Despite being in use for a long time, decompressive craniectomy remains an established procedure to lower intracranial pressure due to malignant brain swelling, and it is still undergoing technical improvements. Therefore, cranioplasty will remain a necessity in neurosurgery as well.

The surgical correction of skull defects has 2 main purposes: protection of the brain and a satisfying cosmetic result. The implanted material has to be durable and provide a low repulsion rate by the host. Because of immunological compatibility, the reimplantation of the patient’s own bone flap is usually the treatment of choice. Nevertheless, age, difficulties with storage, timing of surgery, and anatomical conditions can lead to the loss of the bone flap in a large number of cases. Various techniques are currently being discussed to rescue infected bone flaps or improve their preservability, but as of yet none of these offers results superior to the ones achievable with nonbioresorbable materials. Recent developments are looking toward osteoconductive bioresorbable materials, tissue engineering, osteoinduction by growth factors, and gene therapy, but despite promising experimental results in animals and preliminary studies, these new technologies still have to prove their worth in large-scale long-term clinical settings.

Until then the surgeon has the choice between various cranioplasty techniques. Computer-assisted design and modeling of craniofacial materials has improved the cosmetic outcome as well as minimized the procedure time needed for plate insertion. Numerous materials have shown high biocompatibility and clinical reliability, such as PMMA, titanium, numerous ceramics such as HA, carbon materials such as CFRP, and others (Table 1).
Nevertheless, it is unclear which material provides the best overall result. The CAD/CAM titanium plates offer an excellent choice for cranioplasty based on their strength, low infection rate, biocompatibility, handling characteristics, and suitability for postoperative imaging techniques, but they are often avoided because of their high costs. However, it may be advisable to take into account that the long-term suitability of this material could compensate its higher production costs. Furthermore, operative time, infection, and revision rates as additional cost factors have to be calculated as well. There are few long-term studies of cranioplasties in the literature. In this long-term follow-up study, we examined 25 patients with large calvarial defects who underwent cranioplasty with titanium plates. We observed these patients for up to 12 years after the procedure, and we reviewed the existing literature focusing especially on complications, removal rates, and long-term follow-up results of cranioplasties.

### Methods

Between 1983 and 2002, 241 patients underwent craniectomy for various reasons in our department. The bone flap was reinserted in 149 cases. Since 1996, CAD/CAM titanium plates (Fig. 1) have been inserted for a variety of large skull defects (Table 2).

Between 1996 and 2002, 26 patients (15 men and 11 women) underwent cranioplasty with CAD/CAM titanium implants (Cranio Construct; Bochum GmbH) due to a posttraumatic nonrestorable large skull defect, lysis, or infection of the bone flap after severe head trauma (13 patients); cerebral infarction (5 patients); meningioma (4 patients); and dysplasia, bone erosion as a result of a growing arachnoidal cyst, herpes encephalitis, and brain abscess (1 patient each). In 6 of these patients 2 plates were implanted. One patient underwent bilateral cranioplasty with titanium (Fig. 2). Four patients underwent bifrontal cranioplasty (Figs. 3 and 4).

The titanium implant was inserted after exposure of the margins of the skull defect without opening the dura mater. If necessary, plate insertion was supported by hyperventilation or lumbar CSF drainage for several minutes. Central dural tenting sutures were placed routinely. Between 1996 and 1998, the fastening of the plates was performed with titanium miniplates from various companies. Since 1998, CranioFix titanium clamps (Aesculap AG) have been used to fasten the plates. A wound drain was placed for 3 days in all cases.

