BONESUPPORT Capital Market Day September 1st, 2022

Introduction

Emil Billback, CEO

Agenda

14.00	**Introduction**	Emil Billbäck, CEO
	Clinician Evidence	
14.15	Clinical overview put into context	Dr Michael Diefenbeck, Chief Medical Officer, EVP clinical affairs
14.35	CERAMENT in clinical practice	Prof. Anand Pillai
15.00	Q&A	
15.15	**Break**	
15.30	**CERAMENT G Launch US**	Mike Roth, General Manager and EVP North America
16:00	**Updated Guidance**	Håkan Johansson & Emil Billbäck
16.10	**Q&A**	
16.30	**Meeting ends**	

Recap on the BONESUPPORT journey -2022

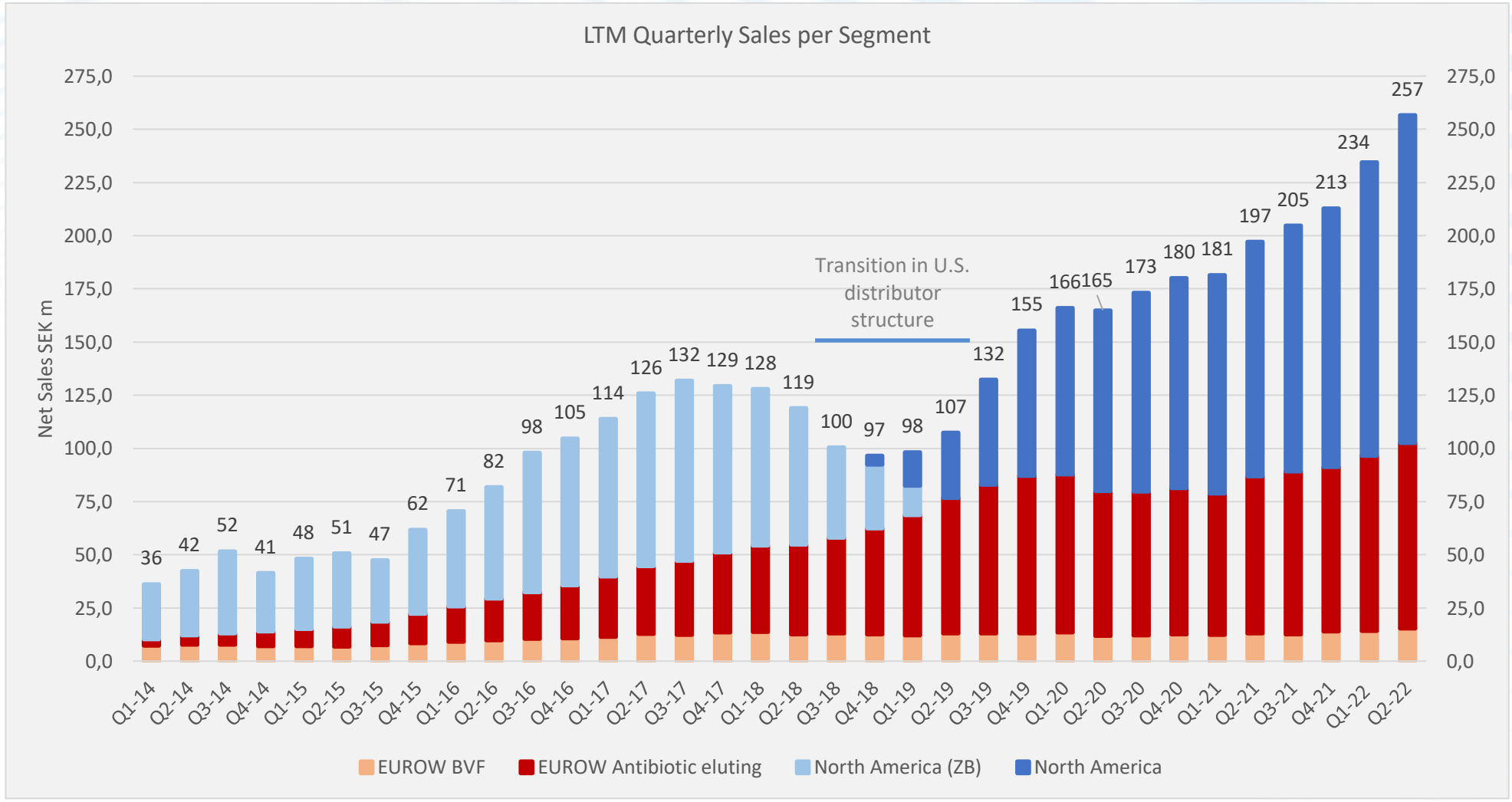
- Origin
  - Invented in Lund, Sweden, by orthopedic clinicians seeking a solution to a well-known problem
  - Unique technology, mimicking natural healing, through bi-phasic remodeling
  - Addition of antibiotic (2013) created a market disruptive breakthrough solution


Prof Lars Lidgren

- New strategy 2018
  - Make the transformation from academic world to making a clinical difference
  - Focus on leveraging exceptionally strong clinical data to drive innovation and market penetration
  - Investments in commercial infrastructure to reach out (market access) to clinicians and hospitals
  - Focus on getting CERAMENT G to the US market – market grant order May 17th 2022
  - Guidance of 40% annual a sales growth

- COVID
  - Disrupted the entire health care market (….and all other markets)
  - High negative impact on market access, especially on “new” therapies

