Bone Remodeling using a novel, injectable bioceramic (CERAMENT™) in foot and ankle reconstruction with long term follow-up:

A CASE SERIES REVIEW

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Introduction

Bone healing is a complex array of multifactorial physiological processes. Medical interventions, such as bone graft technologies, are commonly employed to assist in this process. Currently, several methods exist to regenerate bone, autologous bone grafting being the most prevalent. Although useful for a wide spectrum of clinical applications, limitations of autografts have prompted the development of demineralized bone matrix formulations and new synthetic products to promote bone generation.

Bone grafting with synthetic products is fast becoming the prevailing treatment alternative to autologous bone grafting. Unlike bone harvesting procedures, synthetic ceramic materials reduce the risks of post-operative complications secondary to the harvesting technique; further eliminating the necessity of a secondary surgical site and the perils associated with a limited graft yield. The ideal synthetic bone substitute should be derived from a material that is highly osteoconductive and exhibits a high degree of porosity. As such, synthetic bone grafts are commonly derived from bioceramics such as calcium phosphates (Hydroxyapatite and Tricalcium Phosphate) and calcium sulphate.

Interest in calcium-based bioceramics as a bone graft substitute is supported by its bioactive properties. Specifically its ability to provide biocompatible scaffolding for mature osteoblasts allows the formation of new bone, a process known as osteoconduction. Moreover, some can induce the formation of new bone directly onto the bioceramic material itself by influencing the cellular differentiation of mesenchymal stem cells into chondroblasts and osteoblasts. Despite the favorable intrinsic properties, not all bioceramics are equally efficacious. Differences in both the chemical and physical properties, including the mechanical integrity and structural pore architecture, will significantly impact positional stability and sustained integration.

A newly developed bioceramic bone substitute CERAMENT™ BONE VOID FILLER, BONESUPPORT AB, Sweden which delivers highly osteoconductive hydroxyapatite particles embedded in an injectable and curable calcium sulphate paste combined with the water-soluble radiocontrast agent iohexol, employs the properties necessary for successful bone remodeling and fracture stabilization. Clinical studies evaluating patients with osteoporotic vertebral compression fractures treated with CERAMENT™ demonstrated significant improvements in pain relief, quality of life and subsequent recurrence of remote and adjacent fractures. In addition, several animal and human studies have successfully demonstrated incorporation, new bone growth and bone remodeling after treatment with CERAMENT™. This was achieved with sustained durability and virtually no complications.

In reconstructive foot and ankle surgery the use of bone grafting is common. Whether for trauma, acquired or congenital deformities, arthrodesis, bone loss from fractures, bone tumor resection or joint replacement, the need for a viable and efficacious alternative to autografting would be welcomed. Therefore, it is the purpose of this study to present multiple clinical case reports evaluating the efficacy and long-term durability of the CERAMENT™ bioceramic bone substitute in foot and ankle reconstruction.

IDEAL CHARACTERISTICS OF IMPLANTABLE BIOCERAMICS

- A. Biocompatible with host tissues.
- B. Non-Antigenic.
- C. Non-Inflammatory.
- D. Sufficiently porous and osteoconductive.
- E. Ability to stimulate bone induction.
- F. Resorbable & replaceable by bone.
- H. Stable in varying temperatures.
- I. Achieve fracture stability quickly and efficiently and with long-term durability.
- J. Reduce or eliminate secondary fractures and post-operative complications.
- K. Inexpensive.
Limb Salvage of a Diabetic Mid-Foot Ulcer with Osteomyelitis using CERAMENT™

A 46 year old male with a body mass index (BMI) > 30 kg/m² presented with diabetes mellitus, diabetic peripheral neuropathy and a diabetic foot ulcer of the cuboid region of the left foot with osteomyelitis secondary to malalignment (figures 1-2). Bone biopsies of the tarsal region confirmed chronic long standing osteomyelitis.

Intravenous antibiotics were administered for 6 weeks prior to treatment. A gastrocnemius recession was performed to correct an equinus contracture of the ankle secondary to the foot pathology. An “internal amputation” of the involved tarsal bones was successfully achieved (figure 3). The mid-foot bone void was occupied with an internal fixation device to support realignment arthrodesis, while the injectable, curable ceramic bone substitute, CERAMENT™, was administered to provide structural cancellous support within the void and residual gaps (figure 4).