The size of the skull defects and plates ranged from

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**TABLE 1: Review of the literature regarding clinical studies dealing with alloplast graft cranioplasty**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Study Design</th>
<th>Material</th>
<th>No. of Patients</th>
<th>Mean Follow-Up Duration (mos)</th>
<th>Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joffe et al., 1999</td>
<td>prospective</td>
<td>titanium</td>
<td>148</td>
<td>12</td>
<td>1 infection (0.6%)</td>
</tr>
<tr>
<td>Blake et al., 1990</td>
<td>retrospective</td>
<td>titanium</td>
<td>20</td>
<td>52</td>
<td>no removals (0%)</td>
</tr>
<tr>
<td>Eufinger et al., 1998</td>
<td>retrospective</td>
<td>titanium</td>
<td>22</td>
<td>24</td>
<td>1 infection (4.5%)</td>
</tr>
<tr>
<td>Kamiyama et al., 2001</td>
<td>retrospective</td>
<td>titanium</td>
<td>76</td>
<td>8</td>
<td>2 impaired healings (2.6%)</td>
</tr>
<tr>
<td>Matsuno et al., 2006</td>
<td>retrospective</td>
<td>titanium</td>
<td>77</td>
<td>64</td>
<td>2 infections (2.6%)</td>
</tr>
<tr>
<td>Matsuno et al., 2006</td>
<td>retrospective</td>
<td>PMMA</td>
<td>58</td>
<td>8</td>
<td>8 infections (13.8%)</td>
</tr>
<tr>
<td>Matsuno et al., 2006</td>
<td>retrospective</td>
<td>autogenous bone</td>
<td>54</td>
<td>14</td>
<td>1 infection (5.9%)</td>
</tr>
<tr>
<td>van Gool, 1985</td>
<td>retrospective</td>
<td>PMMA</td>
<td>45</td>
<td>39</td>
<td>2 removals (4.4%)</td>
</tr>
<tr>
<td>Moreira-Gonzalez et al., 2003</td>
<td>retrospective</td>
<td>autogenous bone</td>
<td>312</td>
<td>39</td>
<td>22 infections/exposure (7%)</td>
</tr>
<tr>
<td>Kriegel et al., 2007</td>
<td>retrospective</td>
<td>PMMA</td>
<td>36</td>
<td>44</td>
<td>removal of 2 implants (4.5%)</td>
</tr>
<tr>
<td>Kriegel et al., 2007</td>
<td>retrospective</td>
<td>autologous bone graft (Tutoplast)</td>
<td>25</td>
<td>15</td>
<td>removal of 2 implants (8%)</td>
</tr>
<tr>
<td>Marchac &amp; Greensmith, 2008</td>
<td>retrospective</td>
<td>PMMA</td>
<td>32</td>
<td>8.2*</td>
<td>4 removals (12.5%)</td>
</tr>
<tr>
<td>Friedmann et al., 2000</td>
<td>prospective</td>
<td>HA</td>
<td>38</td>
<td>24</td>
<td>3 infections (7.9%)</td>
</tr>
<tr>
<td>Costantino et al., 2000</td>
<td>retrospective</td>
<td>HA</td>
<td>21</td>
<td>15</td>
<td>no removal (0%)</td>
</tr>
<tr>
<td>Verheugen &amp; Merten, 2001</td>
<td>retrospective</td>
<td>HA</td>
<td>11</td>
<td>6</td>
<td>1 impaired healing (9%)</td>
</tr>
<tr>
<td>Durham et al., 2003</td>
<td>retrospective</td>
<td>HA</td>
<td>9</td>
<td>11</td>
<td>2 infections (22.2%)</td>
</tr>
<tr>
<td>Eppley et al., 2003</td>
<td>retrospective</td>
<td>HA</td>
<td>62</td>
<td>24</td>
<td>3 infections (5%)</td>
</tr>
<tr>
<td>Poetker et al., 2004</td>
<td>retrospective</td>
<td>HA</td>
<td>76</td>
<td>13</td>
<td>2 infections (2.63%)</td>
</tr>
<tr>
<td>Saringer et al., 2002</td>
<td>retrospective</td>
<td>CFRP</td>
<td>29</td>
<td>39</td>
<td>0 infections</td>
</tr>
<tr>
<td>Sanus et al., 2008</td>
<td>prospective</td>
<td>acrylic resin (Cortoss)</td>
<td>13</td>
<td>24.3</td>
<td>0 removals or infections</td>
</tr>
<tr>
<td>Scolozzi et al., 2007</td>
<td>case report</td>
<td>PEEK</td>
<td>1</td>
<td>12</td>
<td>0 removal</td>
</tr>
</tbody>
</table>

* This follow-up duration was reported in years.
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65 to 155 mm (mean 112 mm). The patients’ age at operation ranged from 6 to 63 years (mean 35.6 years), and the follow-up period ranged from 6 to 12 years (mean 8.1 years). The span of time between the removal of the bone flap and the insertion of the CAD/CAM titanium plate ranged from 2 to 14 months (mean 6.5 months).

