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DOI:

[10.1016/j.jcms.2016.03.010](https://doi.org/10.1016/j.jcms.2016.03.010)

Document Version

Peer reviewed version

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Citation for published version (APA):

Williams, L., Fan, K., & Bentley, R. (2016). Titanium cranioplasty in children and adolescents. *Journal of Cranio-Maxillofacial Surgery*. Advance online publication. <https://doi.org/10.1016/j.jcms.2016.03.010>

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Accepted Manuscript

Titanium cranioplasty in children and adolescents

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PII: S1010-5182(16)00088-3

DOI: [10.1016/j.jcms.2016.03.010](https://doi.org/10.1016/j.jcms.2016.03.010)

Reference: YJCMS 2325

To appear in: *Journal of Cranio-Maxillo-Facial Surgery*

Received Date: 27 November 2015

Revised Date: 17 March 2016

Accepted Date: 21 March 2016

Please cite this article as: Williams L, Fan K, Bentley R, Titanium cranioplasty in children and adolescents, *Journal of Cranio-Maxillofacial Surgery* (2016), doi: 10.1016/j.jcms.2016.03.010.

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Titanium cranioplasty in children and adolescents

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SUMMARY AND KEYWORDS

SUMMARY

Full thickness calvarial defects present considerable challenges to reconstructive surgeons. In paediatric cases, the use of biomaterials as a substrate for cranioplasty rather than autologous bone is controversial. Alloplastic cranioplasty in adults is supported by several large case series however long term outcome of biomaterial use in paediatric cases is limited. Retrospective seven year analysis of departmental database and clinical records identified 22 patients aged under 18 who had undergone 23 custom made titanium cranioplasties by a single surgeon using the same technique. Data including patient demographics, reason for craniectomy and complications experienced following surgery was obtained. The mean age at operation was 12 years 9 months. The mean defect size was 44.3cm². No significant complications related to the cranioplasty were recorded in the early post operative period or during long term review (average follow up 4 years 6 months). No cranioplasty implant required removal. This retrospective case series shows that custom made patient specific titanium cranioplasty is a viable alternative to autologous bone as a reconstructive material in paediatric patients under specific circumstances.

KEYWORDS

Cranioplasty, calvarial reconatruction, paediatric, biomaterials, patient specific implants

MAIN TEXT

Introduction

The use of biomaterials rather than autologous bone grafts in paediatric cranioplasty is controversial (Gosain et al., 2009). Despite several decades of technique refinement no single method has proved superior and gained widespread acceptance. Full thickness calvarial defects arise from numerous pathologies including congenital defects, osteomyelitis, trauma, tumour resection, decompressive procedures and infected or resorbed bone flaps replaced following conventional neurosurgery. Calvarial defects expose brain to trauma and can create significant cosmetic morbidity, especially if the defect is large, and can have significant negative impact on active, school age children. The most common donor sites for full thickness calvarial defects are split calvarial grafts and split ribs (Tessier et al., 2005; Jackson et al., 1986). Autogenous bone provides a biological reconstruction that has the potential to grow with the patient and once revascularised has minimal long term infection risk, however limitations include donor site morbidity, limited availability of sufficient bone, difficulty in contouring grafts adequately (Frodel et al., 1993) and high incidence of resorption compared to adults (Grant et al., 2004). Biomaterials in current use include acrylics, ceramics, polyethene, polyetheretherketone (PEEK) and titanium (Cho and Gosain., 2004; Hanasono et al., 2009). Each material has relative merits and disadvantages, however the principle concerns in using biomaterials in paediatric cranioplasty relate to the possible deleterious effects of a rigid material on normal cranial growth, intracranial migration of reconstruction components and high incidences of failure through infection, adverse tissue reactions and material breakage (Resnick et al., 1990; Wong et al., 2011; Yaremchuk et al., 1994; Beck et al., 2002; Papay et al., 1995; Kosaka et al., 2003; Josan et al., 2004; Moreira-Gonzalez et al., 2003).