The radiopacity enhancing component contains water soluble iohexol which is rapidly excreted from the body and CERAMENT™. This allows us to be able to observe, the gradual resorption of CERAMENT™ incorporating into new bone growth and eventually remodeled completely into newly formed trabecular bone, without being obscured by radiopaque enhancement of the iohexol. At the 7-month follow-up period we observe adequate wound and bone healing allowing us to remove the internal fixation device (figure 5). The foot was maintained in a planti-grade position and at 20-months post-operative follow-up we observe the mid-foot free of ulceration and infection (figure 6). The use of the CERAMENT™ composite assisted in successful realignment arthrodesis and amelioration of the osteomyelitis.

Figure 1. Pre-operative diabetic foot ulcer with associated osteomyelitis and malalignment.

Figure 2. Pre-operative radiograph of a malaligned lateral column of the foot with osteomyelitis.

Figure 3. Intra-operative radiograph of an “internal amputation” of the infected cuneiform, navicular, cuboid and talus bones.

Figure 4. Intra-operative realignment of the mid-foot with internal fixation and CERAMENT™ employed as a bone void filler.

Figure 5. A post-operative lateral radiograph following hardware removal and mid-foot realignment.

Figure 6. A well-healed diabetic foot ulcer following a realignment arthrodesis at 20-months post-treatment.
Limb Salvage of a Diabetic Charcot Arthropathy with Osteomyelitis using CERAMENT™, a Bi-Phasic Ceramic Bone Substitute

A 57 year old male presented with a diabetic long-standing mid-foot ulcer secondary to a neuropathic charcot deformity with accompanying instability noted at the ankle, sub talar joints and the mid-foot. Exposure of the talar head allowed bone biopsy and subsequent diagnosis of osteomyelitis (figure 1). Radiographic evidence revealed the extent of the neuroarthropathy and tarsal deformity (figure 2). Application of an external fixator for stabilization and bone debridement followed by intravenous antibiotics and local wound care were performed.

Approximately 6 weeks after the wound was resolved, ankle and foot reconstruction was planned in two separate surgical stages to restore stability of the ankle and hind foot, then the mid-foot to prevent future recurrence. The first stage consisted of a complete talectomy and application of an intramedullary retrograde nail (figure 3 & 4). The talus bone void was replaced with a combination of allogenic bone and autologous blood. The allogenic bone was washed in autologous blood and applied directly into the bone void. CERAMENT™ bi-phasic ceramic bone substitute was administered within the void and residual gaps in order to enhance cancellous bone integrity and provide structural support (figure 5).

Following adequate stabilization of the ankle, the second stage of the reconstruction was performed, post first stage, in order to stabilize the mid-foot. The second stage consisted of bone resection and arthrodesis via a locking plate. The resected bone void was back filled as before and CERAMENT™ was again utilized to fill in residual gaps and to incorporate new bone growth, thus providing enhanced structural support (figure 6).

Postoperatively, for each reconstruction, the patient was immobilized in a below the knee cast for two months. At 4-months post second reconstruction (mid foot), the patient was full weight bearing and regeneration of solid bone was seen progressing at each monthly visit. At 6-months post treatment the bone appeared to be fully incorporated and mature (figure 7 & 8). At 4-years the patient continues to exhibit excellent results. The CERAMENT™ bone substitute was instrumental in achieving successful arthrodesis and stability.
Back Filling of a Calcaneal Autograft Site with CERAMENT™, a Bi-Phasic Ceramic Bone Substitute

A 51 year old African-American male presented with a non-union of the first metatarsophalangeal joint (MPJ), (figure 1). His primary complaint was pain and discomfort when fully weight bearing or walking. Our goal was to achieve subjective improvement of the patient’s level of pain and walking tolerance. In addition, we hoped to objectively restore first ray stability, thus alleviating symptoms of MPJ overload. The procedure will also restore great toe alignment and length, correcting lesser digital misalignment after restoration of full halluc position.

