What happens to the bone flap? Long-term outcome after reimplantation of cryoconserved bone flaps in a consecutive series of 92 patients

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Abstract: BACKGROUND: Reimplantation of cryoconserved autologous bone flaps is a standard procedure after decompressive craniotomies. Aseptic necrosis and resorption are the most frequent complications of this procedure. At present there is no consensus regarding the definition of the relevant extent and indication for surgical revision. The objective of this retrospective analysis was to identify the incidence of bone flap resorption and the optimal duration of follow-up. METHODS: Between February 2009 and March 2012, 100 cryoconserved autologous bone flaps were reimplanted at the Department of Neurosurgery, Inselspital Bern. Three patients were not available for follow-up, and five patients died before follow-up. All patients underwent follow-up at 6 weeks and a second follow-up more than 12 months postoperatively. A clinical and CT-based score was developed for judgment of relevance and decision making for surgical revision. RESULTS: Mean follow-up period was 21.6 months postoperatively (range: 12 to 47 months); 48.9 % (45/92) of patients showed no signs of bone flap resorption, 20.7 % (19/92) showed minor resorption with no need for surgical revision, and 30.4 % (28/92) showed major resorption (in 4 % of these the bone flap was unstable or collapsed). CONCLUSIONS: Aseptic necrosis and resorption of reimplanted autologous bone flaps occurred more frequently in our series of patients than in most reports in the literature. Most cases were identified between 6 and 12 months postoperatively. Clinical observation or CT scans of patients with autologous bone flaps are recommended for at least 12 months. Patient-specific implants may be preferable to autologous bone flaps.

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What happens to the bone flap? Long-term outcome after reimplantation of cryoconserved bone flaps in a consecutive series of 92 patients

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ABSTRACT

Background: Reimplantation of cryoconserved autologous bone flaps is a standard procedure after decompressive craniotomies. Aseptic necrosis and resorption are the most frequent complications of this procedure. At present there is no consensus regarding the definition of the relevant extent and indication for surgical revision. The objective of this retrospective analysis was to identify the incidence of bone flap resorption and the optimal duration of follow-up.

Methods: Between February 2009 and March 2012, 100 cryoconserved autologous bone flaps were reimplanted at the Department of Neurosurgery, Inselspital Bern. Three patients were not available for follow-up and 5 patients died before follow-up. All patients underwent follow-up at 6 weeks and a second follow-up more than 12 months postoperatively. A clinical and CT-based score was developed for judgment of relevance and decision making for surgical revision.

Results: Mean follow-up period was 21.6 months postoperatively (range: 12 to 47 months). 48.9% (45/92) of patients showed no signs of bone flap resorption, 20.7% (19/92) showed minor resorption with no need for surgical revision and 30.4% (28/92) showed major resorption (in 4% of these the bone flap was unstable or collapsed).

Conclusions: Aseptic necrosis and resorption of reimplanted autologous bone flaps occurred more frequently in our series of patients than in most reports in the literature. Most cases were identified between 6 and 12 months postoperatively. Clinical observation or CT scans of patients with autologous bone flaps is recommended for at least 12 months. Patient-specific implants may be preferable to autologous bone flaps.

Keywords: aseptic bone flap necrosis, bone flap, bone flap resorption, hemicraniectomy
INTRODUCTION

Reconstruction of skull defects is currently a standard procedure in neurosurgery and maxillofacial surgery. Reconstruction techniques date back to ancient times; Artico et al provide a good overview of the historical development.[3] More recently, artificial materials have been developed that provide very good replacements, but are quite costly. For this reason, and following the paradigm that autologous material should always be preferred over artificial replacements, reimplantation of a bone flap is usually the first choice to close a bone defect.[10] The material provides perfect biocompatibility, shape and fusion with the surrounding bone.[12] For preservation of an explanted flap until the delayed reimplantation, the material is either implanted into a subcutaneous pouch [2,13] or cryoconserved.[1,14] However, several major complications are related to reimplantation of autologous bone; e.g., epidural and subgaleal fluid collections and bleedings, infections, and resorption (aseptic necrosis) of the bone flap.

MATERIAL AND METHODS

Patients

Between February 2009 and March 2012 we reimplanted 100 cryoconserved autologous bone flaps at the Inselspital in Bern, Switzerland. Five patients died during follow-up (no perioperative deaths) and three patients were not available for follow-up. Of the 92 patients included in the present retrospective study, 60 were male and 32 female. The mean age was 46.2 years (standard deviation [SD] 18.0). Pathologies leading to craniectomy were: 39 cases of head trauma, 18 cerebrovascular insults, 17 intracerebral hemorrhages, 14 subarachnoidal hemorrhages, and four cases of infectious disease leading to malignant brain swelling. The mean follow-up time was 21.6 months (SD 1.5). This retrospective analysis was approved by the local ethics committee (Kantonale Ethikkommission Bern, Switzerland, approval number 155124, 20.02.2013).