Several large case series exist of cranioplasty using biomaterials in adult populations (Wehmöller et al., 2004; Joffe et al., 1999; Shoakazemi et al., 2009; Marchac and Greensmith 2008), however the

data concerning cranioplasty using an alloplastic material as a substrate in children is limited. A retrospective analysis was carried out to determine outcome of all custom made patient specific titanium cranioplasties performed by the senior author (RPB) in paediatric patients. A literature search was carried out in addition to identify case series of cranioplasty in the paediatric population to assess current methods of calvarial reconstruction and limitations associated with these techniques in this age group.

Materials and Methods

Ethical approval was not required for this study. Custom made titanium cranioplasty plates were used in this series of patients. A fine cut spiral CT of the head is obtained (0.5mm slice, 0° gantry angle) and the DICOM data from this used to generate an STL format file which is then used to produce a model of the patient's skull using additive manufacturing. This biomodel is then used to reconstruct the defect in plaster before using the reconstructed bio-model in a hydraulic press to cold form 0.8mm thick titanium sheet. This results in an accurately fitting, low profile onlay implant that precisely reconstructs normal cranial volume and projection of the skull. Several holes are drilled in the plate to prevent extradural accumulation of fluid and to allow for titanium screw fixation. The plate is anodised, etched with nitrofluoric acid and autoclaved prior to insertion.

In all cases incisions utilise previous scars or are planned to allow best access without compromising vascularity of the overlying scalp and to avoid closing scalp wound margin directly over the cranioplasty plate. The defect is exposed in sub-periosteal plane and the cranioplasty plate is secured using titanium screws ensuring rigid fixation. The scalp is closed in layers over suction drains that are generally removed at 48 hours post procedure. Antibiotic prophylaxis is given for the procedure and continued for a total of one week.

Departmental database and laboratory records were used to identify paediatric patients who underwent titanium cranioplasty using the described method by a single surgeon. The clinical

records were then analysed and data collected using a proforma. Data collected included pathology leading to calvarial defect, site of defect, patient age at which the calvarial defect was acquired, age at cranioplasty, length of inpatient stay, length of follow up and complications recorded. Accurate surface area calculations of defect size using CT scan DICOM data was possible in 12 of the 22 cases due to some patients having planning scans done at external institutions.

Literature search

A search of Pubmed, ScienceDirect and Scopus was undertaken to assess the current methods in use for reconstruction of full thickness cranial defects in paediatric patients and to compare the published data with this series of patients. The search terms used were: “pediatric” and “cranioplasty”, “pediatric “ and “calvarial reconstruction”, and “cranioplasty”. Full articles were included in the comparative data if the authors stated that the series related to paediatric cranioplasty. Published abstracts only were excluded. Data relating to patients less than 18 years of age was abstracted from larger series where possible. Inclusion criteria included publication since 1997, cases reporting ≥ 3 patients and full thickness defects. Data abstracted included modality of reconstruction and, where stated, mean age and range, size of defect mean and range, mean length of follow up and range, effect on cranial growth and modality of assessment, and complications requiring second cranioplasty procedure.

Results

The characteristics of the patients in this series are tabulated in Table 1 and summarised in Table 2.

Between 2002 and 2009, 22 consecutive patients under the age of 18 underwent 23 custom made titanium cranioplasties. One patient had bilateral frontal defects and required two cranioplasty plates inserting during a single operation. The average age at cranioplasty was 12 years and 9 months (range: 6 years 2 months to 17 years 9 months). Four patients were female. The indications for cranial defect were as a result of decompressive craniectomy in 8 cases (36%), infected bone flap

following conventional neurosurgery in 4 cases (18%), osteomyelitis in 3 cases (14%), traumatic loss in 3 cases (14%), congenital defects in 2 cases (9%) and growing fractures in 2 cases (9%).

Figure 1 illustrates the site of the defects. It was possible using CT scan data to accurately measure 12 defect sizes. Of the 12 defects the average surface area was 44.3cm^2 (range 5.3cm^2 to 116.5cm^2). Seven known defect sizes were less than 40cm^2 however several very large reconstructions were undertaken.

