Displaced intra-articular calcaneal fractures treated with open reduction internal fixation (ORIF) combined with an injectable and bone remodeling bone substitute (CERAMENT™): A preliminary report.

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Abstract

Displaced intra-articular calcaneal fractures Sanders 3 and 4 leaving a large bone void after reposition, continue to pose a therapeutic challenge. The purpose of this study was to determine the effects of open reduction and internal fixation (ORIF) combined with the injectable bone substitute CERAMENT™|BONE VOID FILLER in patients with a bone gap > 2 cm after reduction. Twelve consecutive cases were included and followed for one year. Two cases underwent minor revisions due to superficial infections.

A bone biopsy in one patient, taken after 5 months, showed bone formation at multiple sites in the implanted material. In all patients, full bone healing was demonstrated on X-ray after one year, with no deterioration of the Böhler angle. From this preliminary report, it is concluded that filling large bone defects with CERAMENT™ results in full bone remodeling and a preserved Böhler angle after one year.
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Introduction

Intra-articular fractures of the calcaneus are severe injuries, often with devastating, life-altering consequences. Many patients remain incapacitated for 3 to 5 years after injury and often never return to full function. The majority of fractures involve young working males, and the economic impact of these fractures is substantial (Epstein et al). The treatment of calcaneal fractures remains a debated topic with non-conclusive study results, especially in displaced intra-articular calcaneal fractures Sanders 3 and 4 with significant voids after reduction and a risk of secondary collapse and reduced Böhler angle.

Although bone grafts have been used for decades (Palmer et al, Leung et al), conventional bone grafting appears to not accelerate healing or reduce the time to weight-bearing, while causing significant morbidity from the harvest site. Thus, it has been claimed that with proper surgical technique, bone grafting can be avoided (LeTournel 1984, Le Tournel 1993, Stephenson et al, Sanders et al, Longino & Buckley).

However, more recently the introduction of synthetic biologic materials has opened new prospects for treatment. Thus, the use of calcium phosphate cements have been reported to allow earlier weight-bearing in calcaneal fractures (O’Farrell et al, Mermelstein et al, Xu et al, Welch et al, Horstmann et al, Larsson et al, Morgan et al, Constantz et al), and in a study on Norian SRS, biopsies showed nearly complete bone apposition, areas of vascular penetration, and reversal lines illustrating progressive cycles of resorption and new bone formation (Schildhauer et al). Curing calcium phosphate cements do, however, have the drawback of slow bone remodeling (Kopylov et al), with a risk of late material fracture or hematogenous osteomyelitis facilitated by the presence of a foreign body.

We have experienced a number of cases with significant bone defects after treatment with ORIF LCP without filling the void, that have demonstrated loss of calcaneal height of the posterior facet and reduction of Böhler’s angle following full weight bearing. We thus decided to use an injectable composite ceramic cement that fully remodels to bone within a year (CERAMENT™ [BONE VOID FILLER, BONESUPPORT AB, SWEDEN] in a series of patients with displaced intra-articular calcaneal fractures (DIACFs) Sanders 3 and 4, and a significant bone defect after reposition.
Material and Methods

During two years, patients older than 20 years with displaced intra-articular calcaneal fractures (DIACFs) and a significant bone defect over 2 cm after open reduction and internal fixation (ORIF), were included in the study. Exclusion criteria were a history of anaphylactic reaction to iodine-based radiocontrast agents, known bleeding disorders, hyperthyreosis or thyroid adenoma.

After appropriate antibiotic prophylaxis, a pneumatic thigh tourniquet was applied and inflated to 350 mm Hg. All surgeries were performed by the same surgeon with lateral approach and a full-thickness flap, followed by K-wire repositioning of articular bone fragments under fluoroscopy, and fixation with LCP plate and cancellous screws. After full fixation, a flowable and curing bone substitute (CERAMENT™|BONE VOID FILLER, BONESUPPORT AB, Sweden) was applied under fluoroscopy. CERAMENT™ consists of highly osteoconductive hydroxyapatite particles embedded in an injectable calcium sulphate (CaS) paste, which is prepared 3 minutes before application by mixing with the water-soluble radiocontrast agent iohexol and water in a closed system. Once implanted, CERAMENT™ has a wet compressive strength of 5 MPa, which is comparable to that of healthy trabecular cancellous bone. Due to the microporosity of the CaS, an immediate flow of tissue fluids with nutrients and growth factors are allowed to penetrate the implant, which promotes osteoclasts and macrophages to enter the implant and create macropores resulting in a widespread ingrowth of early bone. The end result is full transformation and remodeling into mature bone after 9-12 months (Abramo et al, Hatten & Voor).