Technique of bone flap preservation and reimplantation

After explantation of the bone flap and intraoperative decision for a delayed reimplantation, the bone was freed from adherent soft tissue residuals and washed carefully with 0.9% NaCl with gentamycin 320 mg/l (provided by hospital pharmacy).
Afterwards the bone flap was packed and sealed into a sterile plastic bag which was stored at -80°C.

For reimplantation the bone was taken directly from the freezer and thawed in the operating room in sterile 0.9% NaCl solution with gentamycin 320 mg/l at 37°C. After preparation of the surrounding skull the flap was reimplanted and fixed using titanium plates and screws (Low Profile Neuro 0.6mm self-drilling screws, 4-5mm length, 400.83x), and Double-Y- or burr-hole-cover plates, 0.5mm thick (product numbers 421.516 and 421.528; Synthes, Oberdorf, Switzerland).

**Follow-up**

All patients received a CT scan on the first postoperative day to detect possible hygroma, epidural or subdural hematoma, intraparenchymatous hemorrhage on the ipsi- or contralateral side, or hydrocephalus. Most patients were discharged to continue stationary rehabilitation after 3 to 5 days. After 6 weeks all patients received a clinical check-up in the outpatient clinic to identify cases of wound healing disturbance or delayed malresorptive hydrocephalus. In case of a questionable condition the patient received an additional CT scan. All patients were scheduled for a second clinical follow-up after at least 12 months to rule out delayed resorption of the bone flap. In case of questionable resorption the patients received another CT scan at the 12-month visit.

**Judgment of bone resorption**

At the 12 month follow-up visit (or later), after reimplantation of the bone flap the patients were asked about headaches, palpable holes in the reimplanted bone or gaps around its margins. They were also asked about palpable instability and changes in appearance. Afterwards, the bone flap was examined by a physician through careful palpitation. In case of a stable, cosmetically good and clearly non-resorbed bone flap we dispensed with an additional CT scan to avoid unnecessary exposure to ionizing radiation. For identified holes, gaps and instability we assigned scores as described in Table 1.

Depending on the score, we derived indications for further follow-up and surgical revision in accordance with Table 2. As instability cannot be accepted in a reimplanted
bone flap, we decided to assign 3 additional points for this condition. Thus, instability alone was considered indicative for surgical revision.

RESULTS

Surgical outcome and complications
Mean dimensions of the craniectomies approximated in the 2D-lateral CT-scout were 112 cm² (SD 22). Complications, including bone flap resorptions, are listed in Table 3. Reimplantations of bone flaps were performed an average of 2.6 months after explantation (SD 1.5 months, range 0.3 to 7.4 months).

Bone flap resorption
Resorption of the bone flap occurred in a considerable number of patients. Minor resorption as defined in Table 2 occurred in 20.7% (19/92) of patients and major resorption leading to surgical revision and replacement with a patient-specific implant (PSI) occurred in 30.4% (28/92). Four patients (4.3%) showed a relevant dislocation of the bone flap (Table 3). In 29.3% (27/92) of patients a PSI implantation was performed subsequently. The median time until identification of relevant bone resorption in clinical follow up or imaging was 15.9 months (average 20.0, SD 15.1, range 1.0 through 47.7). Only five of the 28 cases were identified before 12 months after reimplantation.

Statistical methods and power
Only descriptive statistical methods were used. Ninety-two patients were included. The incidence of relevant bone resorption (grade 3 or higher) was 30.4%, which led to a 95%-confidence interval of 20.8 to 40%.

