

Research Article

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Preliminary results of Highly Injectable Bi-Phasic Bone Substitute (CERAMENT) in the treatment of benign bone tumors and tumor-like lesions

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Abstract: Background: CERAMENT™|BONE VOID FILLER is an injectable and moldable ceramic bone substitute material intended for bone voids. The material consists of hydroxyapatite and calcium sulfate hemihydrate. The aim of this study is to present the first long-term results following open curettage of benign bone tumors and tumor-like lesions and void filling with this novel injectable and synthetic bone graft. Methods: Thirty three patients were enrolled into the study between June 2013 and October 2014. Totally, we treated 24 women and 9 men with a median age of 47 years (range: 22-74). All patients suffered from primary musculoskeletal system disorders (enchondroma 63,6%, giant cell tumor 18%, aneurysmal bone cyst 9%, fibrous dysplasia 9%, Gaucher disease 3%). We performed curettage of pathological lesions, then the bone substitute was administered by means of needle to the void. Results: The average follow-up was 13 months (range: 2-13 months, median 10 months). No metastasis or recurrence had been detected. We received significant clinical improvement relating to VAS, MSTs, and oncological results. Conclusions: The results of our study report that CERAMENT can be successfully used as a bone substitute in patients with various bone diseases, as well as benign bone tumors. CERAMENT can provide an effective and

long-term solution for reconstructive procedures following curettage of bone tumors and tumor like lesions.

Keywords: Bone tumor; Bone defect; Bone substitute

1 Introduction

Benign bone tumors and tumor-like lesions are a heterogeneous group of bone lesions and much more frequent than malignant bone tumors among the total number of skeletal neoplasms [1]. All age groups are affected and any bone can be involved. They usually cause no symptoms and frequently are found incidentally during an unrelated radiographic examination [2, 3].

Bony lesions that are symptomatic, grow rapidly or are radiologically unclear, must be biopsied. After histological investigation an appropriate therapy is initiated. Intralesional curettage and the void reconstruction is the treatment of choice. Various options of bone defect filling have been reported including cancellous bone autograft as a gold standard. This modality has many desirable graft properties [3-6]. However autogenous bone grafting has some restrictions, such as donor site morbidity, the limited availability of grafts of sufficient size and shape, and additional procedures for harvesting. Complication rates of 20% have been reported. Similarly, allografts have a high complication rate [7-9].

Searching for an alternative to overcome the limitations of autografts and allografts, a variety of synthetic bone substitute materials have been developed [10, 11]. Unlike bone harvesting procedures, synthetic ceramic materials reduce the risk of post-operative complications secondary to the harvesting technique; further eliminating the need for 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.

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Table 1: Patient demographics and indications for surgery.

	Total	Women	Men
Patient number	33	24	9
Median age [years]	47	48	26
Musculoskeletal system condition:			
Enchondroma	21	21	-
Giant cell tumor	6	3	3
Aneurysmal bone cyst	3	-	3
Fibrous dysplasia	3	-	3
Gaucher disease	1	1	-

Such, synthetic bone grafts commonly derive from bio-ceramics, such as calcium phosphates (Hydroxyapatite and Tricalcium Phosphate) and calcium sulphate. Bone graft substitutes possess different characteristics with regard to their mechanical properties and resorption rates [12].

The CERAMENT concept is based on research from the Medical Faculty, Lund University, Sweden and the research group of Lars Lidgren, Professor in Orthopedic Surgery.

It started as a research project in the mid 1990s and has resulted in approximately 40 preclinical scientific publications and several dissertations, among them especially the thesis by Malin Nilsson, “Injectable Calcium Sulphate and Calcium Phosphate Bone Substitutes” that was publicly defended and approved in 2003. In 1999 the first patent applications were filed, and in 2001 the Medtech Company BONESUPPORT was founded. First treatment was a vertebroplasty with CERAMENT SPINESUPPORT in 2003. First market approval was for CERAMENT BONE VOID FILLER in US, 2006.

CERAMENT™|BONE VOID FILLER is an injectable and moldable ceramic bone substitute material intended for bone voids. The material consists of a powder and a liquid component. The major constituents of the powder are hydroxyapatite and calcium sulfate hemihydrate. The liquid component contains iohexol (C-TRU) as a radio-opacification enhancer. Mixing the components, with the combined mixing injection (CMI) device, results in a viscous material suitable for percutaneous injection into a bone void. By combining hydroxyapatite and calcium sulfate an optimal balance is achieved between implant resorption rate and bone in-growth rate. Calcium sulfate acts as a resorbable carrier for hydroxyapatite. Hydroxyapatite has a slow resorption rate, high osteo-

conductivity that promotes bone in-growth and gives long term structural support to newly formed bone. The ceramic bone substitute material is placed into the bone void under visual inspection or under radiographic monitoring.

The aim of this study is to present the first long-term results of (i) durability and radiological healing efficacy; (ii) the functional outcomes of the patient; (iii) and the complications following open curettage of benign bone tumors and tumor-like lesions and void filling with this novel injectable and synthetic bone graft.

