software platform widely utilized for visualization, analysis, and processing of medical imaging data. In the present study, 3D Slicer was used to quantify mineralized volume at the immediate postoperative and follow-up timepoints within five different zones: the central region of the flap, flap edge (peripheral region of the flap), the burr holes, kerf (the region between flap edge and peripheral cranium), and the peripheral cranial region as shown in Table 1 [13]. [Table 1].

The CT datasets, at immediate post-op and follow-up, were loaded in Slicer (v5) with a constant threshold of 500 to 2000 HU (Hounsfield Units) applied to preferentially select mineralized bone and reject metallic hardware. The outlines of the flap, burr-holes, and surrounding bone were marked manually using the scissors tool on an orthographic projection of the immediate post-op skull [Fig. 1]. These markups were used to generate extruded zones for measurement of mineralized volume [Fig. 1D]. These zones were 1) central flap – material at the center of the flap, at least 5 mm away from the kerf, 2) flap edge – material at the edge of the flap, within 5 mm of the kerf,

**Table 1** Measurement zones in and around the cranial flap

| Zone | | 3D Zones |
|---|---|---|
| z1 | Flap central |  |
| z2 | Flap edge | |
| z3 | Burrholes | |
| z4 | Kerf | |
| z5 | Peripheral | |
| Flap edge and peripheral bone are 5 mm wide. | | |

