

CERAMENT™ *WHITE PAPER*

Preliminary Results of a Highly Injectable Biphasic
Bone Substitute in Acute Trauma Surgery

A Prospective Case Series on CERAMENT™|BONE VOID FILLER

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Abstract

In orthopedic trauma surgery autologous bone grafts are considered the gold standard for reconstructive procedures and filling of voids. However, donor site morbidity and limited availability of graft material are the limiting factors of this technique. Allografts can be useful but they possess a slow incorporation rate and have a risk of disease transmission and immunogenic host-versus-graft reactions. Synthetic bone graft substitutes can overcome these limitations and provide a valuable alternative for both autografts and allografts in many indications.

A newly developed bioceramic bone substitute, CERAMENT™|BONE VOID FILLER (BONESUPPORT AB, Sweden), which delivers highly osteoconductive hydroxyapatite particles embedded in an injectable and curing calcium sulfate paste combined with the water-soluble radiocontrast agent iohexol, seems to employ the properties necessary for successful bone remodeling and fracture healing. CERAMENT™ can be used in a minimally invasive fashion to fill voids and assist in bone regeneration and the high radiovisibility helps the surgeon to avoid leakage in e.g. fractures adjacent to a joint. To further evaluate its safe and effective use as a bone graft substitute in orthopedic trauma we conducted a consecutive series on 20 patients with various fractures involving calcaneus, tibial condyles, distal radius, and proximal humerus.

In connection to surgery, a mean volume of 9.4 ± 1.9 ml CERAMENT™ was given and the follow-up time will be 12 months or until the fracture is radiologically healed. In this interim report, we describe the results after a mean follow-up of 4 ± 4 months (range 1-12 months) in all 20 patients. Eight of those twenty patients have hitherto attained full bone healing and successful remodeling of CERAMENT™ after 8 ± 3 months (range 4-12). No failures have been detected during this follow-up time. It is preliminarily concluded that CERAMENT™ completely remodels to bone within 12 months and that this might be an efficient alternative to autologous bone grafting.

Introduction

It is estimated that up to 600,000 bone grafting procedures are performed each year in the United States ¹, of which the majority is autologous bone from the iliac crest. Autologous bone is desirable mainly because of its inherent osteoconductive properties, but the harvesting procedure is associated with complications and certain co-morbidity ².

As a result, new synthetic bone graft substitutes have emerged to provide the surgeon with a minimally invasive, safe, and effective treatment alternative for bone defects and voids.

Calcium sulfate is a soluble osteoconductive material that, after curing, hardens to form a substance that can be used to fill defects ³ and support fixation devices ⁴. Calcium sulfate products tend to resorb too quickly, leaving the bone void without proper osteoconductive matrix to support the bone regeneration ⁵. Calcium phosphate-based products like e.g. hydroxyapatite have on the other hand a slow resorption rate which hinders the full replacement with new bone ⁶ and leaves a foreign body, sometimes for years. A proper combination of the two materials may be of benefit for bone regeneration, and for subsequent remodeling to mature bone, and may allow some stability during healing ⁷⁻⁸.

One such product that has recently been introduced is a bioceramic bone substitute consisting of hydroxyapatite particles embedded in an injectable synthetic calcium sulfate carrier that is mixed with the radiocontrast agent iohexol. The compressive strength provided by this minimally invasive, injectable bioceramic is similar to that of cancellous bone to ensure at least the same mechanical stability as with autografts ⁹. The aim of this case series is to present the first long-term results of durability and stabilizing/healing efficacy of this new injectable and synthetic bone graft used in trauma surgery.

Materials & Methods

Between August 2011 and November 2012, twenty patients undergoing bone surgery, and in need of autologous bone transplant, received a synthetic bone graft substitute (CERAMENT™|BONE VOID FILLER, BONESUPPORT AB, Sweden) to avoid bone harvesting. CERAMENT™ is a biphasic material consisting of hydroxyapatite (HA) particles (40 weight-%) delivered by a calcium sulfate (CaS) paste that is prepared immediately prior to surgery by adding water and the water-soluble radiocontrast agent iohexol (180 mg/ml). The HA-CaS powder is pre-packed in a closed and sterilized mixing device that is conveniently transformed to a delivery device. After addition of the liquid component, the powder and liquid is mixed for 30 seconds to create a paste. At 3 minutes the viscous paste is ready for injection during 4-5 minutes, and moldable for another 3-4 minutes. Due to the high flowability, also in a high viscosity state, minimally invasive procedures are possible with a low pressure injection that entails good intraosseous spread.

The curing process takes one hour and it is not necessary to immobilize the treated region, since in contrast to calcium phosphate products, the crystallization of CERAMENT™ restarts if interrupted. Once cured, the hydroxyapatite component triggers the body to precipitate an endogenous calcium phosphate layer on the surface of the implant⁹, which stabilizes the implant and retards the CaS resorption substantially. Thus, in most applications the resorption rate is similar to that of bone regeneration and remodeling to cancellous bone, which results in a complete bone healing within one year^{10,11}.

The patients were recruited consecutively if considered in need of autologous bone harvesting and filling of residual bone voids in connection with the procedure.

Results

Patient demographics and the indication for surgery are presented in Table I.