Eight consecutive all-time-high, strong traction in both regions



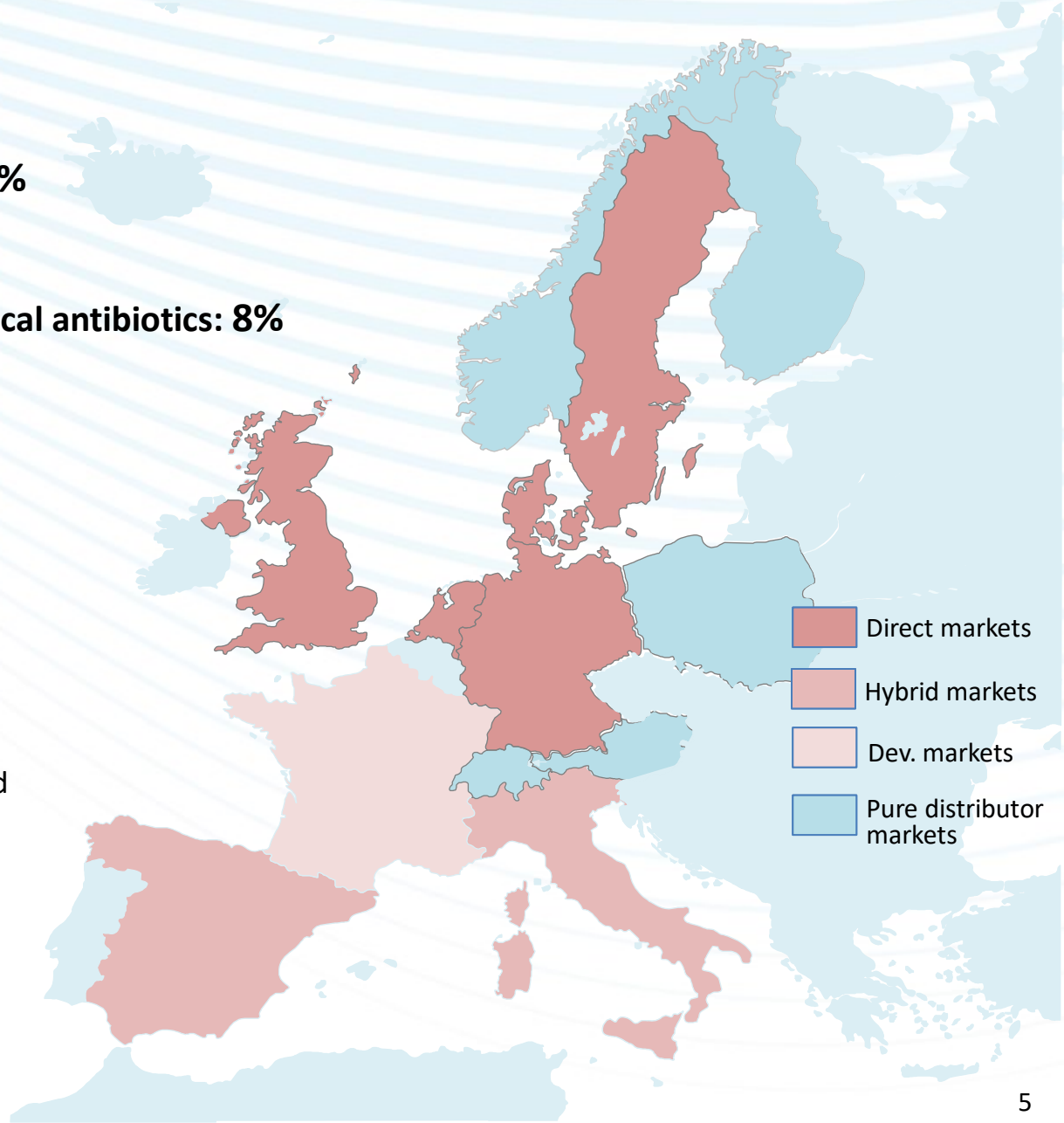
EUROPE – rapid market share gains in early-stage market entries

Top EU5 total: 335 k

Direct markets:	000 procedures/ year
UK	70
Germany	80
Nordics	25
	175

CERAMENT total market share : 4% (procedures)

CERAMENT (G/V) Market share local antibiotics: 8% (procedures)



Market penetration with proven model:

- **Expanded sales team in Germany, Scandinavia and UK, 2018-2019**
- **Direct market established in Netherlands (16 k procedures), 2020**
- **Hybrid set up Spain and Italy (100 k procedures), 2021:** Distributors appointed and own sales development staff hired.
- **France (70 k procedures):** CONVICTION study running with Crioac centers; **Data expected for 2025**.
- **Regulatory process for Japan (120 k procedures) initiated**

BONESUPPORT Strategy

Innovation

- 3 levels of innovation:
  - Tactical
    - Ancillary offerings to support CERAMENT sales
  - Organic
    - Next generation CERAMENT G, V and BVF
  - Breakthrough
    - Osteoporosis
    - Bone active substances

Clinical and Health Economic evidence

- Over 160 peer-to-peer reviewed clinical publications
- Convincing Health Economic benefits

Commercial platform

Clinician interactions

- Market access
- Medical education

BONESUPPORT Capital Market Day September 1st, 2022

Clinical overview

Michael Diefenbeck, Chief Medical Officer

Introduction:

Michael Diefenbeck, MD, PhD
Orthopaedic Surgeon

Chief Medical Officer, BONESUPPORT AB since April 2017

EVP Clinical and Medical Affairs since Jul 2018

Honorary Consultant, Nuffield Orthopaedic Centre, Oxford University Hospitals, NHS in 2016

Founder of “Scientific Consulting in Orthopeadic Surgery and Traumatology”, Hamburg in 2014

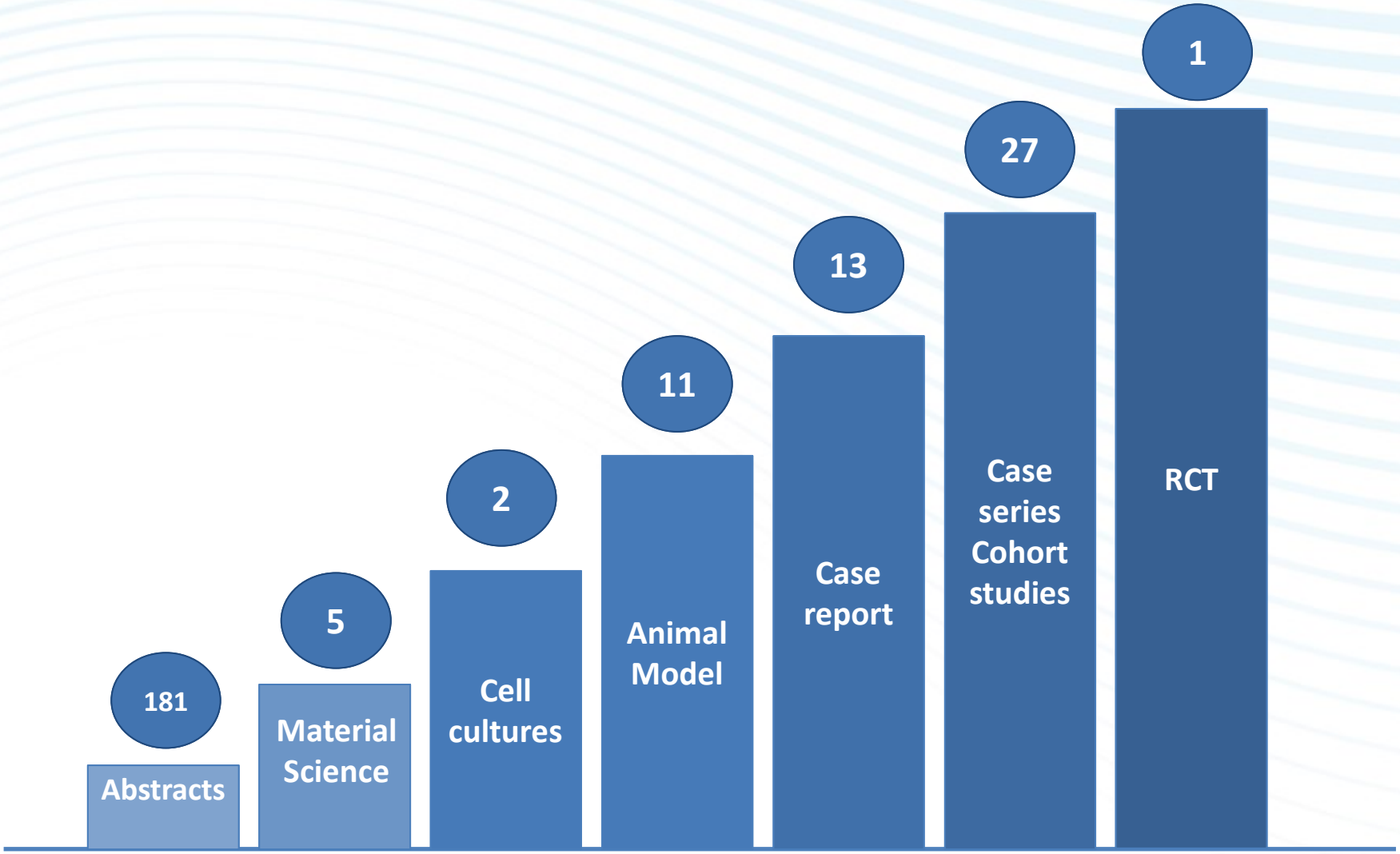
Clinical positions at:

- Schön Klinik Hamburg Eilbek, Bone infection unit, Consultant for orthopaedic surgery, 2012-14
- University Hospital Jena, 2006-12
- BG Kliniken Bergmannstrost Halle/Saale, 2004-06
- BG Unfallklinik Murnau, 2000 – 03



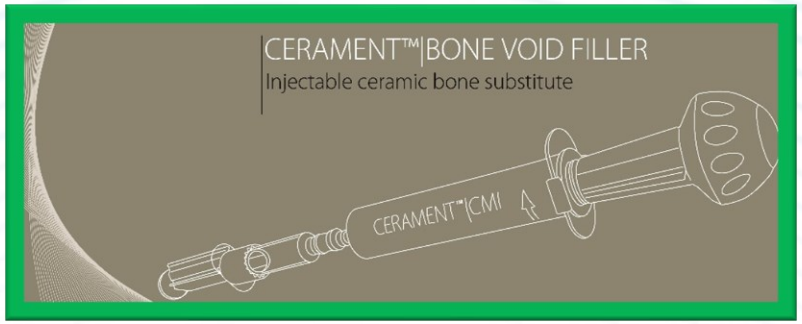



Strong clinical evidence for CERAMENT builds strong foundation



Reference: Clinical Evaluation Reports 2021

CERTiFy further strengthens CERAMENT's clinical evidence



CERTiFy
CERAMENT™|Tibia Fracture Study

Reference: Clinical Evaluation Reports 2021

Basic evidence for C BVF or CG or combination of both

CERTiFy paves the way for CERAMENT BONE VOID FILLER

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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