The follow-up examination included a questionnaire covering subjectively experienced pain and satisfaction with the cosmetic result based on two 100-mm-long VASs: the VASPI and VASC. Overall satisfaction with cranioplasty as a whole was evaluated using the Odom criteria. Furthermore, eventual changes in the quality of life after cranioplasty were evaluated, and the patients were asked if they would have chosen cranioplasty again. Postoperative CT scanning was routinely performed.

One patient died of a heart attack 6 years after plate insertion and was lost to the last follow-up. At the 1-year follow-up, this patient reported no specific complaints, but he did not fill out the questionnaire. Therefore, a total of 25 patients were evaluated.

Results

Analysis of the Odom criteria showed that 68% of the patients (17 of 25) noted excellent, 24% (6 of 25) good, 0.8% (2 of 25) fair, and 0% poor results. Overall, 84% (21 of 25) did not suffer any pain, and 88% (22 of 25) were satisfied with the cosmetic result of titanium cranioplasty with a score of > 75 mm on the VASC (Fig. 5).

Only 2 female patients, one with a history of a severe head injury and the other with a left brain infarction suffered pain periodically with an intensity of 48 and 61 mm on the VASPI, respectively. The patient with the left brain infarction was dissatisfied with the cosmetic result and scored 43 mm on the VASC.

Another female patient with a history of left brain infarction noted a suboptimal cosmetic result and scored 51 mm on the VASC, but suffered no pain. One patient scored 71 mm on the VASC. Clinical evaluation and imaging did not reveal any objective reasons for impaired cosmetic results such as asymmetry, swelling, or ill fitting of the plates in these cases. All patients would have chosen to undergo cranioplasty again, noting a considerable improvement in their quality of life following calvarial reconstruction.

Despite artifacts, follow-up imaging of the 4 patients undergoing removal of meningiomas was possible. Nevertheless, the quality of follow-up images in these patients was regarded as suboptimal. Imaging quality was acceptable in the follow-up of the other cases. Extraaxial collections without midline shift were seen on postoperative CT scans in 4 cases, but no surgical intervention was required in the clinically unaffected patients.

The operation time ranged from 60 to 219 minutes (mean 118 minutes). The costs for the titanium plates, including instances in which 2 plates were used, ranged from €2500 to €5050 (mean €3733).
None of the implanted titanium plates had to be removed. Due to a postoperative hypertrophy of the temporal muscle and a resulting asymmetry of the face 4 months after insertion of the titanium plate, a reduction of the temporalis muscle was performed in 1 case. In this case, a transient palsy of the frontal ramus of the facial nerve occurred postoperatively.

**Discussion**

We presented a long-term follow-up study of 26 patients after placement of CAD/CAM titanium for cranioplasty. None of the plates had to be removed, and almost 90% of the patients were satisfied with the cosmetic result and overall outcome. The cosmetic and overall outcomes of our patients did not differ substantially from other studies dealing with CAD/CAM implants, but we focused on long-term results, patients’ satisfaction, and quality of life. Cranioplasty is the surgical correction of skull defects and has 2 main purposes: protection of the brain and a satisfying cosmetic result. Furthermore, cranioplasty affects cerebral metabolism positively and may facilitate patient rehabilitation.43,44

Because of issues of immunocompatibility, a patient’s own bone flap is considered the material of choice for a cranioplasty, and we support this point of view. If the bone flap is lost to osteolysis or infection, autologous bone from other parts of the body is rarely used for calvarial reconstruction because of donor site morbidity and shaping problems. In these cases alloplastic implants are more frequently used. The decision for one of the many available materials often depends on the surgeon’s preference and experience as well as costs and availability of modeling techniques. The most frequently used cranioplasty materials are PMMA, HA, and titanium.45