Seven patients had previous infection at the surgical site. The minimum interval between cranial defect and reconstruction for this group of seven patients was 10 months (average 2 years 6 months). No particular precautions were taken in these patients other than standard peri-operative antibiotic prophylaxis and a one week post-operative course. The average inpatient episode was four days. One patient had five previous interventions at the cranioplasty site, the remainder had two or less interventions. None of the patients previously had radiation therapy to the cranium and none required tissue expansion prior to cranioplasty insertion.

No complications were recorded intra-operatively or during admission. One seroma was noted on early review which settled without intervention. One patient died five months following cranioplasty from causes unrelated to the reconstruction. The remaining patients had an average follow up of 4 years 7 months (range: 1 year 3 months to 8 years 9 months). No long term complications have been observed over this time and no cranioplasty has required removal.

Review of the literature identified 22 studies reporting outcomes of paediatric cranioplasty since 1997. These studies are summarised in Table 3 (Barone and Jimenez 1997; Blum et al., 1997; Choi et al., 1998; Durham et al., 2003; Cohen et al., 2004; Grant et al., 2004; Josan et al., 2004; David et al., 2005; Pang et al., 2005; Gosain et al., 2009; Biskup et al., 2010; Singh et al., 2010; Rogers et al., 2011; Wong et al., 2011; Frassanito et al., 2012; Lin et al., 2012; Piedra et al., 2012; Bowers et al., 2013; Stefani et al., 2013; Martin et al., 2014; Piitulainen et al., 2015; Greene et al., 2008)

Discussion

Currently there are two sources of material for calvarial reconstruction; autologous bone or a biomaterial. Autologous cranioplasty substrates are either the preserved craniectomy bone flap or a bone graft, most commonly split calvarium or split rib. Biomaterials in adults, particularly titanium, are supported by several large case series (Joffe et al., 1999; Eufinger et al., 2005) however due to concerns regarding intracranial migration of implants and on disturbance of skull growth the use of biomaterials in paediatric cases is controversial and autogenous bone is generally advocated.

Autogenous bone is considered the gold standard reconstruction as there is the potential for revascularisation and growth with the patient. Literature review identified six studies reporting the use of preserved, either frozen or autoclaved, bone flaps in paediatric cranioplasty. Graft resorption and infection are the most frequently cited reasons for failure of replaced bone flaps with second cranioplasties being required in 18-100% of patients (Grant et al., 2004; Josan et al., 2004; Frassanito et al., 2012; Piedra et al., 2012; Bowers et al., 2013; Martin et al., 2014). In a series of 23 cases reported by Martin et al, bone flap resorption or infection requiring bone flap removal was seen in 43% of cases with decreasing age associated with increased risk of resorption (Martin et al., 2014). Grant et al reported 50% of paediatric patients undergoing cranioplasty with a fresh frozen bone flap following decompressive craniectomy had sufficient graft resorption to warrant a second reconstruction (Grant et al., 2004). In contrast, in adult cranioplasty bone flap resorption is less frequent, but still significant, with second cranioplasty seen in up to 25.9% of adults with an autoclaved, frozen bone flap (Matsuno et al., 2006). Although a preserved bone flap is an attractive option for paediatric cranioplasty the high incidence of resorption mandating further cranioplasty, particularly in patients under 7 years, suggests this technique should be used only in older children (Martin et al., 2014; Bowers et al., 2013).

