

CERAMENT[®] G with Gentamicin
CERAMENT[®] V with Vancomycin

VALUE GUIDE

Proven bone remodeling with
local antibiotic elution

Get it right the first time

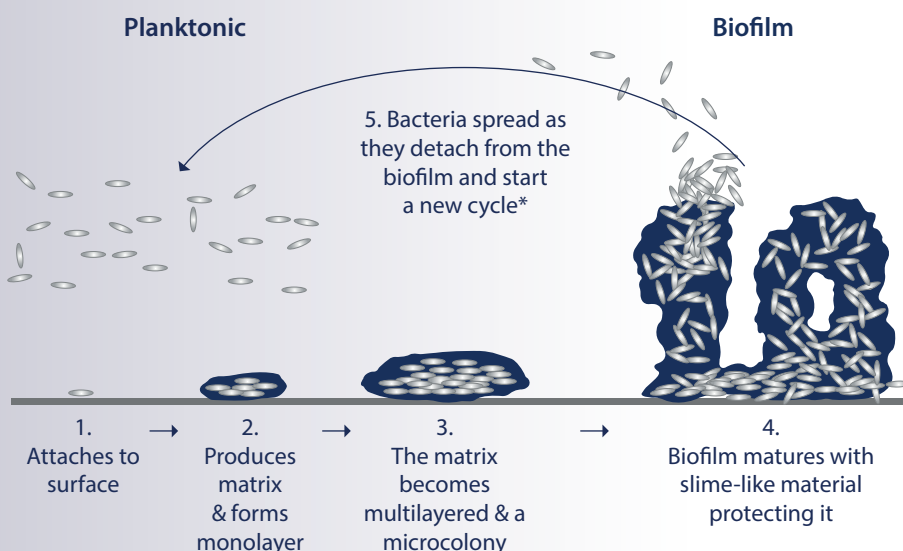


THE BURDEN OF BONE INFECTION

Biofilm formation

Bone infection (osteomyelitis) is an infection of the bone that can arise from fractures, placement of implants, or diabetic foot ulcers. It can be debilitating and can lead to limb amputations.

Bacteria naturally accumulate and form sedentary colonies, commonly referred to as 'biofilm'. Once biofilm forms, susceptibility to antibiotic therapy is significantly reduced and surgical debridement is required.



*adapted from Vasudevan et al. 2014¹

Unmet needs

Despite systemic antibiotics and medical advancements, bone infections are common and impose a significant burden:

1 in 5 infections recur²

1 in 7 open tibial fractures become infected^{3,4}

20 - 30% diabetic foot infections involve bone⁵

6 times higher cost when fracture-related infection is present⁶

Moreover, bone infection is associated with an increased risk of amputation. There is a call for effectively promoting and protecting bone healing when bone infection is present.

¹ Vasudevan, R., 'Biofilms : Microbial Cities of Scientific Significance', Journal of Microbiology and Experimentation, 1.3 (2014), 84–98.

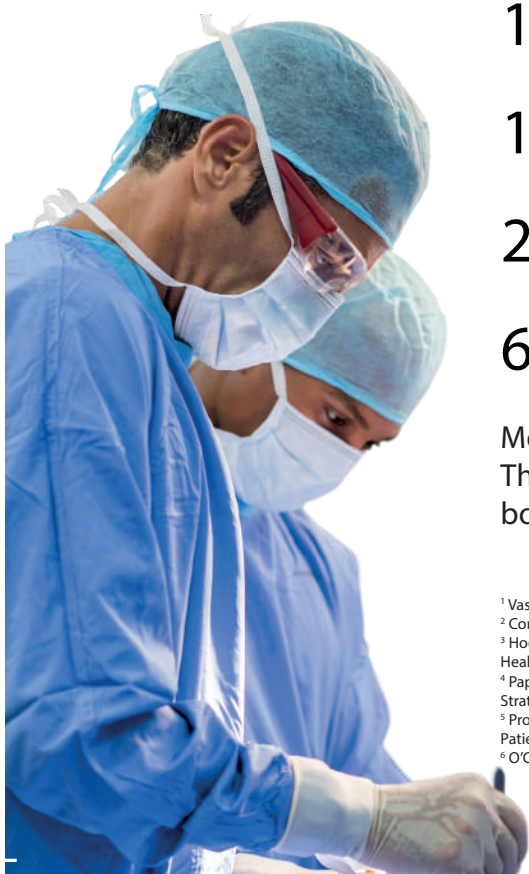
² Conterno, L.O., Turchi, M.D. Antibiotics for treating chronic osteomyelitis in adults. Cochrane Database Syst Rev. 2013;2013(9).