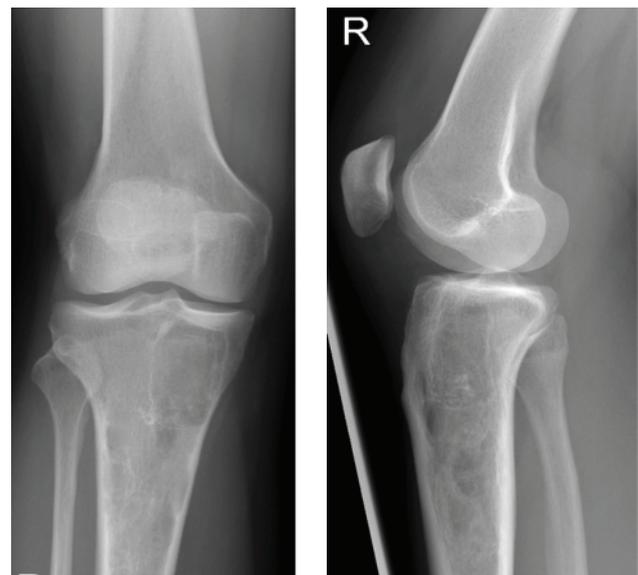
**Figure 1:** Pre-operative antero-posterior and lateral plain radiograph demonstrating large enchondroma of the proximal tibia.



Figure 2: Intraoperative insertion of CERAMENT into the calcaneus following curettage of the giant cell tumor.



Figure 3: Intraoperative view of CERAMENT filling the void of the calcaneus.



Figure 4: Intraoperative view after curattage of a large lesion of the Gaucher disease of the distal part of femur.



Figure 5: Intraoperative view of CERAMENT filling the void of the distal part of the femur together with the allogenic bone debris.



Figure 6: Intraoperative insertion of CERAMENT into the humerus following curettage of enchondroma.

2 Material and methods

Thirty three patients hospitalized at the Department of Orthopedics, Traumatology and Orthopedic Oncology of Pomeranian Medical University in Szczecin, Poland, were enrolled to our study between June 2013 and October 2014. Totally, we treated 24 women and 9 men with a median age of 47 years (range: 22-74). All patients were suffering from musculoskeletal system conditions (enchondroma 63,6%, giant cell tumor 18%, aneurysmal bone cyst 9%, fibrous dysplasia 9%, Gaucher disease 3%). They required curettage of pathological lesion and administration of bone substitute (Table 1). The diagnosis was established by biopsy and X-ray picture. The lesions were localized in proximal part of the tibia (18%), calcaneus (18%), proximal part of humerus (18%), distal part of femur (8%), proximal part of femur (8%), II metacarpal (9%), talus (9%) and distal part of the tibia (9%) (Fig. 1).



Figure 7: Immediate post-operative antero-posterior plain radiograph demonstrating filling the void with CERAMENT after curettage of the enchondroma of the humerus.



Figure 9: Immediate post-operative antero-posterior plain radiograph demonstrating filling the void with CERAMENT after curettage of the GCT of the talus.



Figure 8: CT-scan of the proximal tibia at 8 weeks demonstrating progressive resorbtion of the CERAMENT and early replacement with new bone.

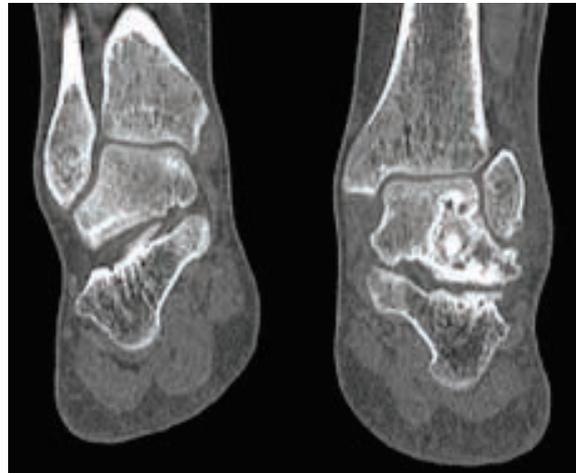


Figure 10: CT-scan of the talus at 5,5 months demonstrating further resorbtion of the CERAMENT and filling with new bone.

All patients had completed and signed a consent form before surgery. Peri-operatively, all patients received a prophylactic broad-spectrum antibiotic. In the operating theater under general or spinal anesthesia we performed curettage of pathological lesions. Then the bone substitute was administered by means of needle to the void. The volume of CERAMENT injected ranged from 5 to 18 ml, with easy handling and proper injectability in all cases (Fig. 2, 3, 6).

In one case (Gaucher disease), we decided to fill the void with the allogenic bone debris first and then to administer CERAMENT bone substitute (Fig. 4, 5).

CT scans and X-rays were carried out post-procedure to assess bone remodeling, intra-osseous CERAMENT distribution and any signs of its leakage (Fig. 7 - 11). Clinical outcome was to quantify using VAS score (0–10) and the musculoskeletal tumor society (MSTS) scoring system



Figure 11: CT-scan of the talus at 5,5 months demonstrating further resorbtion of the CERAMENT and filling with new bone.