Split and particulate calvarial grafts are reported in 3 series of paediatric cranioplasty since 1997 (Barone and Jimenez 1997; Josan et al., 2004; Rogers et al., 2011). Low incidences of resorption and infection are seen (Frodel et al., 1993) although limitations include unpredictable splitting of the inner and outer tables due to poorly developed diploe in children under the age of five (Hockley et al., 1990), a weakened donor site calculated to a mean of 36% loss of strength for a harvest area of 40mmx40mm (Laure et al., 2010), and the quantity of bone available may not be enough for large defects. Rib grafts have been previously documented in small series or case reports for cranioplasty (Munro and Guyuron, 1981; Takumi and Akimoto, 2008), with only one series reporting 13 cases since 1997 (Taggard and Menezes, 2001). Compared with split calvarial grafts, rib grafts undergo greater resorption (Blair et al., 1980). This observation was initially thought to be due to the difference in the endochondral origin of rib rather than the membranous origin of calvarium although it is now evident that calvarium, being dense cortical bone, is revascularised at a slower rate thus resorption occurs at a slower rate (Rosenthal and Buchman, 2003; Ozaki and Buchman, 1998). The most common complications associated with rib harvesting are scarring, chest wall deformity due to non-regenerated ribs and pain in the early post-operative period, which can be considerable. At the graft site the most common complications are contour irregularity giving a “washboard” effect and resorption that can necessitate further surgery in up to 25% (Blair et al., 1980).

In adults, biomaterials are widely used including titanium, methylmethacrylate, polyetheretherketone, polythene and ceramics such as hydroxyapatite (Cho and Gosain 2004; Hanasono et al., 2009). Since 1997 fifteen studies report biomaterials in paediatric cranioplasty (Blum et al., 1997; Choi et al., 1998; Durham et al., 2003; Cohen et al., 2004; Josan et al., 2004; David et al., 2005; Pang et al., 2005; Gosain, et al., 2009; Singh et al., 2010; Wong et al., 2011; Lin et al., 2012; Stefani et al., 2013; Martin et al., 2014; Piitulainen et al., 2015; Frassanito et al., 2012).

Hydroxyapatite cements have been reported in 6 studies of cranioplasty, principally in small defects, with the largest stated mean defect size 37cm² in these studies. (Biskup et al., 2010). Minimal complication rates are seen with short term follow up, however Wong reported 75% of full thickness calvarial reconstructions failing due to infection with a mean follow up of 51 months leading the authors to discontinue the use of hydroxyapatite cement in paediatric cases (Wong et al., 2011). In adults hydroxyapatite cements have been associated with significant complication rates such as infection, material exposure, fragmentation and inflammatory tissue reaction and although they may be suitable for select cases for contouring purposes their use for full thickness defects is generally discouraged (Moreira-Gonzalez et al., 2003; Matic and Manson, 2004; Zins et al., 2010; Wong et al., 2011). Custom made hydroxyapatite ceramic implants have been reported by one large study of 114 patients since 1997 with no reported failures, although the defect size and length of follow up are not stated (Stefini et al., 2013). Polymethylmethacrylate has been reported in 3 studies since 1997 (Blum et al., 1997; Josan et al., 2004; Martin et al., 2014). Blum et al reported the largest series of 75 cases followed up for a mean of 10 years and reported a 23% failure rate (Blum et al., 1997). The other biomaterials commonly used in adults are under-reported in paediatric cranioplasty: polyethylene has a total 12 reported cases (Gosain et al., 2009; Lin et al., 2012), titanium 1 reported case (Josan et al., 2004) and bioactive glass 10 cases (Gosain et al., 2009; Piitulainen et al., 2015).

The advantages of these biomaterials over bone grafts include elimination of donor site morbidity, limitless availability of material and excellent fit and contour can be achieved from prefabrication using CT derived biomodels. Operative time is generally reduced and the reconstruction, particularly when titanium or polyetheretherketone are used, provides instant, durable protection to the brain. The obvious disadvantage is that biomaterials will not grow with the child's skull potentially resulting in "false migration" into the cranial cavity or in asymmetry of growth and deformity. The reported cases of false migration of mini-plates and fixation wires have predominantly occurred in infants

who had surgery for craniosynostosis at less than one year of age (Papay et al., 1995; Kosaka et al., 2003) and it has not been reported in implant reconstruction of non-synostosis calvarial defects.