³ Hoekstra, H., Smeets, B., Metsemakers, W.-J., Spitz, A.-C., Nijs, S. Economics of open tibial fractures: the pivotal role of length-of-stay and infection. Health Econ Rev. 2017 Sep;7(1):32.

⁴ Papakostidis, C., Kanakaris, N.K., Pretel, J., Faour, O., Morell, D.J., and Giannoudis, P.V., 'Prevalence of Complications of Open Tibial Shaft Fractures Stratified as per the Gustilo-Anderson Classification', Injury, 42.12 (2011), 1408–15.

⁵ Prompers, L., Huijberts, M., Apelqvist, J., Jude, E., Piaggese, A., Bakker, K., et al., 'High Prevalence of Ischaemia, Infection and Serious Comorbidity in Patients with Diabetic Foot Disease in Europe. Baseline Results from the Eurodiale Study', Diabetologia, 50.1 (2007), 18– 25.

⁶ O'Connor, O., Thahir, A., Krkovic, M., 'How Much Does an Infected Fracture Cost?', The Archives of Bone and Joint Surgery, 135.10(2) (2022), 135–40.



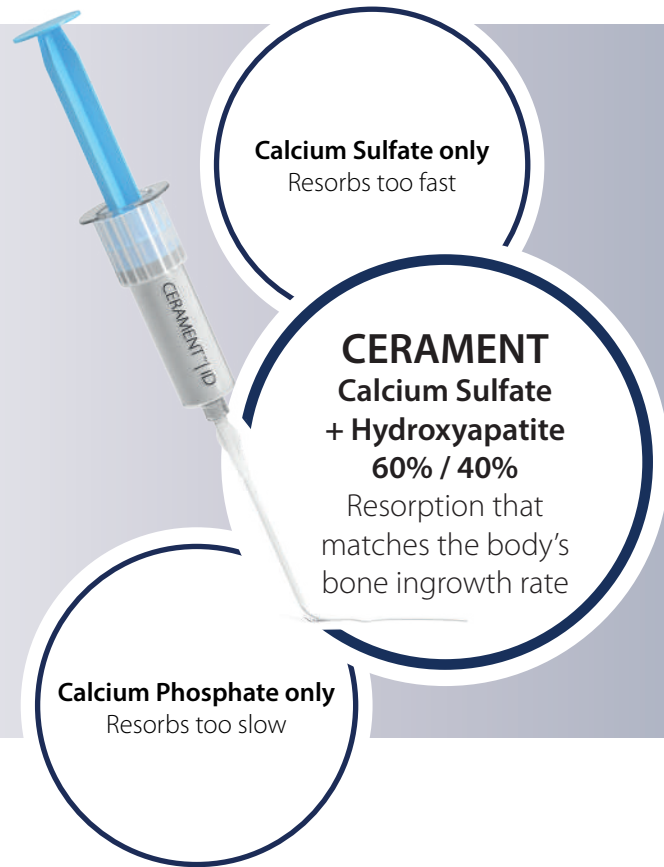
MANAGING BONE INFECTION WITH CERAMENT®

Promote bone remodeling

The traditional way of managing bone infection is to first clear the infection site from any dead and/or poorly perfused bone by surgical debridement, thus leaving a void in the bone.

CERAMENT® technology has the ideal characteristics for a bone substitute to manage bone voids and gaps:

- It resorbs at the same rate as bone naturally forms because of its unique composition (see diagram to the right)
- It is injectable into bone voids so that there is no dead space for bacteria to grow in