Alexander Hofmann, MD, PhD, Stanislav Gorbulev, PhD, Thorsten Guehring, MD, PhD, Arndt Peter Schulz, MD, PhD, Rupert Schupfner, MD, Michael Raschke, MD, PhD, Stefan Huber-Wagner, MD, PhD, and Pol Maria Rommens, MD, PhD, on behalf of the CERTiFy Study Group*

CERTiFy
CERAMENT™ Tibia Fracture Study

Design: Randomized Clinical Trial
Patients: 135 (18 to 65 Y)
Indication: Tibia plateau fractures
Treatment: Autologous Iliac Bone Graft vs. CERAMENT BONE VOID FILLER
Centers: 20 orthopedic trauma centers in Germany

Outcome:
Primary: SF-12 Physical Component Summary at 26 weeks
Co-primary: Pain level at 26 weeks
Secondary: SF-12 Mental Component Summary & SF-12 PCS at 1,6 and 12 weeks
Bone-healing radiographs

Designed to show non-inferiority of CERAMENT BVF vs autograft

CERTiFy paves the way for CERAMENT BONE VOID FILLER

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Autologous Iliac Bone Graft Compared with Biphasic Hydroxyapatite and Calcium Sulfate Cement for the Treatment of Bone Defects in Tibial Plateau Fractures

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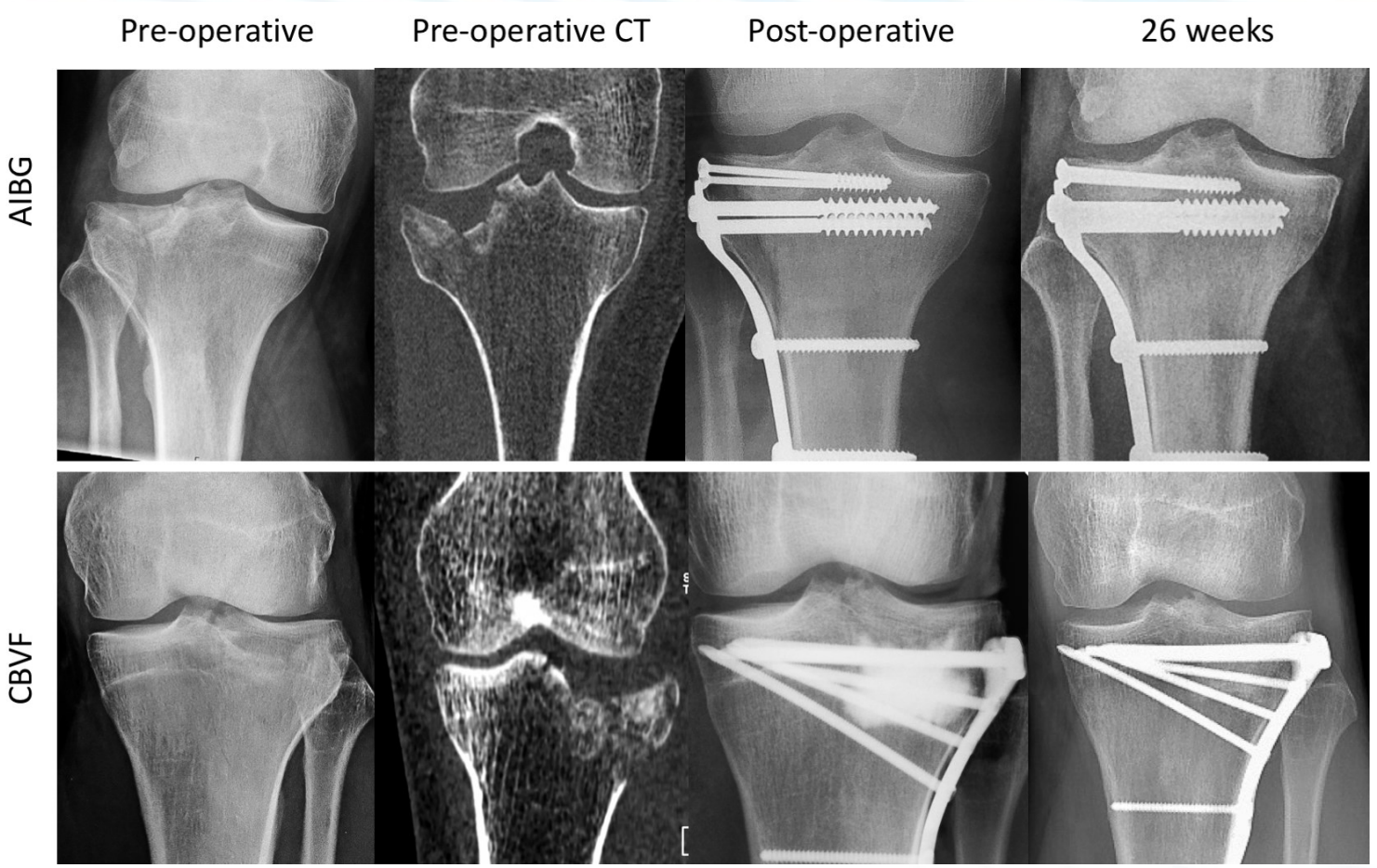
Primary: ✓ SF-12 Physical Component Summary at 26 weeks
Co-primary: ✓ Pain level at 26 weeks
Secondary: ✓ SF-12 Mental Component Summary & SF-12 PCS at 1,6 and 12 weeks
✓ Bone-healing radiographs

