The Use of Bone Graft Substitute in Hand Surgery
A Prospective Observational Study

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Abstract
Bone defects are a very common problem in hand surgery, occurring in bone tumor surgery, in complicated fractures, and in wrist surgery. Bone substitutes may be used instead of autologous bone graft to avoid donor site morbidity. In this article, we will review our experience with the use of Cerament bone void filler (Bonesupport, Lund, Sweden) in elective and trauma hand surgery. A prospective clinical study was conducted with 16 patients treated with this bone graft substitute in our department over a period of 3.5 years. Twelve patients (2 female, 10 male; with an average age of 42.42 years) with monostotic enchondroma of the phalanges were treated and 4 patients (1 female, 3 male; with an average age of 55.25 years) with complicated metacarpal fractures with bone defect. Data such as postoperative course with rating of pain, postoperative complications, functional outcome assessment at 1, 2, 3, 6 months, time to complete remodeling were registered. Postoperative redness and swelling after bone graft substitute use was noticed in 7 patients with enchondroma surgery due to the thin soft-tissue envelope of the fingers. Excellent total active motion of the involved digit was noticed in 10 of 12 enchondroma patients and in all 4 fracture patients at 2-month follow-up. In summary, satisfying results are described, making the use of injectable bone graft substitute in the surgical treatment of enchondromas, as well as in trauma hand surgery a good choice.

Abbreviations: CRPS = chronic regional pain syndrome, DASH = disabilities of the arm shoulder and hand, SNAC = scaphoid nonunion advanced collapse, TAM = total active motion, VAS = visual analogue scale.

Keywords: bone graft substitute, enchondromas, metacarpal fracture

1. Introduction
Bone defects are a common problem in hand surgery. They occur in bone tumor surgery, in complicated fractures, and in wrist surgery, for example in the reconstruction of a scaphoid pseudarthrosis. In these cases cancellous, cortical, or cortico-cancellous bone grafts are the treatments of choice. Autologous bone is desirable mainly because of its inherent osteoconductive properties, but the harvesting procedure is associated with complications and certain comorbidity, such as haematoma or fracture or pain at the donor area. To avoid donor site morbidity, a bone substitute may be used instead of bone graft—especially in emergency situations where bone graft requirements are unpredictable.

Enchondromas are the most common benign bone tumor of the hand.[2] They present as solitary, cystic bone tumors in the phalanges but may occasionally be polyostotic, for example in Ollier disease or Maffucci syndrome.[3] They grow asymptptomatically and commonly present as a pathological fracture.[4]

Hand surgeons aim to remove the tumor to prevent pathological fractures.[5] The purpose of the procedure is to allow histological diagnosis, to prevent future pathological fractures, and to avoid recurrence of the tumor.[6]

The treatment of choice for enchondroma is curettage of the tumor and filling of the resultant cavity with cancellous bone graft. However, there are also hand surgeons who advocated simple curettage as sufficient; thus, additional bone grafting or the use of bone substitutes is discussed controversially in the treatment of enchondromas.[7] Schaller and Bae[7] showed by measuring bone density after curettage for enchondroma that mid-term bone structure is comparable both with and without additive bone grafting.[7]

In the literature, articles on the use of different bone substitutes were only identified for the treatment of enchondromas with hand surgery. Regarding the final treatment of complicated phalangeal or metacarpal fractures with bone defects using bone substitute, there are, to our knowledge, no references in the German and English literature.

In this article, we will review our experience with the use of bone graft substitute in elective and trauma hand surgery, with a follow-up of up to 3 years.

2. Patients and methods
We conducted a prospective clinical study with 16 patients treated with Cerament bone void filler (Bonesupport, Lund, Sweden) in our Hand Surgery Department over a period of 3.5 years. For Cerament bone void filler, one of the widely used injectable bone substitute materials, it had been reported that it promotes cancellous bone healing and reproducible remodeling in bone defects. It consists of calcium sulfate (60%) and
hydroxyapatite (40%) together with Iohexol as a liquid radiopaque contrast medium, which is fully resorbed after 7 days.\(^9\) Iohexal has high radio-visibility, enabling its precise delivery while minimizing the risk of leakage.