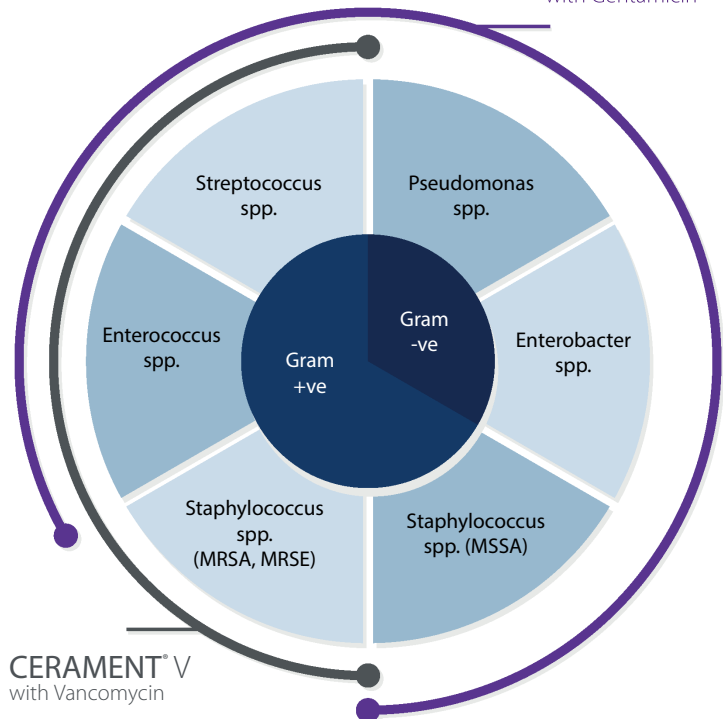
Protect bone healing

CERAMENT G and CERAMENT V are the antibiotic-eluting variants of the CERAMENT technology*. Our patented mixing system is specially designed to enable the safe and reliable local elution of antibiotics, gentamicin and vancomycin respectively.

Using CERAMENT G and CERAMENT V protects bone voids against colonization with a broad range of gram positive and gram negative (CERAMENT G only) bacteria.

*CERAMENT Bone Void Filler (BVF) is the third product of the CERAMENT technology which does not contain antibiotics

CERAMENT® G
with Gentamicin



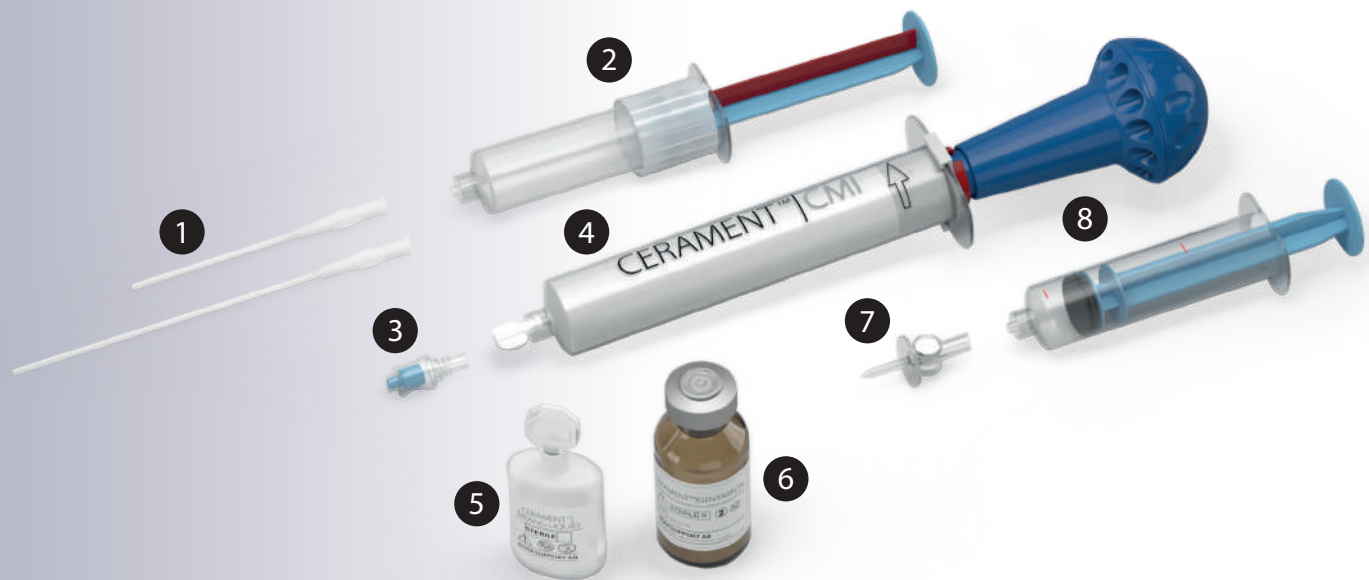
Gentamicin is a broad-spectrum antibiotic that is active against both gram positive and gram negative bacteria.

Vancomycin is active against gram positive bacteria only. Spp. means 'species pluralis' or multiple species.