DISCUSSION

Complications after reimplantation of cryoconserved bone flaps
Due to the long time period required for performing surgery involving cryo-protected tissue, the number of publications dealing with the complications is rather small, especially in adult patients. Table 4 provides a summary of the literature, with an emphasis on the major complications reported. Age of patients, technique of bone flap
preservation, time until reimplantation and underlying pathology differ considerably between these publications. Still, it is amazing how different the incidence of complications is, particularly the incidence of bone flap resorption. Grant et al [6] found no bone resorption in children when the defect was smaller than 75 cm². On the other hand, they found 60% relevant resorption in larger defects. Fragmentation of the bone flap and duration until reimplantation did not seem to influence rate of resorption.[6] The next most important study is from Gruber et al., who reported 33% relevant resorption in a series of nine patients, with signs of minor bone resorption in all of the patients.[7] One very recent study, by Schuss et al [16] examined 254 patients retrospectively and provided a follow-up of more than one year for all cases. The patients were mainly adults and the incidence of resorption was low (3.9%).[16] Unlike Grant et al., they found a significant influence of multi-fragmentation of the bone flap on the incidence of resorption. Schuss et al confirmed that timing of reimplantation was not relevant. Dünisch et al [4] reported the largest series so far: 372 cases. Complications were well documented and the mean follow-up was nearly one year. They found a very high rate of relevant bone resorptions of about 22%.[4] Unfortunately, for all the studies listed in Table 4 (except the present one), ‘bone flap resorption’ is not clearly defined. Schuss et al define it as prospective skull defect, instability or cosmetic deformation.[16] Dünisch et al define a relevant resorption as necrosis of tabula interna and externa.[4] The striking differences between the studies concerning this complication has its origin not only in the different ages of the patients, but also in the different definitions of relevant resorption and the different lengths of follow-up.

**Reporting of bone resorption: Illustrative case**

One of the findings that was most surprising for us was that patients did not spontaneously report an occurrence of bone resorption. One typical example was a 17-year old boy who suffered a severe head trauma in a fistfight. A large subdural hematoma with major dislocation of the midline and consequent brain swelling led to decompressive hemicraniectomy. The bone was cryoconserved at -80°C until the reimplantation 6 weeks later. The patient was seen in the outpatient clinic 6 weeks after reimplantation and the only neurological deficit was a minor gait disturbance. The bone flap fit perfectly, there
were no signs of resorption, and the wound-healing was good. The patient completed in-
patient rehabilitation for 2 weeks and went back to work afterwards. In this young man
the fast regrowth of curly black hair quickly covered the operated hemisphere. When the
patient presented in our outpatient clinic for a late follow-up 6 months after the
reimplantation, which was initiated by the hospital and not by the patient himself, he
presented with major resorption, which was palpable as a 4 cm by 4 cm hole in the bone
and retraction of the skin, but which was covered by his hair. The patient was aware of
the skull defect but still did not realize that it was a problem.

Major resorptions were also identified in a similar manner in other patients. It appeared
that patients with good recovery from the initial trauma/insult were satisfied with being
able to lead a normal life again and did not want to complain about what they considered
minor imperfections or perhaps were reluctant to undergo additional surgery. This lack of
patient initiative may contribute to the low incidence of bone resorption reported in the
literature, where the follow-up is generally short and clinical controls are initiated by the
patient or the general practitioner.

**Definition of ‘relevant’ bone resorption**

The term ‘bone resorption’ must be defined in terms that will enable comparison between
different centers and techniques currently in use or techniques that will be developed in
the future. The reimplanted bone must at least fulfill the criteria given by Schuss et al.: to
protect the brain and be cosmetically acceptable.[16] The best possible result would be
fusion of the surrounding bone with no resorption (even histologically). Such fusion is
unlikely, as histological and radiographic examinations by Prolo et al showed signs of at
least minor bone resorption in all cases.[15] A clear delineation between the indication
for a surgical revision and a tolerable resorption is needed. We suggest the system
described in Tables 1 and 2. This system can be applied to clinical parameters or to a CT
scan. Instability or large holes in the bone flap indicate a need for immediate revision of
the bone flap. Small holes and thinning of the bone flap may contribute, but are not by
themselves sufficient to require revision of the bone flap.

**The Bern experience: High incidence of bone resorption**
In our series of patients the incidence of bone flap resorption is rather high compared with the literature. It corresponds best with the findings of Dünisch et al, reporting 21% of patients with relevant bone resorptions.[4] We found relevant resorption (according to the definition described above) in 30.4% of cases and performed reoperation and replacement with a patient-specific implant (PSI) in 27 cases (29.3%). Three patients with clear indication for bone flap replacement rejected the offer, despite the fact that in one case the dislocated bone flap was cosmetically unfavorable. We did not find a correlation with the patient’s age, but the subgroup of patients under 20 was very small (8 patients, 37.5%) and the study population was not powered for a subgroup-analysis.