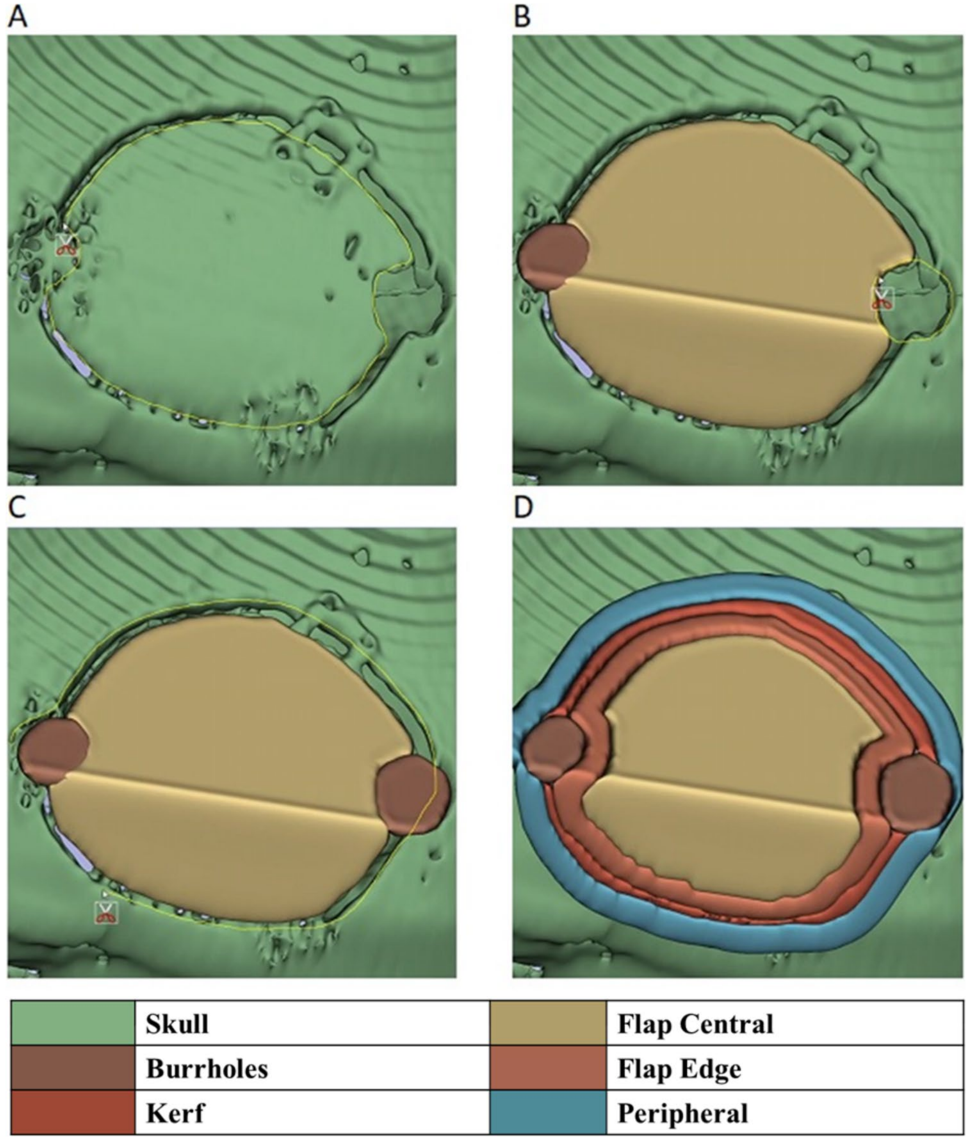



**Fig. 1** Manual markup of cranial flap; **A**) flap, **B**) burr-hole, **C**) surrounding bone, and **D**) Extruded volume measurement zones

3) burrholes – material within the burr-holes, 4) kerf—material within the kerf, and 5) peripheral – material in the surrounding area, within 5 mm of the kerf. The follow-up dataset was aligned with the post-op skull using the transforms and fiducial registration modules of Slicer. At least three landmarks, that were simultaneously identifiable on the immediate post-op and follow-up skulls, were placed to obtain rough alignment of the two timepoints before fine-tuning the alignment using the transforms module. The extruded zones were then intersected with the thresholded immediate post-op and follow-up skulls to measure the mineralized volumes within each zone. Typical resulting segments at the two time points are shown in Fig. 2. [Fig. 2] Additionally, the empty kerf volume in each cranial flap was estimated by multiplying the kerf circumference with the average thickness of cranial flaps (6.28 mm) and the kerf width (2.25 mm).

## Statistical analysis

Descriptive statistics were used for all the continuous variables. A Pearson-correlation was used to analyze the association of the various segments of the bone flap (central flap, edge, kerf, burr-holes and kerf). A linear and logistic regression analysis was performed to analyze the association of the change in the volumes and the various continuous and categorical clinical variables respectively. A multivariate regression analysis was conducted to adjust for potential confounders influencing variations in bone volume. The covariates included in the model were age and sex of the patient, craniotomy location, surgical indications, and postoperative complications. A p-value of $<0.05$ was established as an indicator of significance. R Studio 4.2.3 was used for performing the various statistical tests [14].