ALL IN ONE: CLOSED MIXING SYSTEM IN ONE COMPLETE KIT

How this system improves efficiency in operating theatres:

- All-in-one kit for bone void filling
- Standardized mixing procedure
- Reproducible elution of local antibiotic
- Customizable filling using tip extenders
- Overall less exposure to antibiotics to staff



CERAMENT G kit

- | | |
|---|---|
| <ol style="list-style-type: none"> 1. 2 x 11G tip extenders with tapered ends in 50mm & 100mm lengths 2. Injection Device (ID) syringe 3. Valve 4. Combined Mixing and Injection (CMI) syringe pre-filled with hydroxyapatite (HA)/calcium sulfate (CaS) powder | <ol style="list-style-type: none"> 5. Mixing Liquid, sodium chloride 9 mg/mL liquid 6. Gentamicin sulfate, provides 17.5 mg gentamicin/mL paste 7. Dispensing pins 8. Syringe for preparing the gentamicin solution |
|---|---|

CERAMENT G



Size availability
5ml, 10ml

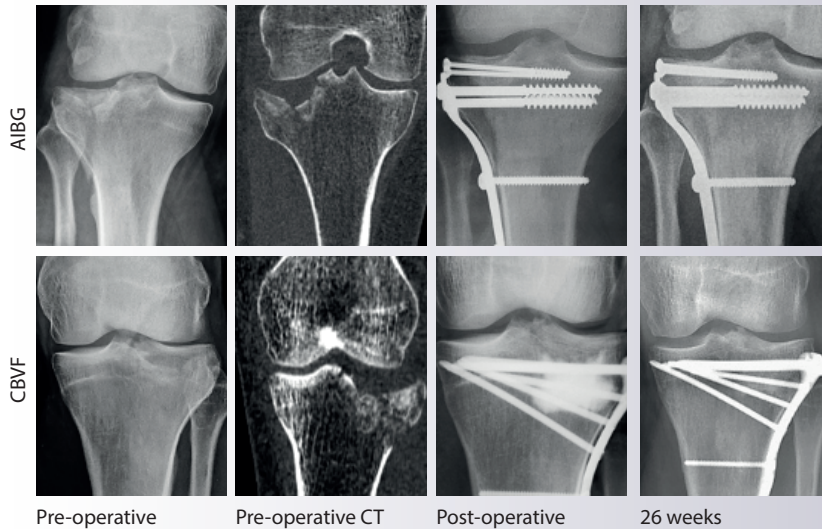
CERAMENT V



Size availability
10ml

No additional mixing equipment needed.

ROBUST EVIDENCE ON CERAMENT® TECHNOLOGY



Evidence-based bone healing

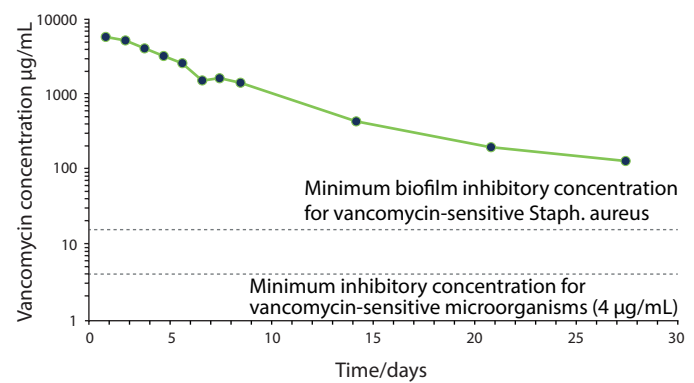
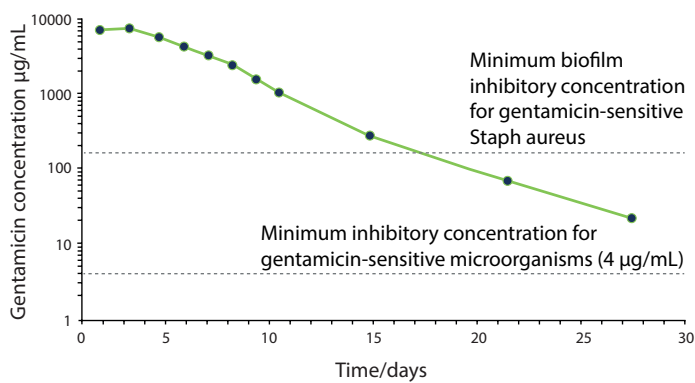
- Largest amount of pre-clinical and clinical data of any bone substitute on the market (240+ publications and counting)
- Level 1 randomized controlled trial (RCT) – the CERTIFY study involves 135 patients and shows that CERAMENT Bone Void Filler (BVF) is as good as autograft (AIBG) in bone remodeling¹
- One and only orthobiologic product with robust long-term evidence: 94% infection-free after 6 year follow-up²



Safe and reliable antibiotic elution

- High burst of local antibiotic with sustained release above the minimum inhibitory concentration (MIC) for at least 28 days (see elution curves)^{3,4}
- No evidence of renal impairment caused by local gentamicin elution up to 525 mg⁵