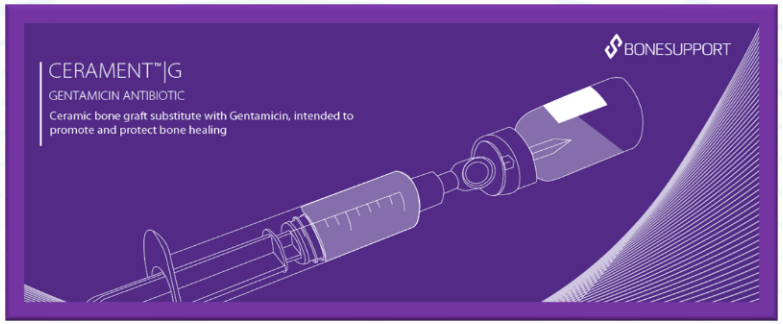
✓ CERAMENT BVF is non-inferior vs autograft

CERTiFy paves the way for CERAMENT BONE VOID FILLER



Hofmann A, Gorbulev S, Guehring T, 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.
J Bone Joint Surg Am. 2020;102(3):179-193.

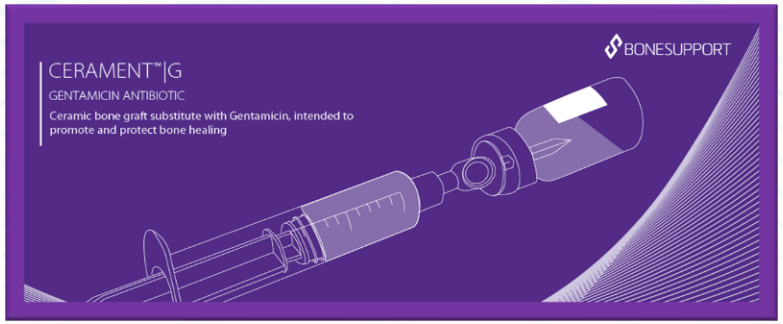
Solid clinical evidence for CERAMENT G



Reference: Clinical Evaluation Reports 2021

Basic evidence for C BVF or CG or combination of both

Solid clinical evidence for CERAMENT G



Basic evidence for C BVF or CG or combination of both

Reference: Clinical Evaluation Reports 2021

Fracture-related Infection

Fracture related infection

In 2018 the Fracture Related Infection Consensus Group (an international group of experts) published a consensus definition:

Infection related to a previous internal fixation that is confirmed by at least one clinical, microbiological, or histopathological confirmatory criteria

Confirmatory Criteria

Clinical Signs
- Fistula, Sinus or wound breakdown (with communication to the bone or the implant)
- Purulent drainage or presence of pus during surgery

Microbiology
- Phenotypically indistinguishable pathogens identified by culture from at least 2 separate deep tissue/implant specimens

Histopathology
- Presence of microorganisms in deep tissue specimens, confirmed by using staining techniques for bacteria and fungi

Metsemakers, W. J., Morgenstern, M., McNally, M. A., Moriarty, T. F., McFadyen, I., Scarborough, M., Athanasou, N. A., Ochsner, P. E., Kuehl, R., Raschke, M., Borens, O., Xie, Z., Velkes, S., Hungerer, S., Kates, S. L., Zalavras, C., Giannoudis, P. V., Richards, R. G., & Verhofstad, M. (2018). Fracture related infection: A consensus on definition from an international expert group. *Injury*, *49*(3), 505–510. https://doi.org/10.1016/j.injury.2017.08.040

Key clinical evidence for CERAMENT G - **Fracture-related Infection**

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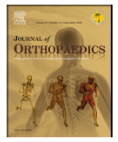
Fracture related infection

Journal of Orthopaedics 17 (2020) 173–179

Contents lists available at ScienceDirect

Journal of Orthopaedics

journal homepage: www.elsevier.com/locate/jor



Augmented debridement for implant related chronic osteomyelitis with an absorbable, gentamycin loaded calcium sulfate/hydroxyapatite biocomposite

Efstathios Drampalos*, Hasan Raza Mohammad, Anand Pillai

Department of Orthopaedics, Orthoplastic Unit, Wythenshawe Hospital, Manchester NHS University Foundation, NHS Trust, UK

Design:	Prospective case series
Patients:	52 patients, mean age 53 years [range 22-81]
Treatment:	Surgical debridement, application of CERAMENT G bone stabilization and optional local or free flap
Center:	Wythenshawe Hospital, Manchester University
Follow-up:	7 months [range: 12-48]
Results:	**Infection was eradicated in 48 patients (92.3%)**

Infection
https://doi.org/10.1007/s15010-020-01418-3

REVIEW

Treatment of fracture-related infection of the lower extremity with antibiotic-eluting ceramic bone substitutes: case series of 35 patients and literature review

Sebastian Pesch[1] · Marc Hanschen[1] · Frederik Greve[1] · Michael Zyskowski[1] · Fritz Seidl[1] · Chlodwig Kirchhoff[1] · Peter Biberthaler[1] · Stefan Huber-Wagner[1]