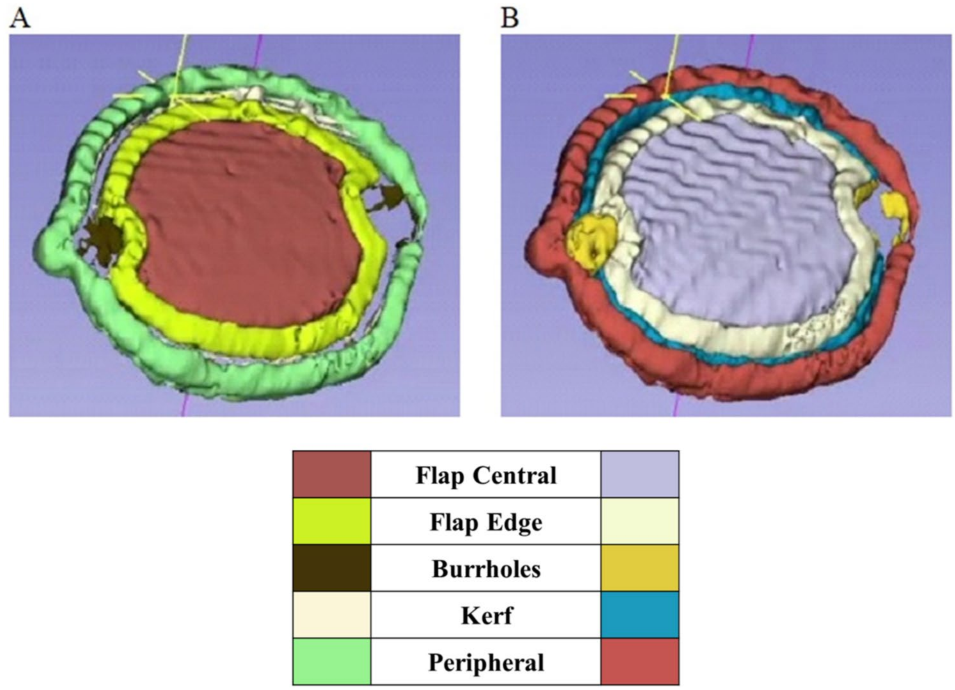



**Fig. 2** Typical measurement segments at **A**) immediate post-op, and **B**) follow-up

## Results

From an initial number of 125 participants, a total of 34 patients were included in the study with a mean age of 59.29 ± 17.77 years and a 16:18 male: female ratio [Fig. 3]. The predominant indication for initial craniotomy was tumor (n = 22), followed by traumatic brain injury (n = 5), vascular or intracranial hemorrhage (n = 4), functional disorder (n = 2), and infective pathology (n = 1). The frontal region was most operated upon in these patients (n = 22), followed by parietal (n = 20), temporal (n = 10) and occipital (n = 3). Fixation involved the utilization of plates and screws, with no reported cases of implant migration. Postoperative outcomes revealed significant pain at the hardware fixation site in 4 patients (11.76%), while cerebrospinal fluid leakage occurred in 1 patient (2.94%), and no surgical site infections were noted. The mean period of follow up between the initial post-operative CT scan and the follow-up was 357.4 ± 62.67 days. During this period, 31 patients (91.18%) required readmission, although none were related to procedure related complications and no patient underwent revision surgery. [Table 2].