CERAMENT G and CERAMENT V elution curves from in vitro data



¹ Hofmann, A., Gorbulev, S., Guehring, T., Schulz, A.P., Schupfner, R., Raschke, M., et al., 'Autologous Iliac Bone Graft Compared with Biphasic Hydroxyapatite and Calcium Sulfate Cement for the Treatment of Bone Defects in Tibial Plateau Fractures: A Prospective, Randomized, Open-Label, Multicenter Study', *The Journal of Bone and Joint Surgery. American Volume*, 102.3 (2020), 179–93

² McNally, M.A., Ferguson, J.Y., Scarborough, M., Ramsden, A., Stubbs, D.A., Atkins, B.L., 'Mid- to Long-Term Results of Single-Stage Surgery for Patients with Chronic Osteomyelitis Using a Bioabsorbable Gentamicin-Loaded Ceramic Carrier', *The Bone & Joint Journal*, 104-B.9 (2022), 1095–1100

³ Stravinskas, M., Horstmann, P., Ferguson, J.Y., Hettwer, W., Nilsson, M., Tarasevicius, S., et al., 'Pharmacokinetics of Gentamicin Eluted from a Regenerating Bone Graft Substitute', *Bone and Joint Research*, 5.9 (2016), 427–35

⁴ S038/2013. Data on file. BONESUPPORT AB, Sweden

⁵ Muir, R., Birnie, C., Hyder-Wilson, R., Ferguson, J., McNally, M.A., 'Does Local Implantation of Gentamicin Impair Renal Function in Patients Undergoing Surgery for Chronic Bone Infection?', *International Journal of Research in Orthopaedics*, 7.3 (2021), 438

WHAT IS VALUE?

Value is about achieving the best outcomes per money spent.

CERAMENT G and CERAMENT V provide great value by enabling strategies to reduce surgical interventions and to increase efficiency in clinical practice. Taking advantage of their unique set of features paves the way for more cost-effective and patient-centered care.

Unique features of CERAMENT G and CERAMENT V

Feature	Importance
Proven bone remodeling	Patients are at greater risk of fractures and (re)infection when there is insufficient bone growth in a void
Proven consistent antibiotic elution above minimum inhibitory concentration (MIC) for a clinically relevant time period	Prolonged low-level exposure to antibiotics may cause antibiotic-resistant organisms to evolve
All-in-one kit for closed mixing and injection (antibiotic included)	One kit used straight off the shelf Overall less exposure to antibiotics No off-label mixing
Reproducible mix & setting times	Standardized procedures minimize errors and ensures consistent delivery
Injectable to completely fill bone voids	Dead space left in a bone void are conducive environments for residual bacteria to grow, thus increasing the risk of infection recurrence
Evidence of sustained clinical effectiveness beyond six years	Bone infection can recur beyond two years of follow-up



IMPROVED CLINICAL OUTCOMES

Bone remodeling

CERAMENT BVF (base technology) vs. autologous bone graft *CERTIFY RCT study*¹

CERAMENT BVF was **non-inferior** to autologous bone graft in terms of patient-reported and radiographic outcomes

Infection recurrence

CERAMENT G vs. Gentamicin-impregnated PMMA beads + autograft^{2, 3}



CERAMENT G vs. Antibiotic-loaded calcium sulphate (CS) carrier^{2, 4}



Evidence of cost savings

A UK health economic study compares the healthcare utilization of a single-stage protocol using CERAMENT G at the Oxford bone infection unit versus the top 10 busiest osteomyelitis centers in England⁵.