Prospective case series

35 patients, mean age 56 years [range 37-75]

Surgical debridement, application of CERAMENT G, bone stabilization, optional local or free flap

Klinikum rechts der Isar, Technical University of Munich, 13 months [range: 2-40]

Infection was eradicated in 32 patients (91.4%)

Benchmark Fracture-related Infection: PMMA beads
Two-stage surgery (min two interventions, min two hospital stays)
Infection eradication rate (published data): **86.7%**[1]
Meta analysis (published data): **86.8%**[2]

1. McNally MA, Small JO, Tofighi HG, Mollan RA. Two-stage management of chronic osteomyelitis of the long bones. The Belfast technique. J Bone Joint Surg Br. 1993 May;75(3):375-80.
2.. Meta-analysis of published data from 7 studies on PMMA-beads as part of treatment of osteomyelitis, submitted to FDA as part of CERAMENT G application

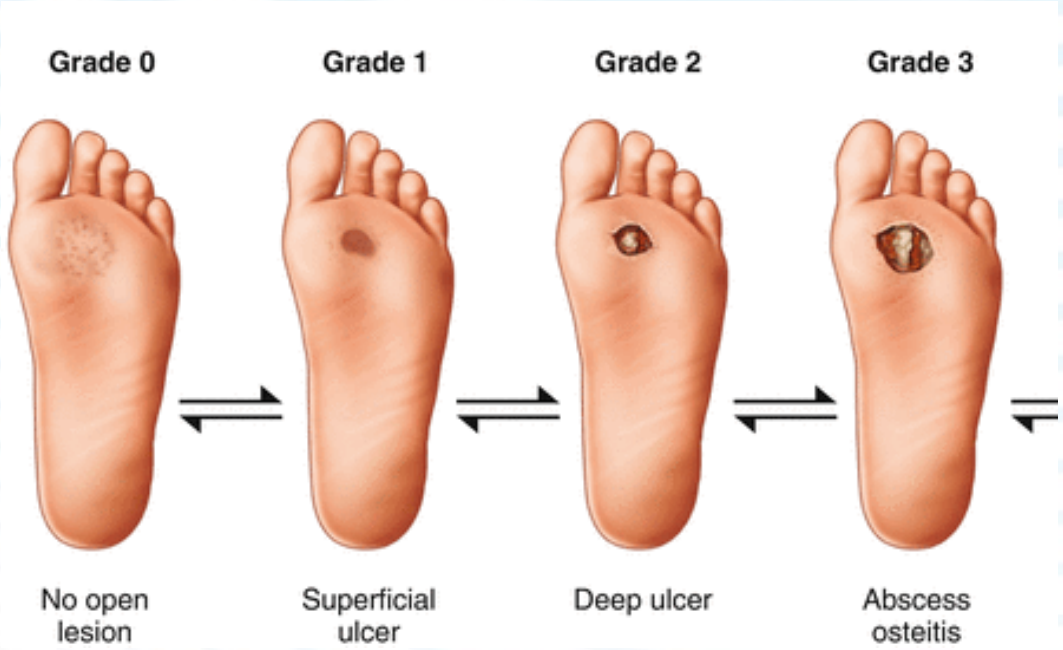
Diabetic Foot Osteomyelitis a hard-to-treat indication

Diabetic Foot Osteomyelitis

Diabetic Foot Osteomyelitis (DFO) is mostly a consequence of a soft tissue infection (e. g. Diabetic foot ulcer) that spreads into the bone, first involving the cortex and then the marrow

The typical sequence is usually:

- Deformity of the foot (shortening of tendons)
- Lack of protective sensation (no pain)
- Superficial foot ulcer / contamination
- Deep foot ulcer with infection
- Bone infection / Osteitis / Diabetic Foot Osteomyelitis
- …
- Amputation



Pinzur, M.S. (2016). The Diagnosis and Treatment of Diabetic Foot Infections. In: Herscovici, Jr., D. (eds) The Surgical Management of the Diabetic Foot and Ankle. Springer, Cham.

Strong clinical evidence in Diabetic Foot Osteomyelitis

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Diabetic Foot Osteomyelitis

The Foot 39 (2019) 22–27

Contents lists available at ScienceDirect

The Foot

journal homepage: www.elsevier.com/locate/foot

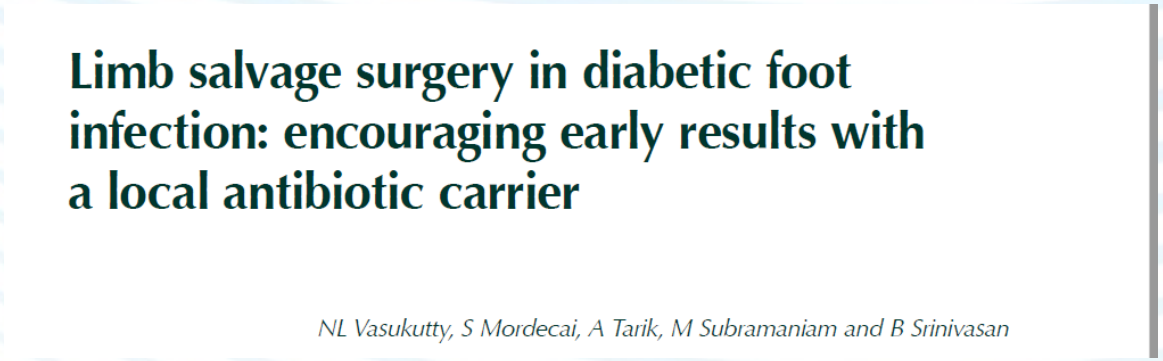
ELSEVIER

Original Article

Adjuvant antibiotic loaded bio composite in the management of diabetic foot osteomyelitis — A multicentre study