Clinical follow up was performed according to clinical practice and included radiographic and clinical examination at 1 year. A CT scan was taken preoperatively to examine the fracture, for surgery planning and for fracture classification according to Sanders.
Results

In total 12 patients with DIACF (8 male), age 48 ± 17 (mean ± SD), were included over a two year period. Three of the patients presented with bilateral fractures. All fractures were treated with ORIF and the average volume of CERAMENT™ used was 10 cm³ (Fig 1). Fracture reduction and correction of the Böhler angle was successful in all cases. Two patients developed superficial infections that were treated with debridement and antibiotics.

Fig 1. a) Displaced intra-articular fracture. b) Postoperative radiogram demonstrating the radiopacity of CERAMENT™, and c) Bone healing after 11 months with full weight bearing at 6 months postoperatively.
In a 54 year old female allowed full weight bearing after 3 months, it was decided to remove the plate after 5 months due to local discomfort (Fig 2), and a bone biopsy was taken from the implant region.

Histology from the biopsy demonstrated residual CERAMENT™ with bone formation at multiple sites, no giant cells, and a tight junction without interposition of fibrous tissue between CERAMENT™ and newly formed bone (Fig 3).

![Fig 2](image-url) Preoperative (a,b) and immediate postoperative radiograms (c,d), with good visibility of the bone void filled with CERAMENT™ containing the radiocontrast agent iohexol. After 45 days (e,f), iohexol is washed out and early bone formation is seen. In the images taken 5 months after surgery and with the plate removed, radiological bone healing is demonstrated (g,h).
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All patients presented with preserved Böhler angle and full bone healing after 12 months, and no re-operations were needed.

Fig 3. Bone biopsy (a) taken 5 months after implantation with CERAMENT™. Newly formed bone interfoliates with CERAMENT™ at multiple sites. Note the direct contact between ingrowing bone and CERAMENT™ without fibrous tissue or foreign body cells (b).
Discussion

The question, whether or not to utilize bone grafts to fill voids in connection with ORIF in calcaneus fractures, goes beyond the scope of this preliminary report. Irrespective of using autogenous or allogenic bone grafts, there exist disadvantages that cannot be overlooked, for instance donor site pain and morbidity, blood loss, infection, slow rate of incorporation and secondary fractures. For these reasons there has been an emergence of bone graft substitutes in the area of trauma and orthopedic surgery. In this study we wanted to investigate the bone forming capacity of a new biphasic and highly biocompatible bone substitute with attractive handling properties. CERAMENT™ bioceramic bone substitute, which consists of hydroxyapatite embedded in a synthetic calcium sulphate carrier and mixed with the radiocontrast agent iohexol to form an injectable and hardening paste, possesses a combination of distinctive advantages that warrant its safe and efficacious use. A passive precipitation of hydroxyapatite on the surface of the implant (Nilsson et al) seems to extend the gradual resorption of the calcium sulphate component over months (Hatten & Voor), allowing the cement to be replaced by ingrowing bone that rapidly remodels to form trabeculae (Wang, Mahan et al).

It can be preliminary concluded that radiological and clinical healing was obtained in all cases of our study. It is also worth noting that no postoperative compression occurred during the follow-up period of 12 months. It is preferable with a compressive strength and stiffness similar to that of the cancellous bone being substituted, and a bone regeneration rate with subsequent remodeling, that takes place over the shortest possible time. In our preliminary results, CERAMENT™ fulfills these requirements. The product delivers hydroxyapatite particles embedded in an injectable and curable calcium sulphate paste combined with the water-soluble radiocontrast agent iohexol. This composite has the porosity and interconnectivity to allow for efficient osteoconduction. Interestingly, histology from a bone biopsy taken after 5 months showed multiple sites of bone regeneration with the new bone interfoliating with CERAMENT™. Thus, instead of a creeping bone substitution starting from the surface, microporosity and high biocompatibility promotes cell invasion and bone formation all over the implant, for quickest possible bone regeneration.

In two patients a superficial infection was seen. Bearing in mind the release pattern of the water-soluble radiocontrast agent iohexol from CERAMENT™, with the major amount released during the first weeks, addition of a prophylactic antibiotic might very well be an attractive alternative in the treatment of complicated calcaneus fractures (Lindberg et al).

In conclusion, CERAMENT™ is a material with attractive handling properties and a fast remodeling to bone, which makes it an attractive alternative to autologous bone or allografts. Although both animal studies (Nilsson et al, Wang) and studies on osteoporotic patients (Abramo et al, Hatten & Voor), have demonstrated bone remodeling after treatment with CERAMENT™, the concept has to be further proven in studies comparing the outcome with that obtained after autologous bone transplant.
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References


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OUR MISSION is to provide an injectable radiopaque bone substitute that has been proven to rapidly remodel into bone, with the potential to be combined with other substances, and is capable of being delivered percutaneously.