Several studies in animals have been carried out assessing the effect of wiring or microplating in craniofacial deformity models (Yaremchuk et al., 1994; L. Wong et al., 1991; Resnick et al., 1990) and these have shown variable effects including restriction of growth locally and distant to the site of intervention and also compensatory expansion at other cranial sites (Resnick et al., 1990). No animal studies have thus far assessed the effects on reconstruction of critical sized calvarial defects and cranial growth. Of the 22 case series reporting biomaterials for full thickness defects in paediatric patients identified in the literature review only 2 studies comprising 16 patients in total state that there were no disturbances of growth observed, although the method used to assess this is not stated in either paper (Lin et al., 2012; Piitulainen et al., 2015). The effects on growth of using biomaterials for reconstruction of large calvarial defects in the growing human skull are largely unknown. Since approximately 90% of cranial growth is achieved by 5 years of age it seems reasonable to hypothesize that after this age rigid biomaterials can be used for reconstruction with minimal to no risk of intracranial migration or significant effects on cranial growth. Although absence of reports in the literature is not proof of absence of occurrence, this assumption is supported by the long-term experience in this cohort of patients as well as the other case series of full-thickness paediatric cranioplasty using biomaterials Blum et al., 1997; David et al., 2005; Pang et al., 2005; Lin et al., 2012; Stefini et al., 2013)

The optimum method of cranioplasty in paediatric cases remains controversial. This case series demonstrates custom made titanium can be used with long term success in select patients. It is of note that none of the patients had previous radiotherapy or required tissue expansion. All but one patient had 2 or less previous interventions at the cranioplasty site. The vascularity of the overlying scalp, influenced by the number of previous interventions and irradiation, has a significant effect on the incidence of infection or implant exposure (Cheng et al., 2008; Baumeister et al., 2008; Bruce

and Bruce, 2003), which are likely the reasons for the absence of infections or implant exposures in this study. A significant limitation in this study, in common with other published series, is lack of objective measurements relating to possible alterations in cranial growth as a result of rigid cranioplasty. Eight patients were under the age of ten in this cohort and although it is possible that potential for growth existed in these patients, there does not exist a modality of assessment that would be suitable without exposing the patient to clinically unnecessary radiation. In addition, in the absence of control patients, interpretation of serial cranial measurements in the context of significant calvarial defects would be meaningless, as skulls in these situations would grow abnormally regardless if reconstruction is attempted or not.

The future of cranial defects may lie in tissue engineered bone scaffolds (Chim and Schantz, 2005; Payne et al., 2014) but until that is viable in the clinical setting the select use of custom made titanium offers a predictable and reliable alternative.

Conclusion

Full thickness calvarial defects continue to challenge reconstructive surgeons with several techniques available, each having their own relative merits. It has been shown in our small series that custom made titanium cranioplasty implants have low complication rates compared with published results associated with autologous bone grafting and other biomaterials in situations where there is adequate quality of soft tissue coverage. The utilisation of titanium cranioplasty may be considered where the size of defect or acceptability of donor site morbidity precludes the use of autologous bone in paediatric patients greater than five years of age where cranial growth is largely complete.

ACKNOWLEDGEMENTS AND CONFLICTS OF INTEREST

ACKNOWLEDGEMENTS

Thanks to Dr Steve Connor, Consultant Neuroradiologist, for his assistance in obtaining defect surface area measurements from DICOM data.

CONFLICTS OF INTEREST

Conflicts of interest: none.

FUNDING

None

ETHICAL APPROVAL

Ethical approval was not required for this study.

CONTRIBUTIONS FROM AUTHORS

L Williams – study concept, study design, data collection and analysis, preparation of manuscript

K Fan - study concept, study design, preparation of manuscript

R Bentley – sole surgical operator, study concept, study design, preparation of manuscript

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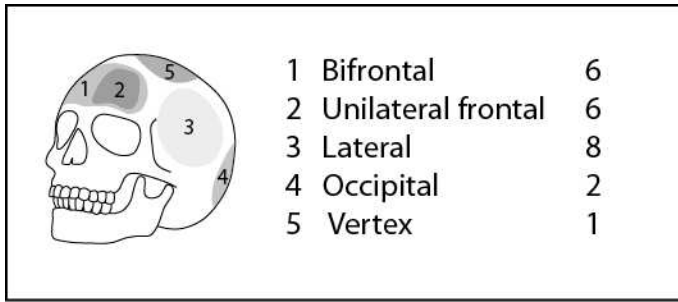