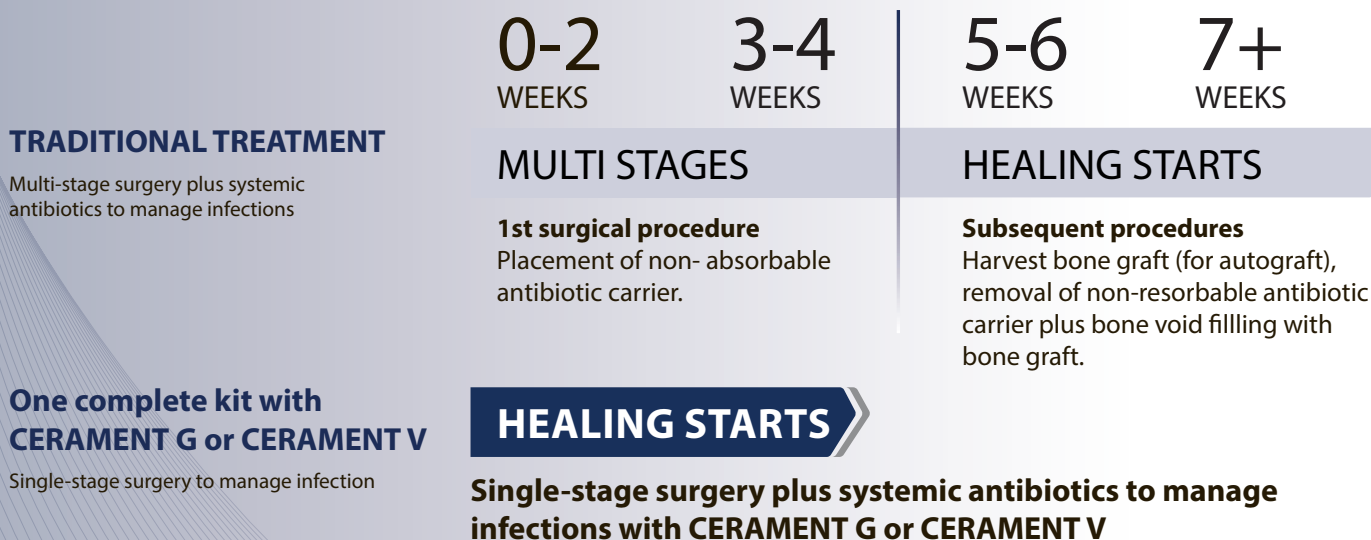
17 less bed days
£8,500 / €9,888
 direct cost savings per patient from reduced length of stay*

*Based on an average cost per bed day of £500; the average annual exchange rate between pound sterling and euro for 2021 was used (£1 = €1.1633); data sourced from the Office for National Statistics (ons.gov.uk).

¹ Hofmann, A., Gorbulev, S., Guehring, T., Schulz, A.P., Schupfner, R., Raschke, M., et al., 'Autologous Iliac Bone Graft Compared with Biphasic Hydroxyapatite and Calcium Sulfate Cement for the Treatment of Bone Defects in Tibial Plateau Fractures: A Prospective, Randomized, Open-Label, Multicenter Study', *The Journal of Bone and Joint Surgery. American Volume*, 102.3 (2020), 179–93
² McNally, M.A., Ferguson, J.Y., Scarborough, M., Ramsden, A., Stubbs, D.A., Atkins, B.L., 'Mid- to Long-Term Results of Single-Stage Surgery for Patients with Chronic Osteomyelitis Using a Bioabsorbable Gentamicin-Loaded Ceramic Carrier', *The Bone & Joint Journal*, 104-B.9 (2022), 1095–1100
³ McNally, M. A., Small, J.O., Tofighi, H.G., Mollan R.A.B., 'Two-Stage Management of Chronic Osteomyelitis of the Long Bones', *British Editorial Society of Bone and Joint Surgery*, 75.3 (1993), 375–80
⁴ Ferguson, J. Y., Dudareva, M., Riley, N.D., Stubbs, D., Atkins, B.L., McNally, M.A., 'The Use of a Biodegradable Antibiotic-Loaded Calcium Sulphate Carrier Containing Tobramycin for the Treatment of Chronic Osteomyelitis: A Series of 195 Cases', *Bone and Joint Journal*, 96 B.6 (2014), 829–36
⁵ Ferguson, J., Alexander, M., Bruce, S., O'Connell, M., Beecroft, S., McNally, M.A., 'A Retrospective Cohort Study Comparing Clinical Outcomes and Healthcare Resource Utilisation in Patients Undergoing Surgery for Osteomyelitis in England: A Case for Reorganising Orthopaedic Infection Services', *Journal of Bone and Joint Infection*, 6.May (2021), 151–63

ENABLING SINGLE-STAGE PROTOCOL

Add convenience to your practice and remove the need for additional surgeries.



Single stage protocols featuring CERAMENT G and CERAMENT V

Name	Clinic	Indication	Description
The Oxford Protocol^{1, 5}	Nuffield Orthopaedic Centre, Oxford University Hospitals, NHS, United Kingdom	Cavitary and segmental bone infection	Biphasic bioceramics such as CERAMENT G and CERAMENT V are assigned for cortico-medullary and combined defects. Evidence of cost savings with protocol
The Fix and Flap^{2, 3}	Wythenshawe Hospital, Manchester NHS University Foundation Trust, United Kingdom	Open traumatic fractures	An ortho-plastic approach where definitive skeletal stabilization and soft tissue coverage are conducted in the same sitting. CERAMENT G is used as adjuvant local antibiotic bio-composite
The Silo Technique⁴	Wythenshawe Hospital, Manchester NHS University Foundation Trust, United Kingdom	Diabetic foot osteomyelitis	Debridement of the dead bone and local delivery of antibiotics in drilled tunnels using CERAMENT G

