

CERAMENT[®] G
with Gentamicin

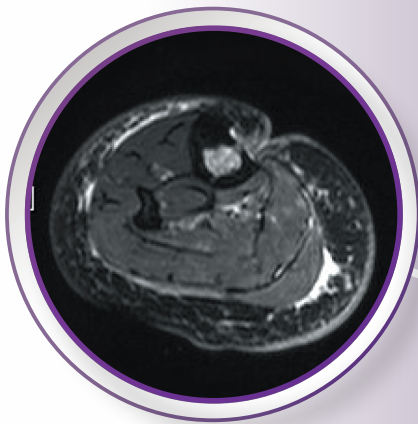
PUBLICATION SUMMARY

Medical Education Series

Single-Stage Treatment of Chronic Osteomyelitis

M. A. McNally et. al

*Nuffield Orthopaedic Centre
Oxford University Hospitals*



Single-Stage Treatment of Chronic Osteomyelitis

INTRODUCTION

The following is a summary of a publication on CERAMENT® G: Single-stage treatment of chronic osteomyelitis with a new absorbable, gentamicin-loaded, calcium sulphate/hydroxyapatite biocomposite: A prospective series of 100 cases as published in *Bone Joint Journal* 2016;98-B:1289-96.

METHODS

One hundred patients with chronic osteomyelitis were treated by a single-stage protocol in 105 bones. All patients were treated by a multi-disciplinary team (MDT) with a single-stage procedure which included debridement, multiple samples, stabilization, dead space management with CERAMENT® G, primary skin closure and culture specific systemic antibiotics.

- Osteomyelitis followed injury or surgery in 81 patients
- 9 patients had concomitant septic arthritis
- 80 patients had comorbidities (Cierny-Mader (C-M) Class B hosts)
- 10 patients had non-unions

Inclusion Criteria:

- Cierny-Mader (C-M) Type III (localized) and Type IV (diffuse)
- Having chronic osteomyelitis symptoms for at least 6 months with clinical and radiological features accompanied by at least one of the following: the presence of a sinus, an abscess or intra-operative pus, supportive histology, or two or more microbiological cultures with indistinguishable organisms.
- Infected non-union with bone loss <1cm at presentation.

Exclusion Criteria:

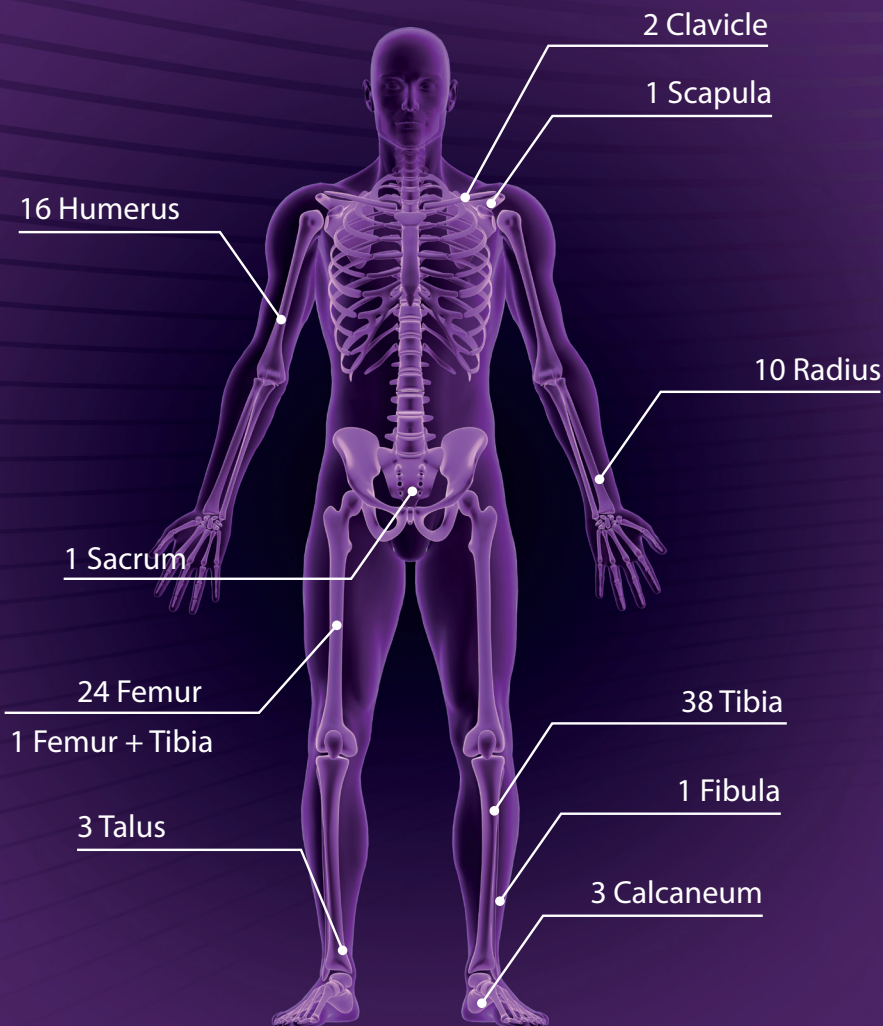
- Diabetic Foot Infections (treated at a different unit at the Nuffield Orthopaedic Centre)
- Contraindications according to the IFU