Twelve patients with monostotic enchondroma of the phalanges and 4 with a complicated metacarpal fracture with bone defect were treated. All patients older than 18 years with an indication for using bone graft substitute were included in the study after an informed consent for surgery had been obtained. An absolute contraindication for Ceramant and exclusion criteria is an allergy to the contrast agent. Because of the inhomogeneity of the study population, we will analyze the data of the 2 patient groups separately. Surgery was performed under regional (brachial plexus block) anesthesia with an upper arm tourniquet to produce a bloodless surgical field. A single-dose perioperative antibiotic prophylaxis (second generation cephalosporin) was used.

In patients with enchondroma, a mediolateral or dorsal incision was used to approach the phalanx and an appropriately sized cortical window about 0.4 × 0.4 cm was cut to expose the tumor. Careful curettage was then performed using a sharp spoon. After inspection to verify the absence of tumor tissue, the bone graft substitute was injected via a flexible venous catheter and the cortical window was used again for reconstruction (Fig. 1).

Postoperatively, a splint was applied for 2 weeks but the physical therapy began on the first postoperative day with passive and active movements.

In patients with metacarpal fractures, a dorsal approach was used. First, reduction of the fracture was performed, followed by the placement of plate and screws. Ceramant was injected into the defect zone and, if necessary, a compound osteosynthesis was performed by inserting additional screws into the bonded Ceramant. Afterward, the periosteum and interosseous muscle fascia were closed with sutures (Fig. 2). Postoperatively, a wrist splint without finger support was applied for 4 weeks and in these cases physiotherapy and lymphatic drainage started on the first postoperative day. After completion of the osteosynthesis, the postoperative course was evaluated.

The following data was registered for each patient: age, sex, digit, follow-up time, operating time, postoperative course with rating of pain on visual analogue scale (VAS) on the first 2 postoperative days under standard pain relief medication (ibuprofen 400mg), postoperative complications, time to complete bone remodeling, and functional outcome at 6 months after surgery. Radiographs were obtained preoperatively, postoperatively and at every follow-up visit to monitor the mechanical integrity of the bone substitute during remodeling. The range of motion was evaluated in these patients at 1, 2, 3, and 6 months after surgery.

The functional outcome was evaluated using the Disabilities of the Arm Shoulder and Hand (DASH) outcome questionnaire. The follow-up was at least 12 months in all patients treated with Ceramant bone void filler, in some up to 3 years. SPSS version 21 (IBM, Illinois, USA) was used for statistical analysis of our study data.

3. Results

Twelve patients (2 female, 10 male) with an average age of 42.42 ± 17.2 years were treated with Ceramant after the curettage of an enchondroma tumor. Complications of grade II according to the Clavien-Dindo classification\(^9\) occurred. In 7 patients (53.8%) redness and swelling appeared, lasting up to 10 postoperative days (Fig. 3). In these cases, an oral antibiotic therapy (second-generation cephalosporin) was initiated on the 2nd postoperative day.
first postoperative day for 7 days. In one of these patients a fracture in the mid zone of the cement appeared 2 weeks after surgery during intensive physiotherapy. This fracture healed well with conservative treatment, but this patient needed the splint for 6 weeks. One patient developed a chronic regional pain syndrome (CRPS), which was treated successfully with intensive conservative treatment and healed without any residual symptoms within 1 year.

Four patients (1 female, 3 male) with an average age of $55.25 \pm 22.69$ years had a complicated metacarpal fracture. In these 4 cases, no postoperative complications occurred. The patients’ demographics are shown in Table 1.

The mean operating time for enchondromas was $41.42 \pm 17.20$ minutes and for fractures $69.75 \pm 15.56$ minutes.