Proper joint preparation of the distal first metatarsal and proximal phalangeal joint surfaces was performed prior to the harvesting procedure (figure 2). A tricortical deep block graft was harvested from the ipsilateral aspect of the calcaneus (figure 3 & 4). The first MPJ was reconstructed with the cancellous calcaneal bone graft. Approximately 10mL of the CERAMENT™, bi-phasic ceramic bone substitute, was injected into the calcaneal defect to encourage union and bone regrowth prior to weight bearing (figure 5). The calcaneal bone graft was cut and contoured to fill the MPJ defect and to restore planti-grade hallux with normal parabolic length and alignment. A low profile locking plate was placed dorsally overlying the midline of the first MPJ. The CERAMENT™ composite was again utilized in the gaps and voids of the recipient site to promote incorporation and stability of arthrodesis. Radiographic outcomes were observed at the donor and recipient sites until healing was confirmed as bridging trabeculation. At the 6-month follow-up period bone incorporation of the calcaneous and MPJ had fully progressed (figure 6). Subjective pain assessment revealed significant pain relief and improvement in overall quality of life. Furthermore, we noted no secondary heel fractures, as is sometimes common for calcaneous harvesting, and the patient was full weight bearing and back to normal activity. After 4 years, the patient remains asymptomatic.
Benign Bone Cyst Removal and Replacement with CERAMENT™ a Bi-Phasic Ceramic Bone Substitute

A 17 year old female presented with intense heel pain secondary to a symptomatic unicameral calcaneal bone cyst. Radiographic lateral views of the calcaneus revealed a central triangular subthalamic radiolucent lesion with sharp edges underlined by a sclerotic rim. The matrix was homogenous, without residual trabeculation (figure 1). The cyst had reached a critical size, defined as >100% intracalcaneal cross section in the coronal plane and >30% in the sagittal plane, placing the patient at risk for fracture.

Bone biopsies were negative for infection and a fluoroscopic curettage of the inner surface of the cavernous cyst wall was performed (figure 2). Filling of the previously cystic cavity with CERAMENT™, bi-phasic ceramic bone substitute, was performed under fluoroscopic guidance and confirmed radiographically (figure 3 & 4).

The flowable CERAMENT™ composite is combined with a water soluble radio-contrast agent, iohexol, which produces a readily injectable paste that was easily introduced into the cystic void via a percutaneous approach and under fluoroscopy. The material was set in less than 15 minutes and was fully stiff and hardened within 1 hour. Within 3-months post treatment, the patient was asymptomatic and was full weight bearing. At 24-months we observed complete consolidation and incorporation of new bone and a clinically stable foot free of any residual pain or complications. Using CERAMENT™ bone substitute is an excellent option for young adults with calcaneal bone cysts who desire early return to athletic activity with minimal risk of postoperative pathological fracture.
Benign Tibial Bone Cyst Removal and Replacement with CERAMENT™, a Bi-Phasic Ceramic Bone Substitute: Eight Years Post Sub Talar Joint Arthrodesis Following Trauma

A 55 year old female with a history of calcaneal fracture and ankle trauma presented with severe ankle pain and discomfort. The patient had previously undergone a sub talar joint arthrodesis to repair the previous trauma. Plain radiographs showed an expansive and well defined tibial bone lesion in the cortex of the medial malleolus extending upward toward the interosseous border (figure 1). Computed Tomography (CT) of the tibia confirmed an osteolytic expansive lesion (figure 2). A subsequent bone biopsy revealed a benign cyst with reparative fibrosis consistent with the previous trauma. Bone cultures were negative.

Fluoroscopic curettage of the bone lesion, which was occupied with solid white tissue, was performed without complications. Following removal of the cyst, the bone void was replaced with the CERAMENT™ bone substitute. Fluoroscopic insertion of the CERAMENT™ composite was performed with no complications or leakage (figure 3).

A 13-G straight injection cannula was percutaneously advanced into the cystic corridor and approximately 15mL of the bone substitute was homogenously spread into the osteolytic void. Intra-operative fluoroscopy revealed immediate curing and excellent cement impregnation, as visualized by the exceptional radiopacity exhibited by the CERAMENT™ bioceramic (figure 4).

At 3-months follow-up the patient was asymptomatic and at 12-months follow-up consolidation and incorporation of new cancellous bone was achieved (figure 5 & 6). Moreover, the patient was full weight bearing with complete ankle stability and no sign of implant-induced adjacent fractures. CERAMENT™ was effective in completely relieving the ankle pain and restoring ankle and tibia structural integrity.

Figure 1. Pre-operative anteroposterior (AP) radiograph of ankle.
Figure 2. Pre-operative lateral CT scan showing cyst.
Figure 3. Intra-operative insertion of CERAMENT™ following curettage.