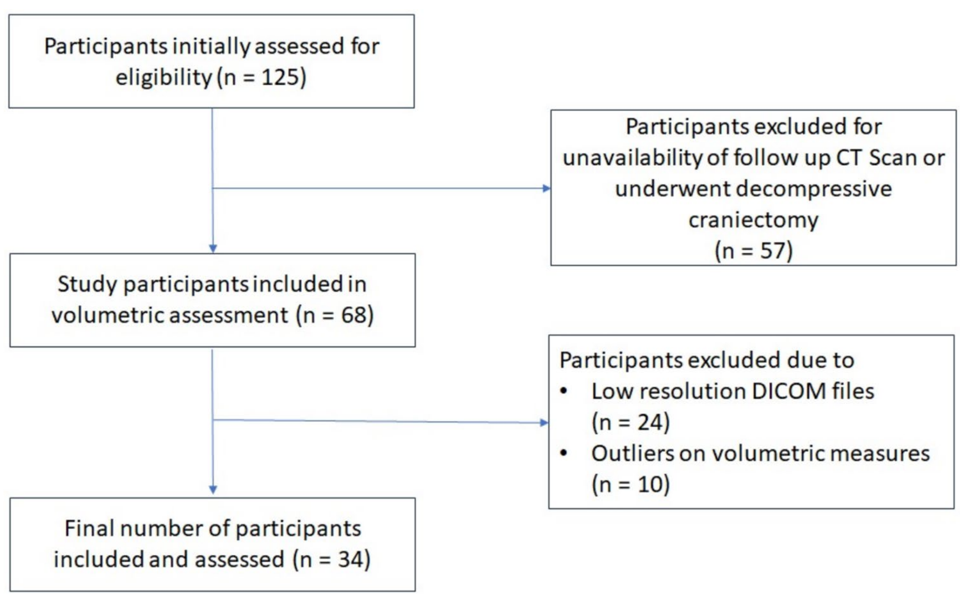



**Fig. 3** Figure describing the inclusion of patients as per the STROBE criteria

At the end of the follow up period, the volumetric changes of central flap, flap edge, kerf, burr-holes, and peripheral bone were assessed. Analysis revealed an overall increase in the mean bone volumes of burr-holes and kerf with 30.6% and 8.56% respectively. A majority of 26 patients (n = 76.5%) for kerf and 24 (n = 70.6%) for burr-holes demonstrated an overall increase in their respective volumes. The kerf and burr-hole volumes are small in the post-op condition, and this percent change through follow-up represents only a small increase in bone volume in these segments, averaging 0.33 cc increase in each segment across all patients, and does not represent fusion across the gap. The average empty kerf space was 3.47 cc and this change only represents bridging of 9.64% of this volume. On the contrary, there was a decrease in the mean volumes of central flap, flap edge and peripheral bone, with overall difference of −1.55%, −1.48% and −3.5% respectively. Of the 34 patients, 21 (61.8%), 24 (70.6%) and 23 (67.6%) exhibited an overall decrease in bone volumes for central flap, flap edge and peripheral bone, respectively. [Table 3].

There was a strong correlation observed between the overall volume change of the central flap and flap edge segments ($r = 0.704$, p-value $< 0.0001$). Similarly, a moderately strong correlation was found between the volume changes of central flap and peripheral segments ($r = 0.612$, p-value $= 0.0001$). However, correlations between the volume changes of other segments were weaker. No significant correlation was observed between the volumetric changes between the flap edge segment and the burr-holes ($r = 0.235$, p-value $= 0.18$) or between the volumetric changes in the peripheral segment and burr-holes ($r = 0.336$, p-value $= 0.052$). [Table 4].

Regression analysis revealed significant associations between volumetric changes in specific segments and patient characteristics. Notably, there was a significant negative correlation between the volumetric change of the peripheral segment and the age of the patients at surgery ($ß = -0.0017$, p-value $= 0.014$), indicating a decrease in peripheral segment volume with increasing age. Additionally, a significant association was found between the volumetric change of the flap edge segment and the sex of the patient ($ß = 0.093$, p-value $= 0.011$), suggesting a positive

**Table 2** Table depicting the demographic characteristics of all the study participants. * N = number of participants; SD = Standard Deviation

| Characteristic | N |
|---|---|
| Age (mean ± SD) (in years) | 59.29 ± 17.77 |
| Range | 24–88 |
| Sex | |
| Males | 16 |
| Females | 18 |
| Site of Craniotomy | |
| Frontal | 22 |
| Parietal | 20 |
| Temporal | 10 |
| Occipital | 3 |
| Indication | |
| Tumor | 22 |
| Vascular | 4 |
| Trauma | 5 |
| Functional | 2 |
| Infective Pathology | 1 |
| **Cerebrospinal Fluid Leak** | 1 |
| **Post-operative Pain** | 4 |
| **Readmission** | 31 |

**Table 4** Table describing the correlation between the volumetric changes in the various bone flap segments at one year follow up. Significant p-value < 0.05

| Bone Segment | Central Flap | Flap Edge | Kerf | Burr-holes | Peripheral |
|---|---|---|---|---|---|
| **Central Flap** | 1 | 0.704 | 0.477 | 0.436 | 0.612 |
| | - | **< 0.0001** | **0.004** | **0.01** | **0.0001** |
| **Flap Edge** | 0.704 | 1 | 0.467 | 0.235 | 0.478 |
| | **< 0.0001** | - | **0.005** | 0.18 | **0.004** |
| **Kerf** | 0.477 | 0.467 | 1 | 0.423 | 0.392 |
| | **0.004** | **0.005** | - | **0.013** | **0.022** |
| **Burr-holes** | 0.436 | 0.235 | 0.423 | 1 | 0.336 |
| | **0.01** | 0.18 | **0.013** | - | 0.052 |
| **Peripheral** | 0.612 | 0.478 | 0.392 | 0.336 | 1 |
| | **0.0001** | **0.004** | **0.022** | 0.052 | - |

**Table 3** Table describing the volumetric changes in the various bone flap segments at one year follow-up

| Segment | Average Volumetric Change (in %) | Standard Deviation (in %) | Increased Bone Volume (n) | Decreased Bone Volume (n) |
|---|---|---|---|---|
| Central Flap | −1.55 | 9.74 | 13 | 21 |
| Flap Edge | −4.48 | 10.99 | 10 | 24 |
| Kerf | 8.46 | 12.92 | 26 | 8 |
| Burr-holes | 30.6 | 49.54 | 24 | 10 |
| Peripheral | −3.5 | 7.28 | 11 | 23 |

correlation between male sex and volumetric changes in the flap edge segment. Furthermore, no significant associations were observed between volumetric changes in various segments and the indication of surgery or the duration of the follow-up period.