**Future aspects**
To learn the true incidence rate of the complications of this very common surgery is far from academic; it is highly relevant for clinical decision-making and outcome. Our own results, as well as publications by Gruber et al [7] and Grant et al [6] suggest that about one third of patients require replacement of the bone flap by allogenous material in an additional surgical approach. The rate of infection was rather low in our own series, but between 2 and 15.8% of patients reported in the literature (Table 4) experienced other complications like hematomas and hygromas (13% and 5% in our own series, respectively). If these results can be generalized, neurosurgeons must consider searching for alternatives to a surgical procedure with an approximately 40% overall complication rate. This question will never be answered satisfactorily on the basis of retrospective data and there has never been a prospective study on this topic. Therefore we suggest -- and are currently planning -- a multicenter prospective study. If our findings will be supported by prospective results, the indication for reimplantation of autologous bone might be questioned in general. Alternatively, industrial patient specific implants might be implanted from the very first. The higher costs for the implants might be put into perspective compared to repeated surgery’s costs and the inconveniences for the patients. On the other hand there are techniques available to use very low-cost intraoperatively molded implants, for example made from polymethylmethacrylate. Those won’t even need to be inferior towards commercial products regarding their cosmetic results and complication rate as we were recently able to show[17].
CONCLUSIONS
Bone flap resorption is a frequent complication after delayed reimplantation of cryoconserved bone flaps. The incidence of complications is dependent on the patient’s age, and is more frequent in children than adults. There is also evidence for an influence of multi-segmentation of the reimplanted flaps[16] and size of the covered defect.[6] The overall incidence of major resorption reported in the literature is between 2 and 60%. In our own series of 92 patients the incidence was 30.4% (95% confidence interval: 20.8% to 40%). To provide a clear definition of what we consider a major resorption, we present a simple scoring system that proved quite useful in our series. Some cases of bone flap resorption become evident only after a long follow-up. A future prospective study is planned to identify the optimal time point for clinical and radiological follow-up. Based on the present study, we expect the optimal follow-up time point to be at least 12 months after the reimplantation.
REFERENCES


### Table 1: Bone flap resorption score

<table>
<thead>
<tr>
<th>CT scan (if available)</th>
<th>Visible/palpable (no CT scan available)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>not palpable or visible</td>
<td>0</td>
</tr>
<tr>
<td>Gaps or holes &lt;2 cm</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>(not temporo-basal) ≥2, &lt;3 cm</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>≥3 cm</td>
<td>palpable/visible</td>
<td>3</td>
</tr>
<tr>
<td>Bone thickness ≥1 mm</td>
<td>cannot be judged</td>
<td>0</td>
</tr>
<tr>
<td>&lt;1 mm</td>
<td></td>
<td>+1</td>
</tr>
<tr>
<td>Bone flap stability, dislocation, collapse &lt; bone thickness</td>
<td>stable</td>
<td>0</td>
</tr>
<tr>
<td>≥ bone thickness</td>
<td>visible or palpable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>instability/dislocation/collapse</td>
<td>+3</td>
</tr>
</tbody>
</table>

**Table 1 legend:** If a computed tomography (CT) scan was available, the resorption of the bone flap was judged based on appearance of gaps and holes, after reduction of bone thickness and stability. If no CT scan was available, bone thickness could not be determined. For a palpable gap or hole in the flap the maximum of 3 points was assigned. In case of palpable instability of the flap or dislocation in the CT scan 3 additional points were assigned.

### Table 2: Indications derived from the bone flap resorption scores

<table>
<thead>
<tr>
<th>Bone flap resorption score</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 points (no resorption)</td>
<td>Clinical follow-up</td>
</tr>
<tr>
<td>1-2 points (minor resorption)</td>
<td>Follow-up with CT scan after 6 months</td>
</tr>
<tr>
<td>≥ 3 points (major resorption)</td>
<td>Indication for surgical revision*</td>
</tr>
<tr>
<td></td>
<td>(replacement, patient specific implant)</td>
</tr>
</tbody>
</table>

* A large gap or hole, or any instability was considered indicative for surgical revision.
### Table 3: Complications after reimplantation of cryoconserved bone flaps

<table>
<thead>
<tr>
<th>Complication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection of unknown origin</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Infection after wound healing disturbance</td>
<td>1</td>
<td>1.1</td>
</tr>
<tr>
<td>Hematoma</td>
<td>3</td>
<td>3.3</td>
</tr>
<tr>
<td>Hygroma</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Hydrocephalus requiring shunt placement</td>
<td>19</td>
<td>20.7</td>
</tr>
<tr>
<td>Dislocation / Collapse</td>
<td>4</td>
<td>4.3</td>
</tr>
<tr>
<td>Minor resorption (score 1-2)</td>
<td>19</td>
<td>20.7</td>
</tr>
<tr>
<td>Major resorption (score ≥ 3)</td>
<td>28</td>
<td>30.4</td>
</tr>
</tbody>
</table>