¹ Mifsud, M., McNally, M.A., 'Local Delivery of Antimicrobials in the Treatment of Bone Infections', Orthopaedics and Trauma, 33.3 (2019), 160-65

² Jahangir, N., Niazi, N., Aljawadi, A., Reid, A., Wong, J., Drampalos, E., et al., 'The Use of Adjuvant Local Antibiotic Hydroxyapatite Bio-Composite in the Management of Open Gustilo Anderson Type IIIB Fractures. A Prospective Review', Journal of Orthopaedics, 16.3 (2019), 278-82

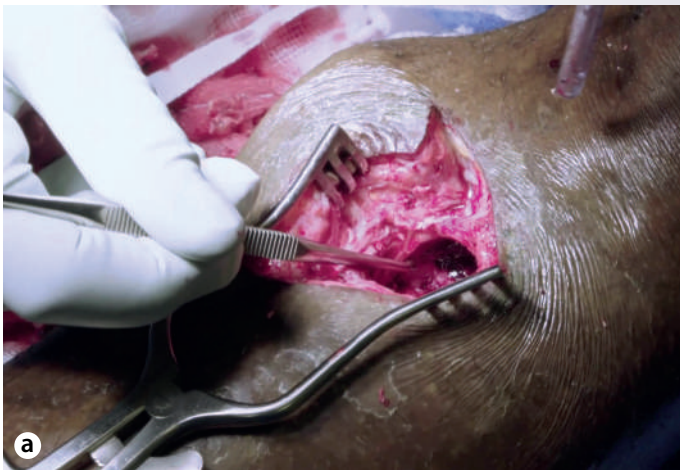
³ Aljawadi, A., Islam, A., Jahangir, N., Niazi, N., Ferguson, Z., Sephton, B., et al., 'Adjuvant Local Antibiotic Hydroxyapatite Bio-Composite in the Management of Open Gustilo Anderson IIIB Fractures. Prospective Review of 80 Patients from the Manchester Ortho-Plastic Unit', Journal of Orthopaedics, 18.December 2019 (2020), 261-66

⁴ Drampalos, E., Mohammad, H.R., Kosmidis, C., Balal, M., Wong, J., Pillai, A., 'Single Stage Treatment of Diabetic Calcaneal Osteomyelitis with an Absorbable Gentamicin-Loaded Calcium Sulphate/Hydroxyapatite Biocomposite: The Silo Technique', Foot, 34 (2018), 40-44

⁵ Ferguson, J., Alexander, M., Bruce, S., O'Connell, M., Beecroft, S., McNally, M.A., 'A Retrospective Cohort Study Comparing Clinical Outcomes and Healthcare Resource Utilisation in Patients Undergoing Surgery for Osteomyelitis in England: A Case for Reorganising Orthopaedic Infection Services', Journal of Bone and Joint Infection, 6.May (2021), 151-63

ENABLING SINGLE-STAGE PROTOCOL

Example of filling a bone void with CERAMENT G in a single-stage protocol



a Dead bone is removed leaving dead space.



b CERAMENT G is injected into the bone void.

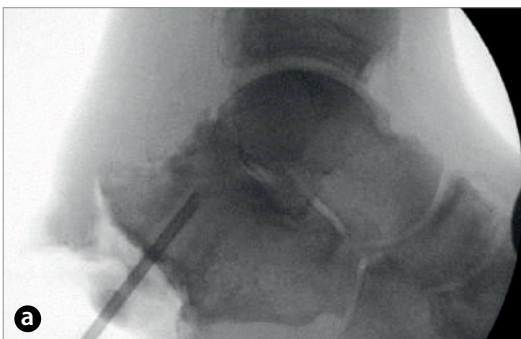


c Bone void is completely filled.



d CERAMENT G has set and wound is closed.

Note: Images are from a chronic osteomyelitis case and they are reproduced with kind permission from the Nuffield Orthopaedic Centre, Oxford UK.



a



b

The Silo Technique.