The mean VAS pain score in the first 2 postoperative days was $2.08 \pm 0.51$ in the enchondroma group and $3 \pm 0.82$ in the fracture group.

The mean DASH score was $3.75 \pm 1.58$ in fracture patients at 6 months after the surgery and $2.45 \pm 5.45$ in enchondroma patients.

Excellent total active motion (TAM) of the involved digit was found in all patients at 2-month follow-up, with the exception of the enchondroma patient with the postoperative fracture in whom the full range of motion was achieved after 3 months and the CRPS patient who finally achieved full range of motion after 1 year.

All patients had returned to the normal daily activities at 2 months postoperatively, and the range of VAS pain scores was 0 to 1 at that time.

In the x-rays, quick remodeling of the bone substitute into bone with restoration of mechanical integrity (Fig. 3) was noted after the first 6 postoperative weeks. Interestingly, the remodeling began in the outer layer of the bone substitute (with the development of a cyst-like formation in the x-rays) and then...
the entire bone substitute was replaced by bone tissue. The radiocontrast agent was completely washed out during the initial postoperative week. No patient failed to achieve complete bone healing within 6 months.

4. Discussion

So far, mainly cancellous bone grafts have been used in the treatment of large enchondromas. In our study, the enchondroma was used as a “test system”; we started to use Cerament bone void filler (Bonesupport, Lund, Sweden) instead of cancellous bone grafts. After establishing this method, we began to treat selected metacarpal fractures with bone defects in this way too.

The ability of calcium-based bioceramics to provide biocompatible scaffolding for mature osteoblasts promotes the formation of new bone, a process known as osteoconduction. Some bioceramics induce the formation of new bone directly onto the material itself by influencing the cellular differentiation of mesenchymal stem cells into chondroblasts and osteoblasts.[10]

Cerament triggers a precipitation of endogenous hydroxyapatite on the implant surface, resulting in a retarded degradation process with parallel bone formation and remodeling.[11]

Injection of bone substitute, even via small approaches, is quick and easy, its distribution inside the bone can clearly be visualized due to the added contrast medium. It does not lead to a significant increase in the temperature, and therefore it does not induce necrosis or apoptosis of surrounding cells. On the other hand, bone graft substitutes can still be expensive and do not possess the features of an autologous graft. Allograft bone is osteoconductive and osteoinductive but lacks the osteogenic properties of the autograft.[12] In addition, another disadvantage of bone substitute may be rejection and slower incooperation.[13]

Even though bone substitutes have been used for a long time in trauma surgery, they have rarely been used in hand surgery—mainly because only small amounts of bone material are usually needed, which can be easily harvested at the olecranon, distal radius or at the iliac crest. Nevertheless, there is often a need for bone material in emergency trauma surgery or in case of complicated fractures, where the patient might not have been informed about or refused to undergo the additional harvesting procedure. These are the main indications, where we see a benefit in the use of bone substitutes.

Because of the uncertainty how bone substitutes would perform in hand surgery, we started with enchondromas as a “test model” under controlled conditions. The application of the bone substitute is fast and simple, the contrast agent provides good visualization under fluoroscopic control. It is less time consuming than harvesting autologous bone and without donor site morbidity, which is of great importance in old multimorbid or immunosuppressed patients with problematic wound healing.

 Clinically, a localized redness and swelling was often observed, which was judged as an infection at the beginning. In 3 cases, we have observed a “milky drainage” up to the fifth postoperative day, which appeared to be liquid Cerament, but was in fact white wound serum since the Cerament remained stable radiologically. This phenomenon may be caused by a chemical reaction involving the bone substitute, which probably takes place in all patients, but is not necessary clinically manifest—especially in cases with thick soft tissue coverage. Therefore, this observation is less common in orthopaedic surgery. In these cases, our recommendation is to keep patients under clinically control and not to proceed to revision surgery early, as we obtained with this approach good results in all cases.