Figure 4. Intra-operative fluoroscopy using CERAMENT™.
Figure 5. Post-operative distal tibia with incorporation of CERAMENT™ at 12-months.
Figure 6. Post-operative AP radiograph of CERAMENT™ fully incorporated at 12-months.
Tendo Achilles Lengthening and a Pantalar Arthrodesis of a Mal-Aligned Charcot Deformity using CERAMENT™ as a Bone Void Filler

A 75 year old female presented with severe lower extremity pain and discomfort secondary to talonavicular displacement and mal-alignment accompanied by a charcot deformity (figure 1 & 2). A bone biopsy was performed ruling out osteomyelitis. Our goal was immediate off-loading and reconstructive surgical intervention to reverse the deformity and restore joint stability. Due to the excessive local inflammation, bone resorption and concern for bone healing and soft tissue reconstruction, an external fixator was applied to provide realignment and support to the ankle and hind foot prior to reconstructive surgery.

After three months of non-weight bearing, surgery was performed. Firstly, Achilles tendon lengthening was used to remove the contracture and relieve the plantar pressure distribution. Secondly, pantalar arthrodesis was performed to repair the significant instability and subluxation of the ankle and hind foot.

Internal fixation was applied and a wedge resection of the posterior talonavicular area was utilized to obtain satisfactory functional position and alignment for arthrodesis (figure 3). Subsequent void fill of the resected area was accomplished with CERAMENT™ bone void substitute (figure 4 & 5).

Three months after the surgery, radiographs showed dense fusion and incorporation of the ankle and talonavicular region (figure 6). In addition, the patient was asymptomatic and full weight-bearing. The CERAMENT™ composite formed a solid, pain free arthrodesis in a biomechanically stable and functional position. Pantalar arthrodesis with CERAMENT™ bone substitute was effective, safe and can eliminate pain and improve function in even the most severely disabled patient.
Discussion

The use of bone grafts for foot and ankle reconstruction has been well documented, specifically, in the areas of nonunion and cystic bone lesions, reconstructive osteotomies and arthrodesis\textsuperscript{13}. Whether 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\textsuperscript{14}. It is for these reasons there has been an emergence of bone graft substitutes in the area of foot and ankle reconstruction.

In our series we presented an assortment of clinically challenging cases employing the use of an innovative bone remodeling technique that relies on the unique properties afforded to the CERAMENT™ bone substitute composite. The immediate pain relief, full weight-bearing recovery, bone consolidation and incorporation as well as the structural bone integrity and durability demonstrated in the case reports indicates that CERAMENT™ can provide a safe and effective long-term solution for reconstructive foot and ankle arthrodesis and back-filling procedures secondary to evacuation of bone cysts.

The CERAMENT™ bioceramic bone substitute, which consists of hydroxyapatite embedded in a synthetic calcium sulphate carrier (ratio 40/60 weight-%), mixed with the radiocontrast agent iohexol, possesses a combination of distinctive advantages that warrant its safe and efficacious use. A passive precipitation of hydroxyapatite on the surface of the implant\textsuperscript{15} seems to extend the gradual resorption of the calcium sulphate component over months\textsuperscript{11}, allowing the cement to be replaced by the in-growing bone that remodels to form trabeculae\textsuperscript{16, 17}. After an initial pliable period, the calcium sulphate hardens to form a microporous filler that can provide the support for fixation devices, as demonstrated in our series. With its consistent and progressive resorption rate that is balanced with new bone growth and remodeling, excellent injection ability and designed compressive strength, the calcium sulphate acts as an effective bone void filler that can be applied using minimally invasive techniques and could conceivably be used for future applications as a drug delivery system.

Meanwhile, the hydroxyapatite particles act as scaffolding that also retards the overall rate of absorption of the calcium sulphate\textsuperscript{11}, while simultaneously providing the osteoconductive template for new bone incorporation. This osteoconductive scaffolding is highly suitable for arthrodesis and back-filling procedures as the microparticles remain in situ over a period of years to provide the matrix for new bone ingrowth with the compressive strength comparable to that of cancellous bone\textsuperscript{19}.

The added benefit provided by the radiocontrast agent (iohexol, 180 mg iodine/mL) allows excellent radiopacity, which aids in the precise delivery of the composite with minimal risk of leakage.

The CERAMENT™ bioceramic bone substitute offers the foot and ankle surgeon a valuable therapeutic that meets the desirable attributes of a bone graft while significantly reducing the risks associated with morbidity. This unique composite also exhibits the necessary qualities needed from a bioceramic that allows safe and effective treatment of a variety of reconstructive ailments.

“CERAMENT™ can provide a safe and effective, long-term solution for reconstructive foot and ankle arthrodesis and back-filling procedures following evacuation of bone cysts.”
References


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.