Figure 1: Defect site

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Table 1 – Patient characteristics

PATIENT	GENDER	AGE AT OP	INDICATION	SITE	NO. OF PREV INTERVENTIONS	INJURY/ OPERATION INTERVAL (YEARS/ MONTHS)	INPATIENT STAY (DAYS)	FOLLOW UP LENGTH (YEARS/ MONTHS)	COMPLICATIONS/ NOTES
1	M	6y 2m	Congenital deformity	Vertex	1	N/A	3	2y0m	
2	F	7y5	Growing fracture	Right lateral neurocranium	0	4y9m	3	7y2m	
3	M	7y10	Decompressive craniectomy	Unilateral frontal	1	11m	5	7y0m	
4	M	8y9	Congenital deformity	Vertex	0	N/A	3	1y0m	
5	M	8y 2m	Decompressive craniectomy	Left lateral neurocranium	1	1y1m	3	8y0m	
6	M	8y 5m	Infected bone flap	Left lateral neurocranium	5	1y6m	5	1y5m	
7	M	9y7	Growing fracture	Occipital	2	8y11m	3	7y8m	
8	M	10y 0m	Post infection	Bifrontal	1	10m	3	1y6m	
9	F	10y9	Post infection	Unilateral frontal	1	7y2m	4	7y7m	
10	M	12y 8m	Post trauma	Left lateral neurocranium	1	1y5m	3	1y9m	
11	M	13y2	Decompressive craniectomy	Left lateral neurocranium	1	9y1m	4	3y4m	
12	M	13y 9m	Decompressive craniectomy	Right lateral neurocranium	1	8m	4	6y7m	
13	M	14y 3m	Post trauma	Right lateral neurocranium	1	2y1m	4	2y8m	
14	M	15y10	Post trauma	Bifrontal	1	1y0m	4	2y7m	
15	M	15y 9m	Decompressive craniectomy	Unilateral frontal x 2	1	4m	5	2y6m	2 unilateral frontal defects
16	M	15y 2m	Decompressive craniectomy	Unilateral frontal	1	1y	11	3y5m	
17	F	16y 2m	Infected bone flap	Bifrontal	2	8m	5	5y8m	
18	F	16y 5d	Infected bone flap	Bifrontal	1	11m	4	-	Died 5 months post procedure unrelated to cranioplasty
19	M	17y 5m	Decompressive craniectomy	Left lateral neurocranium	1	1y1m	7	2y2m	Seroma
20	M	17y 9m	Post infection	Bifrontal	1	11m	4	7y0m	
21	M	17y 0m	Infected bone flap	Bifrontal	2	5y1m	4	3y0m	
22	M	17y 9m	Decompressive craniectomy	Unilateral frontal	1	1y2m	4	8y9m	

Table 2: Summary of patient cohort

Mean age (range)	12y6m (6y2m - 17y9m)
Gender	Male 18 Female 4
Number of previous interventions	1.2 (0 - 5)
Defect - reconstruction interval	2y6m (10m - 9y1m)
Inpatient stay	4.3d (3d - 11d)
Follow up	4y7m (1y3m - 8y9m)
Indication	
Decompressive craniectomy	8 (36%)
Infected bone flap	4 (18%)
Osteomyelitis	3 (14%)
Post-traumatic	3 (14%)
Congenital	2 (9%)
Growing fracture	2 (9%)
Size of defect	
<40cm ²	7
41-80cm ²	2
81-100cm ²	2
>100cm ²	1