Noman Shakeel Niazi[a,*], Efstathios Drampalos[a], Natasha Morrissey[b], Noman Jahangir[a], Alexander Wee[b], Anand Pillai[a]

[a] Trauma and Orthopaedics Department, Wythenshawe Hospital, Manchester University Foundation Trust, United Kingdom
[b] Trauma and Orthopaedics Department, Frimley Health NHS Foundation Trust, Surrey, United Kingdom



Limb salvage surgery in diabetic foot infection: encouraging early results with a local antibiotic carrier

NL Vasukutty, S Mordecai, A Tarik, M Subramaniam and B Srinivasan

Design:	Retrospective case series	Retrospective case series
Patients:	70 patients mean age 68 years [range 22-88]	48 patients, mean age 55 years [range 34-83]
Treatment:	Debridement and Dead Space Management with CERAMENT G	Debridement and Dead Space management with CERAMENT G
Center:	Wythenshawe Hospital, Manchester University	United Lincolnshire Hospitals NHS Trust, Boston, UK
Follow-up:	10 months [range: 4-28]	33 months [range: 13-49]
Results:	Infection was eradicated in 61 patients (87.1%)	Infection was eradicated in 42 patients (88%),
	Amputation rate: 5/70 (7.1%)	Amputation rate: 3/48 (6.3%)

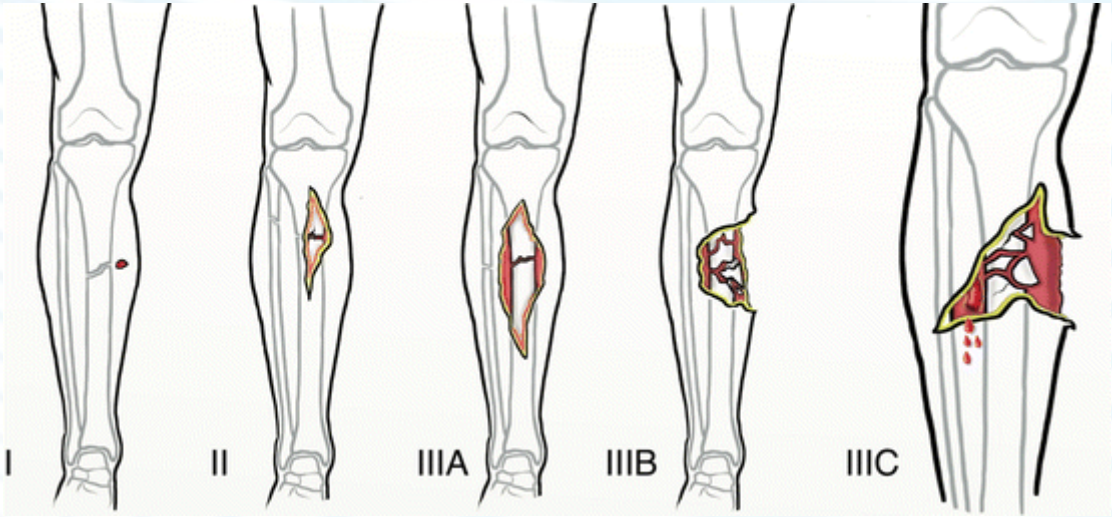
Benchmark: Diabetic Foot Osteomyelitis
Standard of care: Amputation rate up to 24%[1]

[1]Pemayun TG et al. Risk factors for lower extremity amputation in patients with diabetic foot ulcers: a hospital-based case-control study. Diabet Foot Ankle. 2015; 6: 29629

Trauma: Open Fracture

- Open fracture is a fracture with an open wound or break in the skin near the site of the broken bone
- Most often caused by a fragment of bone breaking through the skin at the moment of injury
- Once the skin is broken, bacteria from dirt and other contaminants can enter the wound, potentially causing an infection at the site of injury

Gustilo type	Definition
I	Open fracture, clean wound, wound <1 cm in length
II	Open fracture, wound >1 cm in length without extensive soft-tissue damage, flaps, avulsions
III	Open fracture with extensive soft-tissue laceration, damage, or loss or an open segmental fracture. This type also includes open fractures caused by farm injuries, fractures requiring vascular repair, or fractures that have been open for 8 h prior to treatment
IIIA	Type III fracture with adequate periosteal coverage of the fracture bone despite the extensive soft-tissue laceration or damage
IIIB	Type III fracture with extensive soft-tissue loss and periosteal stripping and bone damage. Usually associated with massive contamination. Will often need further soft-tissue coverage procedure (i.e. free or rotational flap)
IIIC	Type III fracture associated with an arterial injury requiring repair, irrespective of degree of soft-tissue injury.