In multivariate regression analysis, age remained the sole predictor negatively associated with volumetric change in the peripheral segment (ß = −0.0018, p-value = 0.03), reinforcing the inverse relationship between age and peripheral segment volume change. Similarly, male sex continued to be correlated with volumetric changes in the flap edge segment (ß = 0.109, p-value = 0.007), underscoring the positive association between male sex and changes in flap edge segment volume.

## Discussion

Our study is the first to evaluate the quantitative volumetric changes in the craniotomy bone flap at one-year follow-up using a systematic segmentation methodology, while also analyzing the factors that may contribute to bone remodeling. We observed a volumetric increase in the burr-hole and kerf regions (30.6% and 8.56% respectively). This volumetric increase averaged 0.33 cc in the kerf region, accounting for less than 10% of the empty kerf space. Conversely, the central flap, flap edge, and peripheral bone regions exhibited an overall volumetric decrease. Significantly strong correlations were observed between the volumetric changes within the central flap and flap edge, and the flap edge and peripheral bone. Furthermore, regression analysis demonstrated a significant relationship between increasing age and peripheral bone volumetric changes and between male sex and flap edge volumetric changes.

Bone flap resorption and fusion has been widely studied in the cranioplasty population, but remains underreported following craniotomy [5]. *Adaaquah* et al. described fusion based on the presence and extent of bony bridges between the bone-flap and cranium, classifying it as solid, probable or non-fusion [1]. *Jeon* et al. similarly analyzed bone fusion on follow-up CT scans. identifying areas with an overall gap of < 1 mm as fusion [4]. In contrast, our study introduces a novel approach to analyze the extent of bone resorption and fusion by regionally dividing the bone flap and the surrounding cranium into central flap, flap edge, kerf and peripheral bone to assess their respective volumetric changes. Resorption was observed in the central flap (61.8%), flap edge (70.6%), and periphery (67.7%). An increase in the kerf volume was observed in 76.5% of patients, however this was limited to an average of 0.33 cc, which constitutes only 10% of the empty kerf volume and was not suggestive of bony fusion across the gap. Future studies should aim to correlate the volumetric changes within specific regions of the craniotomy bone flap with standardized qualitative assessments to establish quantitative thresholds defining bone fusion.

Several factors influencing the rate of bone resorption or fusion have been identified. A study involving 125 cranioplasty patients reported younger age, bone flap fragmentation, long storage time for bone flap, and lower Glasgow Outcome scores at time of cranioplasty were associated with bone resorption [6]. Conversely, *Adaaquah* et al. observed no association between bone fusion and clinical factors including age, sex, body mass index, type of fusion material or radiation exposure [1]. Our study demonstrated a significant negative association between the peripheral bone volumetric changes and age as well as positive association between the flap edge volumetric changes and male sex. Patient age has previously been identified as a factor that affects bone flap resorption and fusion in patients who had undergone cranioplasty [6, 12]. This could be potentially explained by the differential rate of fusion and resorption owing to age-related changes in bone metabolism and hormonal influences on bone health [15, 16]. Additionally, previous pre-clinical and clinical studies have observed significant differences in bone healing, attributed to the underlying role of sex-hormones on osteogenesis [17]. However, qualitative studies by *Adaaquah* et al. and *Joen* et al. did not observe sex-based differences [1, 4] possibly reflecting methodological differences, as our study employed a quantitative assessment of volumetric changes. A comparison of fusion materials impacting bone remodeling was not possible, as all the patients underwent bone flap placement using plates and screws [18, 19].