Radiologically, as mentioned above, bone regeneration was without complications in our patients during the follow-up period and no patient failed to achieve complete bone healing. In the literature, the full remodeling into mature bone is also described after 6 to 12 months.[14]

Another advantage of using this method in enchondroma surgery and in patients with metacarpal fracture with bone defect is that donor site morbidity is avoided, with the use of autologous bone grafts.[15] However, rejection and slower integration after malunion can occur.[15]

Table 1

Demographic and Clinical Characteristics of the Patients.

<table>
<thead>
<tr>
<th>Patient ’s Number</th>
<th>Age</th>
<th>Sex</th>
<th>Entity</th>
<th>Follow-Up (yr)</th>
<th>Complications</th>
<th>Time of Complete Bone Remodeling (mo)</th>
<th>Finger</th>
<th>DASH After 6 m</th>
<th>Operating Time</th>
<th>TAM After 2 mo</th>
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<tbody>
<tr>
<td>1</td>
<td>68</td>
<td>w</td>
<td>Enchondroma</td>
<td>2</td>
<td>—</td>
<td>2</td>
<td>D1</td>
<td>2</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>54</td>
<td>m</td>
<td>Enchondroma</td>
<td>2</td>
<td>Redness, swelling</td>
<td>3</td>
<td>D5</td>
<td>2</td>
<td>0.9</td>
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<td>1.5</td>
<td>—</td>
<td>3</td>
<td>D4</td>
<td>2</td>
<td>0</td>
<td>41</td>
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<tr>
<td>4</td>
<td>37</td>
<td>m</td>
<td>Enchondroma</td>
<td>1.5</td>
<td>—</td>
<td>2</td>
<td>D5</td>
<td>2</td>
<td>0.9</td>
<td>40</td>
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<tr>
<td>5</td>
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<td>3</td>
<td>Redness, swelling, Fracture</td>
<td>7</td>
<td>D1</td>
<td>1</td>
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<td>Redness, swelling, CRPS</td>
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<td>m</td>
<td>Enchondroma</td>
<td>2.5</td>
<td>Redness, swelling</td>
<td>2</td>
<td>D5</td>
<td>2</td>
<td>0</td>
<td>35</td>
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<tr>
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<td>Redness, swelling</td>
<td>3</td>
<td>D3</td>
<td>2</td>
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<td>3</td>
<td>D5</td>
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<td>—</td>
<td>3</td>
<td>D5</td>
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<td>5.0</td>
<td>93</td>
</tr>
<tr>
<td>14</td>
<td>41</td>
<td>m</td>
<td>Fracture</td>
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<td>—</td>
<td>2</td>
<td>D2</td>
<td>3</td>
<td>5.0</td>
<td>64</td>
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<tr>
<td>15</td>
<td>88</td>
<td>w</td>
<td>Fracture</td>
<td>2.5</td>
<td>—</td>
<td>3</td>
<td>D5</td>
<td>2</td>
<td>1.7</td>
<td>61</td>
</tr>
<tr>
<td>16</td>
<td>39</td>
<td>m</td>
<td>Fracture</td>
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<td>—</td>
<td>4</td>
<td>D5</td>
<td>4</td>
<td>3.3</td>
<td>61</td>
</tr>
</tbody>
</table>

CRPS = chronic regional pain syndrome, TAM = total active motion

* Excellent TAM is 220 to 260 degrees in the finger and 120 to 140 degrees in the thumb.[16]
revision surgery early as in all our cases we achieved good results with antibiotic therapy alone.

5. Conclusion

In summary, satisfying results are described, making the use of injectable bone graft substitute in the surgical treatment of enchondromas, as well as in trauma hand surgery, a good choice. It is especially helpful in the treatment of complicated metacarpal fractures in old multimorbid patients in whom the surgeon wants to avoid potential donor site morbidity and in patients with osteoporotic metacarpal bones. Regarding scaphoid pseudarthrosis, initially experimental studies should be conducted to establish the safety of this procedure, as an unsuccessful surgical procedure may lead to nonhealing, SNAC wrist, chronic pain, and also to unemployability.

References