(0–35), and were performed before the operation as well as 1 month and mean of 13 months of observation after



Figure 12: Immediate post-operative antero-posterior and lateral plain radiograph demonstrating filling the void with CERAMENT together with the allogenic bone debris after the resection of the lesion in the course of the Gaucher disease.



Figure 13: Antero-posterior and lateral plain radiograph at 4 months demonstrating further circumferential resorption of CERAMENT and filling with new bone in the course of the Gaucher disease.

the procedure. Obtained data were compared using paired samples t-test at baseline as well as during follow-up. Statistical significance was accepted as significant at $p < 0,05$.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.



Figure 14: The properly healed wound of the lateral aspect of heel after the procedure.

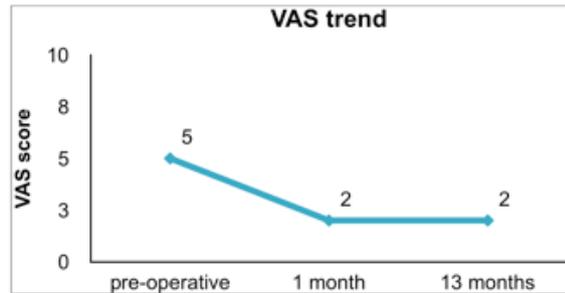


Figure 15: Decrease of VAS score over the follow-up.

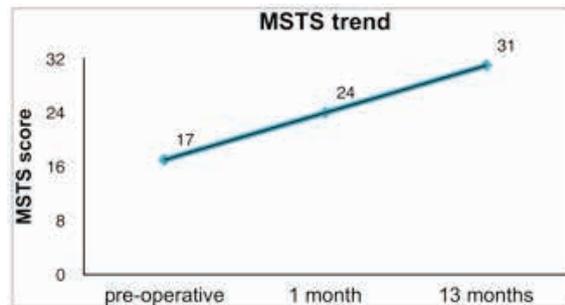


Figure 16: Improvement of MSTS score over the follow-up.

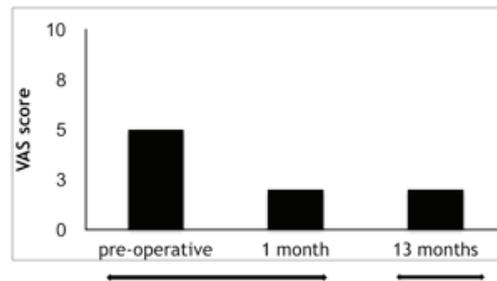


Figure 17: Significant decrease of VAS score over the follow-up.

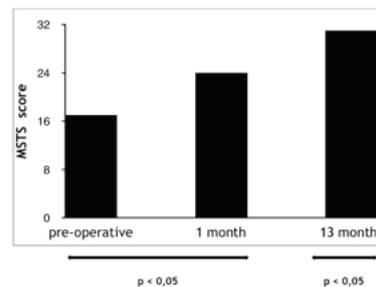


Figure 18: Significant improvement of MSTS score over the follow-up.

3 Results

The average follow-up was 13 months (range: 2-13 months, median 10 months). No metastasis or recurrence had been detected.

The peri-operative radiovisibility of CERAMENT was good. Due to high microporosity, the radio contrast 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. At CT scans and X-rays performed post-procedure, we observed good distribution of the bone cement and visible bone remodeling in all patients (Fig. 12, 13). Moreover there was no leakage of CERAMENT outside the bone.

Neither allergic symptoms, abnormal wound healing nor infections were observed (Fig. 14).

The VAS score assessment showed a decrease over time from a mean of 5 (range 1-9) before operation, to 2 (range 1-4) at 1 month and 2 (range 1-4) at the latest follow-up

Similar results were obtained by analyzing MSTS score at the same time points. In all patients we detected a functional improvement and thereby MSTS score increase, respectively 24 (range 17-29) and 31 (range 27-35) compared to the pre-operative – 17 (range 11-23) (Fig.16).

Both cases showed significant levels with $p < 0,05$ (Fig.17, 18).

4 Conclusion

The results of our study report that CERAMENT can be successfully used as a bone substitute in patients with various bone diseases, as well as bone tumors. CERAMENT can provide an effective and long-term solution for reconstructive procedures following curettage of bone tumors. CERAMENT administration is easy to use, safe and well tolerated by patients. It has also been funded by the National Health System in Poland within the Oncological Package since 2015. It significantly reduces recovery time and improves quality of life. Although the study is still ongoing, new bone formation was clearly demonstrated in all cases with sufficiently long follow-up, with no adverse effects observed. We believe the method should not be compared with other methods results such as bone grafts or steroid injections due to other mechanisms of biological reaction.

It is therefore preliminary concluded that CERAMENT can provide a safe and effective alternative to bone auto- and allografts on the basis of its unique bioactive and osteoconductive reaction without osseogenesis stimulation.

Conflict of interest: The authors have no conflict of interest to declare.

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