Table 3: Summary of literature review

Author (year)	Material	No of Pts	Age range (mean)	Size (mean)	Follow up	Growth disturbance	Complications requiring second cranioplasty
Barone and Jiminez (1997)	Split calvarium	16	13m-41m (21m)	Not stated	0.79y-7.9y (2.3y)	Not assessed	0%
Blum et al (1997)	PMMA	75	6y-18y (12y)	mean 36cm ²	3y-16y (mean 10y)	Not assessed	23% (12 infection, 3 implant detachment, 2 implant fracture)
Choi et al (1998)	Coraline HA cement/ tantalum mesh	10	4m - 19y (6y)	Not stated	1m-43m (26m)	Not assessed	10% (1 infection)
Durham et al (2003)	Tantalum mesh + HA cement	7	1.5m - 16y	40cm - 196cm (140.7cm)	3.5m - 33m (12.6m)	Not assessed	14% (1 infection)
Cohen et al (2004)	Polylactic acid absorbable plates/ carbonated apatite bone cement	34	11m - 18y (7.4y)	1x2cm - 15x15cm (not stated)	3-60m (mean 24.4m)	Not assessed	0%
Grant et al (2004)	Fresh frozen bone flap	40	6w - 19y (9.3y)	14 -147cm ² (99.4)	6m-6y (4.8y)	Not assessed	50% (20 bone resorbtion)
Josan et al (2004)	Autoclaved bone flap	16	9m - 15y (not stated)	Not stated	3m-15y (18m)	Not assessed	18% (3 infection)
	Split calvarial graft	8					0%
	PMMA	3					0%
	Titanium	1					0%
David et al (2005)	HA cement	8	25m-100m (55m)	<30cm ²	23m - 72m (55m)	Not assessed	0%
Pang et al (2005)	HA cement + bioersorbable plates	15	2y - 9.5y (5.5y)	6.25-42.5cm (20.65cm)	2.2y-4.2y (2.9y)	Not assessed	0%
Greene et al (2008)	Particulate cranial graft	38	3-20y (8y)	5 -250cm ² (66.5cm)	0.5y-18y (6.5y)	Not assessed	3% (1 graft resorbtion)
Gosain et al (2009)	Bioactive glass	3	3-5y (4.3y)	Not stated	1y-3y (2.1y)	Not assessed	0%
	Demineralsised bone matrix	8					33% (1 inadequate fill of defect)
	Prefabricated poyethylene (Medpore®)	3					0%
Biskup et al (2010)	HA cement	23	6.5m-14y	46cm - 210cm (37cm)	9m - 19m (12.7m)	Not assessed	0%
Singh et al (2010)	HA cement	78	23m - 18y (9y)	Not stated	1y - 7y (not stated)	Not assessed	0%
Rogers et al (2011)	Exchange calvarial graft	20	9.2m - 22.3y (8.3y)	5.4 -270cm ² (85.2)	24w-3.7y mean 1.57y)	Not assessed	0%
Wong et al (2011)	HA cement	4	4.9y-15.2y (11.75y)	Not stated	37.5m-90m (50.83m)	Not assessed	75% (3 infection)
Frassanito et al (2012)	Frozen bone flap	3	1m-11m (6m)	Not stated	Not stated	Not assessed	100% (3 resorbtion)
Lin et al (2012)	Porous polyethylene	9	2.4-15y (6.8y)	91-231cm (152cm ²)	0.5m-22.4m (3.6m)	Nil recorded	0%
Pierdra et al (2012)	Frozen bone flap	61	not stated (9.3y)	Not stated	24m (2-124m)	Not assessed	36% (18 resorbtion, 4 infection)
Bowers et al (2013)	Frozen bone flap	54	Not stated (6.2y)	Not stated	37.9m (1.5m-168m)	Not assessed	50% (27 resorbtion, 9 infection)
Stefini et al (2013)	Custom made hydroxyapatite implant	114	7-14y (not stated)	Not stated	Not stated	Not assessed	0%
Martin et al (2014)	Bone flap	23	1m-17y (13.3y)	Not stated	21m-155m (81.3m)	Not assessed	43% (8 resorbtion, 2 infection)
	PMMA	4	13-17y (15.75y)	Not stated	79m-125m (102.7m)	Not assessed	0%
Piitulainen et al (2015)	Fibre-reinforced composite bioactive glass	7	2.5-16 (10.4y)	50-253cm	22m - 53m (35.1m)	Nil recorded	29% (2 infection)