Patient Demographics:

- 100 patients
- 65 males / 35 females
- Mean age 51.6 years (23 to 88 years)
- 80 had co-morbidities

LOCATION OF OSTEOMYELITIS BY CIERNY-MADER (C-M) STAGE, SOFT TISSUE MANAGEMENT AND STABILIZATION METHOD

Using the C-M classification, 78 patients were defined as Type III and 22 patients as Type IV. A total of 80 patients (80%) were Class B hosts. 9 patients were diagnosed with septic arthritis of an adjacent joint (3 shoulders, 2 elbows, 3 ankles, and 1 wrist). 10 patients had infected nonunion (4 Tibia, 3 Femur, 3 Humerus). 71 patients presented chronic osteomyelitis after a history of an open fracture or following fixation of closed fractures. 19 patients had hematogenous infection. 6 patients had infection after elective surgery (osteotomy, ligament repair, arthroscopy, or fusion), and four followed soft-tissue injury without fracture.



CIERNY-MADER GRADE

	A	B _{local}	B _{systemic}	B _{I+S}
III	18	25	19	16
IV	2	4	5	11

OVERVIEW OF CASES

The tibia, femur, and humerus were the bones most involved and five patients had 2 bones involved. 21 patients needed stabilization and 5 patients were treated with joint fusion. Direct skin closure was performed in 77 patients; however, 5 patients needed a local flap and 18 required free muscle flap reconstruction. All patients had primary skin closure, and no wounds were left open after initial surgery. There were no second debridement planned in any of the 100 patients.

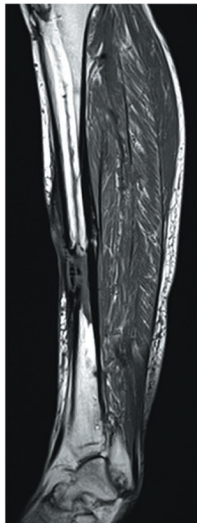


Fig. 1a



Fig. 1b



Fig. 1c



Fig. 1d

1a) Sagittal MR image of the tibia, showing a mid-diaphyseal osteomyelitis with anterior sequestration after intramedullary nailing. The cortex had been drilled six years earlier in an attempt to drain infection; 1b) At operation, the anterior unstable skin and sinus was excised, revealing the dead cortical bone with visible drill holes with surrounding compromised, sclerotic bone and soft tissue; 1c) All dead bone and soft tissue has been excised back to healthy bleeding tissue. The medullary canal was opened proximally and distally. The cavity was then washed and packed with cotton gauze to dry the surface; 1d) 10 mls of CERAMENT G were injected into the cavity 3 minutes after the start of mixing. After 7 minutes, the material was compressed with a gauze swab to improve the contact at the bone surface. The material hardened over a duration of 10 to 15 minutes and the skin defect was covered with a free gracilis muscle flap and split skin graft.

MICROBIOLOGY

Staphylococci were found in 41 cultures (41.8%), with MRSA in 6 patients. *Proteus mirabilis* and *Pseudomonas* spp, were more common in polymicrobial infection, frequently with a gram-positive organism (usually *Staphylococcus aureus*). 16 patients had cultured organisms which were shown to be gentamicin resistant. Some of these organisms displayed inherent (*Salmonella enteritidis*, streptococci) and high-level resistance (enterococci).

Staphylococci	41
MRSA	6
Classified gentamicin resistant	16

The likelihood of gentamicin resistant organisms to be present in patients with hematogenous infection (3/19; 15.8%) was nearly the same as patients following trauma (13/81; 16%). Gentamicin resistant organisms were more likely to exist in patients with polymicrobial infections (9/21; 42.8%) than patients who had single isolates (7/79; 8.9%).

Post operative all patients given parenteral antibiotics for 6 weeks.

SURGERY

Patient: 63 year old male

Ciorny-Mader III Bl+s Tibia

This diabetic patient with severe peripheral neuropathy suffered a burn to front of his leg resulting in skin loss and osteomyelitis. His peripheral circulation was poor and his MRI scan showed cortical and medullary infection over a 6cm region.