We observed regional differences in volumetric changes, suggestive of simultaneous bone fusion and resorption, collectively referred to as bone flap remodeling. Previous studies have reported bone flap resorption rates of 16% in adults and 39.2% in pediatric patients undergoing decompressive craniectomy [20]. Although certain factors including age, bone multifragmentation, and incidence of postoperative complications have been implicated, the underlying mechanism remains unclear [4, 21]. The rate of bone flap fusion varies by cranial region, with frontal and parietal bones supporting a higher density of osteoblasts and vascularity, compared to parietal and occipital regions. Calvarial bone formation occurs via intramembranous ossification, wherein the mesenchymal cells differentiate into osteoblasts, secrete osteoid, and form trabecular bone [1, 22]. In the post-operative period, elements of the process of intramembranous ossification may be reinitiated at bone-flap interface, however, systemic, and cellular factors can disrupt bone regeneration and fusion. While our study provides quantitative evaluation of bone-flap regional volumetric changes, larger prospective studies should evaluate the quantitative rate of bone fusion and resorption and the factors influencing these processes.

Innovative materials for cranioplasty have significantly advanced the field, with materials like polyetheretherketone (PEEK) and porous polyethylene (PE) offering exceptional mechanical strength, biocompatibility, and adaptability for 3D printing, enabling the creation of patient-specific implants [23–26]. Additionally, the development of biodegradable polymers such as poly(lactic-co-glycolic acid) (PLGA) and bioactive glass composites has further expanded the options for effective bone fusion and repair [27]. A novel regenerative bone adhesive, Tetranite, stands out for its ability to bond bone to bone and metal, while also promoting osteogenesis, enhancing the healing process, and has shown to improve fixation strength and CSF leakage resistance in cadaver human skull osteotomies [28].

A major strength of this study was the use of 3D slicer to analyze the regional volumetric changes of the bone flaps with comparatively higher precision, compared to the qualitative approach used in previous studies [1, 4]. The volumetric increase within the kerf region, highlights the need for meticulous opposition of the bone flap and consideration of adjunctive strategies promoting osteogenesis. The study findings suggest investigation into fixation techniques and materials that may improve long-term bone fusion. Quantitative volumetric analysis may help identify patients at risk of incomplete fusion, informing surgical planning and follow-up.

The study is limited by the small sample size, considering exclusion of patients without high-resolution CT scans at one-year follow-up post-craniotomy. The prevalence for MRI in follow-up imaging further reduced the eligible cases. Segmentation for individual cases was performed by a single-trained reviewer, and thus the inter-rater reliability was not assessed. Additionally, we could not account for variables such as radiation exposure, smoking status, existing comorbidities, and use of certain medications due to the limited study cohort and heterogeneity in surgical indications.

Future prospective studies should incorporate multi-reviewer segmentation, histological evaluation of bone fusion and resorption and respective correlation, and stratification by surgical indications and fusion techniques. Given the variability in bone remodeling, patient-related cosmetic outcomes should be evaluated to further understand the clinical and aesthetic implications of post-operative bone remodeling.

## Conclusion

There exists a certain amount of variability with regards to the bone segment volume in patients undergoing craniotomy at one year follow up. An overall decrease in the bone volume was observed in the central flap, flap edge and the periphery, in the majority of the patients, suggestive of bone resorption while kerf and burr-holes demonstrated an overall increase in the bone volume, suggestive of bone regeneration in these areas, but represents at an average less than 10% fusion or bridging of the gap. In fact, in a third of the patients, there was further reduction of bone volume in these segments. While age and sex have been determined to be factors that influence bone fusion and resorption, future studies should explore other demographic and clinical factors that may affect bone flap remodeling.

**Author contribution** Initial design and conception—SB, JKVG, TRS; Data Collection—HA, KB, AP, HH, SS, JLK, JKVG; Data Analysis—HA, SB; Manuscript Draft Writing—HA, SB, AGY, JKVG, CSH; Final Review and Revisions—HA, JKVG, CSH, TRS.

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**Data availability** No datasets were generated or analysed during the current study.

## Declarations

**Ethical approval** The study was conducted under IRB 2015P002352.

**Informed consent** Given the retrospective design of the study, informed consent was waived.

**Competing interests** The authors declare no competing interests.

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