Because of its good biocompatibility and low costs, PMMA is the most frequently used alloplastic material and is still regarded as the material of choice by many authors.26,27 Nonetheless, depending on anatomical conditions as well as the size and shape of the skull defect, intraoperative modeling can be time-consuming and difficult. The disadvantage of inappropriate modeling especially in large skull defects and sensitive cosmetic regions has been solved by the CAD technique, which can be used for PMMA with good results. The CAD/CAM PMMA implants are an acceptable choice even in poorer regions of the world.9,19 Recently, bioactive composite materials consisting of acrylic resins gained access into calvarial reconstruction with good results.38

Hydroxyapatite is probably the most frequently used ceramic and is increasingly used in reconstructive surgery. It is the principal component of bone, has the advantage of osteoconductivity, and allows osteointegration.6,25 Despite high biocompatibility, inflammatory reactions have been described in numerous studies conducted in...
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![Graph showing the clinical results according to the VASPI and VASC.](image)

...the early postoperative period and the few months after surgery. Thus, some authors have regarded HA as a contraindication for craniofacial reconstruction and pediatric populations in special settings. Costantino et al. managed to attain a 0% infection/removal rate, but their small collective comprised mostly patients with small skull defects that occurred after the suboccipital lateral approach for vestibular schwannomas. Furthermore, the costs of HA and other ceramic CAD/CAM implants exceed even CAD/CAM titanium implants.

Carbon and PEEK are other biocompatible materials that provide high strength and radiolucency for postoperative imaging. They have been put to use particularly in orthopedic and spinal surgery with good clinical and radiographic results. In a series of 29 patients, not a single CFRP plate had to be removed. The CAD/CAM PEEK implants for cranioplasty are gaining access in calvarial reconstruction, but larger case studies have not yet been reported in the literature.

Bioactive materials are gaining greater importance and exhibit superior characteristics to classic allografts in biomechanical studies and small clinical short-term settings, but they still have to stand the test of time. Osteoconductive bioresorbable materials, tissue engineering, osteoinduction by growth factors, and gene therapy are only recently gaining access in larger clinical settings. While there are studies in which authors have preferred PMMA or HA as the optimal material for cranioplasty, titanium plates offer a good choice for cranioplasty based on their strength, biocompatibility, handling characteristics, and suitability for postoperative imaging techniques.

While materials such as PMMA and HA show biocompatible and osteoconductive characteristics without significant toxic and immunogenic properties, the best HA series with a complication rate of <2.6% involved only cranioplasties <6 cm following a retrosigmoid approach in most cases. In a small series of 9 patients undergoing large skull defect reconstruction, 22% of HA-based ceramics had to be removed because of infections. The infection rate of titanium implants including large skull defects ranges from 0 to 4.5%. An often-cited reason for the removal of HA and PMMA implants is the proximity to the sinuses, a problem that exists for cranioplasty with titanium as well. In our own study, the frontal sinus was involved in 6 cases.

The costs of large ceramic plates amount to ~$7000, while the costs of large titanium CAD/CAM implants range from €2050 to 5000 and are thus comparable in cost to the CAD/CAM implants used in our series. As patients requiring alloplastic cranioplasty have often already undergone multiple operative procedures, one has to question whether titanium CAD/CAM cranioplasty is actually more expensive than PMMA cranioplasty. In our view, this statement does not take into account the more frequent revision surgery due to higher complication rates of PMMA and the resulting costs. Furthermore, results from clinical series with HA cranioplasty show higher complication rates and higher production costs than titanium cranioplasty.

The suboptimal results of imaging quality due to titanium artifacts for follow-up of the meningiomas in our study cannot be denied. Nevertheless, imaging quality was acceptable in the follow-up of the other cases.

Conclusions

With the aid of CAD technology, all of the currently used alloplastic materials are good choices even for large skull defect cranioplasty. Cranioplasty with CAD/CAM titanium plates is suitable for calvarial reconstruction of all sizes, providing the lowest complication rate, reasonable costs when regarding complications and removal rates over long-term periods, and the possibility of acceptable postoperative imaging. Analyzing our data and the literature, we have come to the conclusion that due to its costs and availability, PMMA is suitable for patients requiring primary cranioplasty or long-term follow-up imaging of tumors. Titanium implants seem to be the material of choice in cases of secondary cranioplasty of large skull defects resulting from decompressive craniectomy after trauma or infarction. Expensive ceramics that are gaining larger access into reconstructive calvarial surgery show no obvious advantage over titanium or PMMA.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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