Table I. Patient demographics and indication for surgery (mean±SD)

		N
AGE (year)	55±17 (range 23-83)	20 (9 females)
Indications:	Calcaneus fractures	5
	Lateral tibia head	5
	Distal radius	3
	Humeral head	3
	Distal tibia	1
	Proximal tibia	1
	Distal femur	1
	Bone cyst femoral head	1

All patients, except one with a bone cyst, were surgically treated with open reduction and internal fixation. The amount of CERAMENT™ given was 9.4 ± 1.9 ml, with easy handling and proper injectability in all cases. In 4 of the 5 patients with comminuted calcaneus fractures, the superficial location resulted in visible drainage with a milky appearance, presumably due to surface dissolution of the cement. The drainage stopped spontaneously within 3 days in all 4 cases. All patients will be followed according to regular hospital routines for 12 months or until the fracture is radiologically healed. In the actual interim report, 8 patients have attained full bone healing and remodelling of CERAMENT™ after a mean follow-up time of 8 ± 3 months (range 4-12). No failures have been recorded. One patient dropped out due to hardware fracture and a need for re-operation. The mean follow-up for the 12 patients not yet radiologically healed was 2 ± 3 months (range 0-7).

The peri-operative radiovisibility of CERAMENT™ was good. Due to high microporosity, the radiocontrast agent is washed out during the initial post-operative weeks, which makes it possible to follow the bone regeneration and the subsequent remodeling to mature, cancellous bone over time (Fig 1-3).



Fig 1. Open calcaneus fracture Grade 3 after fall from height in a 56 year old man. The fracture was treated with 5 ml of CERAMENT™ (black circle). Full bone formation is demonstrated after 6 months (bottom picture).



Fig 2. Humeral head fracture with a posteriorly locked dislocation of the humeral head after bicycle accident in a 53 year old woman treated with 10 ml of CERAMENT™ (white circle). After one year full bone generation is demonstrated (bottom picture).



Fig 3. Bone cyst in a 32 year old male. The cyst was filled with 10 ml of CERAMENT™ (white circle) after open curettage of the cyst walls. After 12 months (bottom picture) the cyst was completely filled with bone.

Discussion

The tested bone graft substitute presents with favorable characteristics such as eliminating the need for a second surgical site to harvest the graft material and minimizing complications related to the harvesting procedure, high flowability also in a viscous state enabling minimally invasive surgery, very easy handling properties, and an excellent radiovisibility. An ideal bone graft substitute should also be sufficiently porous and interconnective to allow tissue to grow in and around the implant over an acceptable time period¹². It is also preferable that the substitute has a compressive strength and stiffness similar to that of the cancellous bone being substituted. In our preliminary results, the newly developed bioceramic bone substitute CERAMENT™ fulfills these requirements. The product delivers hydroxyapatite particles embedded in an injectable and curable calcium sulfate paste combined with the water-soluble radiocontrast agent iohexol. This composite has the porosity and interconnectivity to allow for efficient osteoconduction.

CERAMENT™ acts as an osteoconductive matrix for ingrowth of blood vessels and subsequent bone formation¹³. In contrast to pure calcium sulfate products that sometimes dissolve too quickly in a clinical situation¹⁴, CERAMENT™ triggers a precipitation of endogenous hydroxyapatite on the implant surface, resulting in a retarded degradation process over 6-12 months with parallel bone formation and remodeling^{9,12}. In those cases with sufficient follow-up, radiological and clinical healing was demonstrated after a time span of 4-12 months. No patient failed to present full bone healing within 12 months. In four patients, all of them with comminuted calcaneus fractures, a milky drainage was observed for maximum three days. Since the calcium sulfate carrier is microporous and water soluble, this is not an unexpected finding. It is, however, important to note that this dissolution of calcium sulfate is only a surface phenomenon, since the implanted volume did not decrease on post-operative X-ray. Although it is important to cover the void filled with CERAMENT™ in a proper way to minimize drainage, we did not see any disadvantages in the few patients presenting with drainage. It should also be emphasized that the osteoconductive hydroxyapatite particles remain in place promoting bone generation, but that the calcium sulfate has to be resorbed by the tissues to allow for bone ingrowth. In deeper locations with good blood supply, such as the femoral head or proximal humerus, the calcium sulfate component is transported internally and hence the drainage was not stained white.

Hydroxyapatite forms the chief mineral component of bone and hydroxyapatite particles are known to be very osteoconductive¹⁵⁻¹⁶. When combined with calcium sulfate, the composite forms a matrix to support the attachment of bone-forming cells for subsequent bone formation as clearly demonstrated in the actual report. The added benefit provided by the radiocontrast agent aids in the precise delivery of the composite with minimal risk of leakage, which is especially important in the presence of fracture lines communicating with the joint space.

Other clinical studies evaluating patients with osteoporotic vertebral compression fractures treated with CERAMENT™ demonstrated significant improvements in pain relief, quality of life and fracture healing^{13,17,18}. Additional animal and human studies¹¹⁻¹⁰ have successfully demonstrated incorporation, new bone growth and bone remodeling after treatment with CERAMENT™.

In our report we present a series of cases typical for an orthopedic trauma center employing the use of CERAMENT™. Although the study is still ongoing, bone regeneration was clearly demonstrated in all cases with a sufficiently long follow-up, with no adverse effects observed. It is therefore preliminarily concluded that CERAMENT™ can provide a safe and effective alternative to autologous bone graft harvesting from the iliac crest.

IX. References

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Notes



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.

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