Excision, sampling and irrigation (Aqueous Chlorhexidine solution 0.05%):



In the final image a Gracilis muscle flap is being harvested from the opposite thigh to allow soft-tissue reconstruction.

CERAMENT® G HANDLING

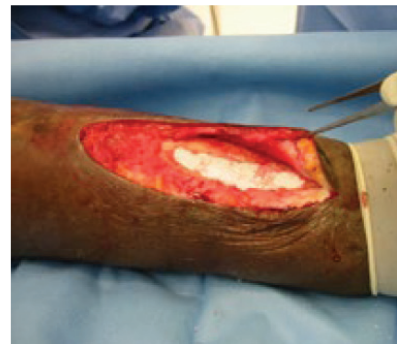
- Inject material 4 to 7 minutes after the start of mixing, for increased viscosity
- 'Compressible' at 8 to 9 minutes after the start of mixing using a gauze swab - this encourages good bone/material contact and intraosseous distribution.

A ONE-STAGE APPROACH

Staged surgical treatment for chronic osteomyelitis is common, with repeated debridement and delayed skin closure. Further operations may be required to remove polymethylmethacrylate (PMMA) antibiotic-loaded beads or to reconstruct bone defects.

There is an increasing interest in a one-stage approach, which might be more patient friendly. This requires effective dead space management, to eradicate the infection and prevent the need for secondary bone grafting.

Our lower rate of infection recurrence with CERAMENT® G may reflect the increased ability of an injectable delivery system to coat the bone over areas which may harbour residual bacteria, or small fragments of biofilm. The high level of a bacteriocidal antibiotic from CERAMENT® G acts at an important time, when most residual bacteria will be in planktonic form, following adequate debridement.



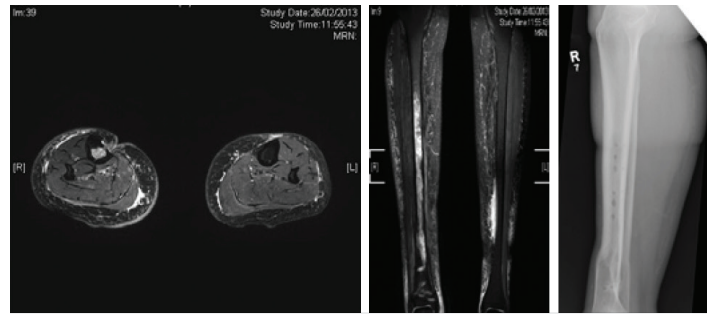
RADIOLOGICAL RESULTS

Patient: 71 year old female

CM IIIBs Tibia

This extensive infection on the medial side of the tibia followed internal fixation of a fracture with a plate. Plate removal did not resolve the infection and the patient presented with a 16cm skin ulcer over the medial tibial border with exposed bone and discharge of pus. MRI confirmed C-M Stage III osteomyelitis.

At operation, a large area of cortex was removed from the medial tibia and the infected medullary bone removed. The defect was filled with 20mLs of CERAMENT® G and a Gracilis muscle flap applied. An external fixator was used to allow full weight-bearing without fracture risk.



Pre operative radiographs and scans



Immediately post operative:

CERAMENT® G is clearly seen.

Filling the bone void, an external fixator has been applied.



13 weeks:

A reaction can be seen throughout the material.



28 weeks:

A reaction can be seen throughout the material.



44 weeks:

There is almost no visible material and there is evidence of organized trabecular bone.

RADIOLOGICAL RESULTS

Patient: 56 years

CM IIIB_{I&S} Tibia

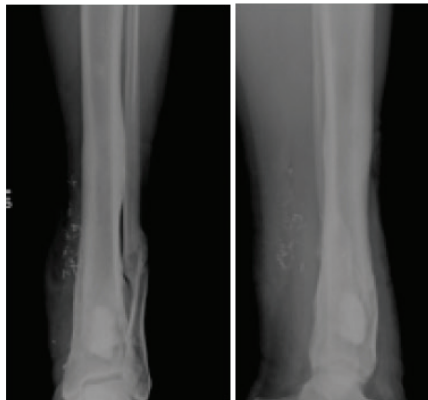
This patient suffered infection after internal fixation of an open ankle fracture. The fracture healed but there was persistent discharge for 3 years despite local excision, VAC therapy, fasciocutaneous flap and prolonged antibiotics.