Silo type tunnels (four to five) are drilled into the os calcis and filled with 5ml of CERAMENT G¹

¹ Drampalos, E., Hasan R.M., Kosmidis, C., Balal, M., Wong, J., Pillai, A., 'Single Stage Treatment of Diabetic Calcaneal Osteomyelitis with an Absorbable Gentamicin-Loaded Calcium Sulphate/Hydroxyapatite Biocomposite: The Silo Technique', Foot, 34 (2018), 40-44

OUTCOMES OF SINGLE-STAGE PROTOCOLS

Clinical outcomes of single-stage protocols that includes CERAMENT G and CERAMENT V

The Oxford Protocol¹
Chronic osteomyelitis
 100 patients,
 mean follow-up:
 6.05 years
94%
 remained infection-free
97%
 did not develop
 a fracture

The Fix and Flap²
Fracture-related infections
 80 patients
 mean follow-up time:
 22 months
98.75%
 infection-free
96.25%
 limb salvage rate
88.30%
 union rate

The Silo technique for midfoot and hindfoot and intramedullary retrograde filling for the forefoot³
Diabetic foot osteomyelitis
 47 patients
 mean follow-up time:
 33 months
94%
 limb salvage rate
88%
 infection-free

CERAMENT G and CERAMENT V are valuable adjunctive therapies to keep a low infection recurrence rate in bone infection cases.

What is the potential savings of having low infection recurrence?

Location of fracture	Potential cost savings from preventing a (re)infection case ⁴ , Cost of infected fracture – Cost of uninfected fracture	
	€	£
Tibia	35,758	30,738
Femur	20,009	17,200
Hip	16,027	13,777

Additionally, bone infection is associated with an increased risk of amputation. For patients with diabetic foot, amputation-related costs can range from £8,394 / €8,078 – £34,023 / €32,740^{5*}.

*Adjusted by PPP exchange rates for 2021 (1 International Dollar = £ 0.693, 1 International Dollar = € 0.704); data sourced from the Organization for Economic Co-operation and Development (oecd.org)

¹ McNally, M.A., Ferguson, J.Y., Scarborough, M., Ramsden, A., Stubbs, D.A., Atkins, B.L., 'Mid- to Long-Term Results of Single-Stage Surgery for Patients with Chronic Osteomyelitis Using a Bioabsorbable Gentamicin-Loaded Ceramic Carrier', *The Bone & Joint Journal*, 104-B.9 (2022), 1095–1100

² Aljawadi, A., Islam, A., Jahangir, N., Niazi, N., Ferguson, Z., Sephton, B., et al., 'Adjuvant Local Antibiotic Hydroxyapatite Bio- Composite in the Management of Open Gustilo Anderson IIIB Fractures. Prospective Review of 80 Patients from the Manchester Ortho-Plastic Unit', *Journal of Orthopaedics*, 18 December 2019 (2020), 261–66

³ Vasukutty, N.L., Mordecai, S., Tarik, A., Subramaniam, M., Srinivasan B., 'Limb Salvage Surgery in Diabetic Foot Infection: Encouraging Early Results with a Local Antibiotic Carrier', 25.2 (2022)

⁴ O'Connor, O., Thahir, A., Krkovic, M., 'How Much Does an Infected Fracture Cost?', *The Archives of Bone and Joint Surgery*, 135.10(2) (2022), 135–40.

⁵ Petrakis, I., Kyriopoulos, I.J., Ginis, A., Athanasakis, K., 'Losing a Foot versus Losing a Dollar; a Systematic Review of Cost Studies in Diabetic Foot Complications', *Expert Review of Pharmacoeconomics and Outcomes Research*, 17.2 (2017), 165–80

A COST-EFFECTIVE STRATEGY FOR HOSPITALS

Get it right the first time - enabling single-stage protocols with CERAMENT G and CERAMENT V reduces the number of surgical procedures and has shown to improve clinical outcomes beyond six years

Having low infection rates achieved by CERAMENT G can generate cost savings – evidence of 17 less bed days on average (£8,500/€9,888 saving)

CERAMENT G and CERAMENT V are all-in-one closed mixing systems – standardized mixing procedure minimizes error and ensures more consistency in bone void filling, overall less exposure to antibiotics to staff

BONESUPPORT is a Swedish orthobiologics company founded in 1999 that develops, manufactures, and markets CERAMENT® – an innovative portfolio of injectable and antibiotic-eluting bone void fillers.



CERAMENT® G with Gentamicin

A synthetic bone substitute with hydroxyapatite, calcium sulfate and the antibiotic gentamicin. Remodels into bone within 6-12 months and elutes gentamicin.

Description	Article Number
CERAMENT® G 5mL	A0450-03
CERAMENT® G 10mL	A0450-01



CERAMENT® V with Vancomycin

A synthetic bone substitute with hydroxyapatite, calcium sulfate and the antibiotic vancomycin. Remodels into bone within 6-12 months and elutes vancomycin.

Description	Article Number
CERAMENT® V 10mL	A0451-03

Ordering details:
E: info@biotechpromed.com



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