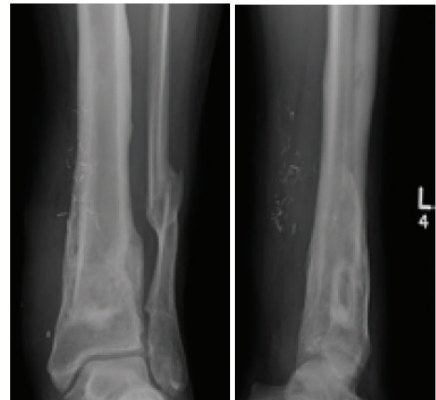
Proximal radiograph



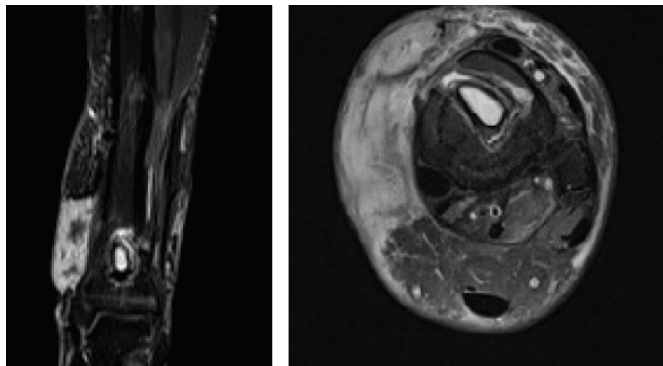
Lateral radiograph



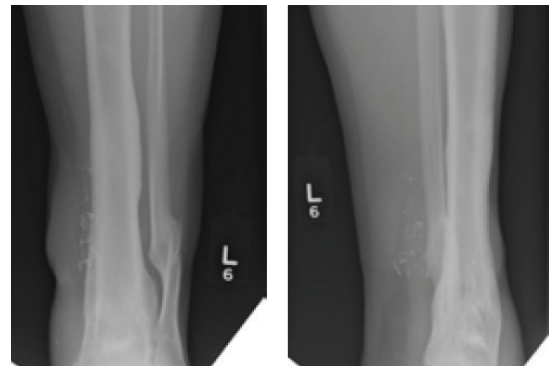
Immediately post operative void filled with CERAMENT® G



At 9 weeks post operative on the lateral radiograph there appears to be a 'void' within the material surrounded by a 'halo'. Patient was clinically well.



MRI at 12 weeks demonstrated a fluid centre surrounded by a 'halo'.



Radiography at 28 weeks shows filling of the 'void' and resorption of the 'halo'. Some material remains visible at the base of the original filled void.

RECURRENCE OF INFECTION

Recurrence of infection occurred in 4 of the 100 patients (4%). Recurrence was no more probable with a resistant organism (1/16; 6.25%) than fully sensitive cultures (3/84; 3.6%). Host class also did not predict the probability of recurrence (Class A - 1/20; 5% vs. Class B - 3/80; 3.75%). At final follow-up all 4 patients were infection free at 13, 16, 17, and 20 months after revision surgery.

The low fracture rate in our study may reflect the higher stability achieved with an injectable in situ hardening material.

RESULTS

One hundred and six consecutive patients were recruited between March 2013 and February 2015. 6 patients were excluded due to intra-operative microbiological and histological samples not meeting the diagnostic criteria.

- Patients were followed up for a mean of 19.5 months (12-34)
- Infection was eradicated in 96 (96%) patients utilizing a single-stage procedure
- All four recurrences were successfully managed with a second surgery
- There were few adverse events, with 3 fractures through the bone voids, 3 unrelated deaths and 6 wound leaks. Wound leakage was infrequent and was mainly related to poor skin cover around the distal tibia.
- Patient outcome was not dependent on C-M host class, microbial culture, wound leakage or presence of nonunion
- Serum Gentamicin levels rose to a maximum of <2mg/l at 24 hours after surgery.
- Bone ingrowth occurred in all cases but incomplete filling was seen in one third.

CONCLUSIONS

The use of CERAMENT® G in a single-stage protocol is an effective treatment for patients with chronic osteomyelitis. The use of CERAMENT® G offers a more patient-friendly treatment compared with other published treatment options.

Thanks to the Bone Infection Unit Team:

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Andrew Woodhouse
Ivor Byren
Tony Berendt

Advancing Osteomyelitis Management

- Bone remodeling to protect and promote bone healing
- Local antibiotic elution that is safe, consistent and clinically significant
- Supports a single-stage surgery



TO ORDER

USA: US.SALES@BONESUPPORT.COM

GLOBAL: ORDER@BONESUPPORT.COM



BONESUPPORT AB
Ideon Science Park,
Scheelevägen 19
SE-223 70 Lund, Sweden

BONESUPPORT, INC.,
60 William St, Suite 330
Wellesley, MA 02481

T: +46 46 286 53 70
F: +46 46 286 53 71
E: info@bonesupport.com

T: +1.877.719.6718
E: us.sales@bonesupport.com
W: bonesupport.com