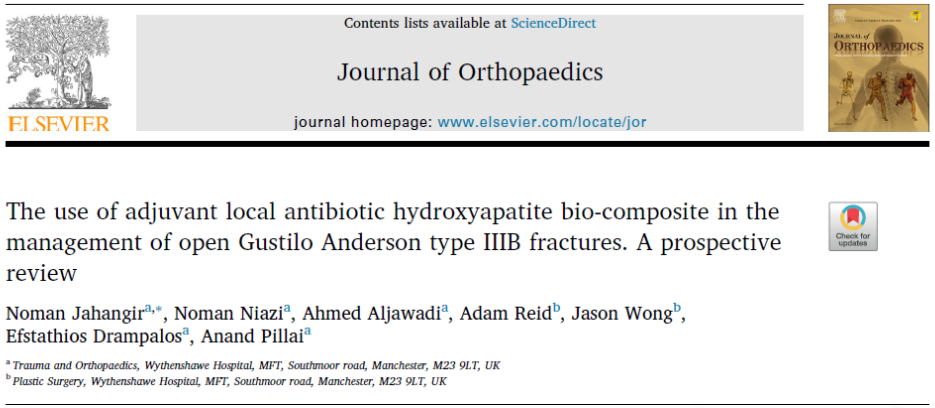


Cross, W. W., 3rd, & Swiontkowski, M. F. (2008). Treatment principles in the management of open fractures. Indian journal of orthopaedics, 42(4), 377–386. https://doi.org/10.4103/0019-5413.43373

Strong clinical evidence in open fracture

BONESUPPORT

Trauma - Open Fracture



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Journal of Orthopaedics

journal homepage: www.elsevier.com/locate/jor

The use of adjuvant local antibiotic hydroxyapatite bio-composite in the management of open Gustilo Anderson type IIIB fractures. A prospective review

Noman Jahangir[a,*], Noman Niazi[a], Ahmed Aljawadi[a], Adam Reid[b], Jason Wong[b], Efstathios Drampalos[a], Anand Pillai[a]

[a] Trauma and Orthopaedics, Wythenshawe Hospital, MFT, Southmoor road, Manchester, M23 9LT, UK
[b] Plastic Surgery, Wythenshawe Hospital, MFT, Southmoor road, Manchester, M23 9LT, UK

Contents lists available at ScienceDirect

Journal of Orthopaedics

journal homepage: www.elsevier.com/locate/jor

Original Article

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**

Ahmed Aljawadi[a,*], Amirul Islam[a], Noman Jahangir[a], Noman Niazi[a], Zak Ferguson[a], Benjamin Sephton[a], Mohammed Elmajee[b], Adam Reid[c], Jason Wong[c], Anand Pillai[a]

[a] Trauma and Orthopaedics, Manchester Foundation Trust, Southmoor Rd, Wythenshawe, Manchester, M23 9LT, UK
[b] ST4 Spine Department, Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, B31 2AP, UK
[c] Plastic Surgery, Manchester Foundation Trust, Southmoor Rd, Wythenshawe, Manchester, M23 9LT, UK

Design:	Prospective case series	Prospective case series
Patients:	51 patients, mean age 40.9 years [range 11-90]	80 patients, mean age 41.28 years [range 10-96]
Treatment:	One stage protocol including debridement, bone stabilization, application of CERAMENT G and optional local or free flap	One stage protocol including debridement bone stabilization, application of CERAMENT G and optional local or free flap
Center:	Wythenshawe Hospital, Manchester University	Wythenshawe Hospital, Manchester University
Follow-up:	13.9 months [range: 6-45]	22 months [range: 9-45]
Results:	Infection rate: 0%	Infection rate: 1.3%

Benchmark: Trauma: Open fracture
Standard of care: Infection rate up to 15%[1]

1Mathews JA, Ward J, Chapman T, Khan U, Kelly M. Single-stage orthoplastic reconstruction of Gustilo–Anderson Grade III open tibial fractures greatly reduces infection rates. Injury. 2015;46(11):2263–2266..

US market approval based on very extensive clinical data

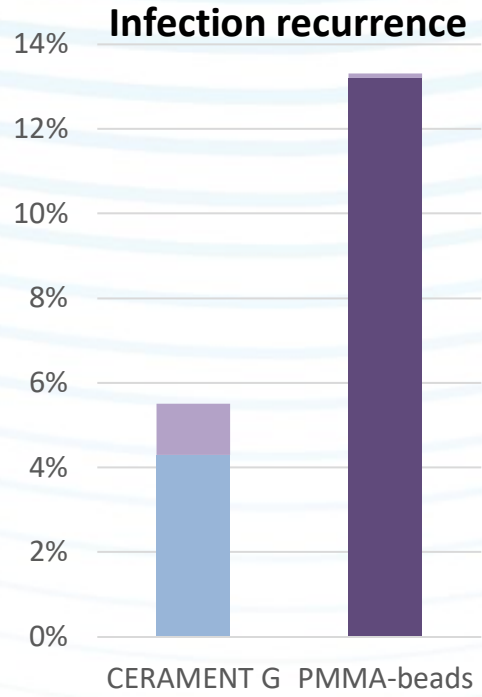
- Clinical data was collected mainly at the Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford University Hospitals, NHS, UK.
- A total of **16950** clinical data points submitted.
- Treatment group bone infection etiology: **Trauma** (Fracture-related infection and osteomyelitis)
- Extensive morphometric measurement and expert interpreted radiographic data confirming bone remodeling

CERAMENT G:

- Single-stage surgery (one intervention, one hospital stay)
- Infection recurrence rate: **4.3%**[1] (2 years follow up) **5.5%** (mean 4 years follow up)

PMMA-beads:

- Two-stage surgery (min two interventions, min two hospital stays)
- Infection recurrence rate (published data): **13.3%**[2]
- Meta analysis (published data): **13,2%**[3]

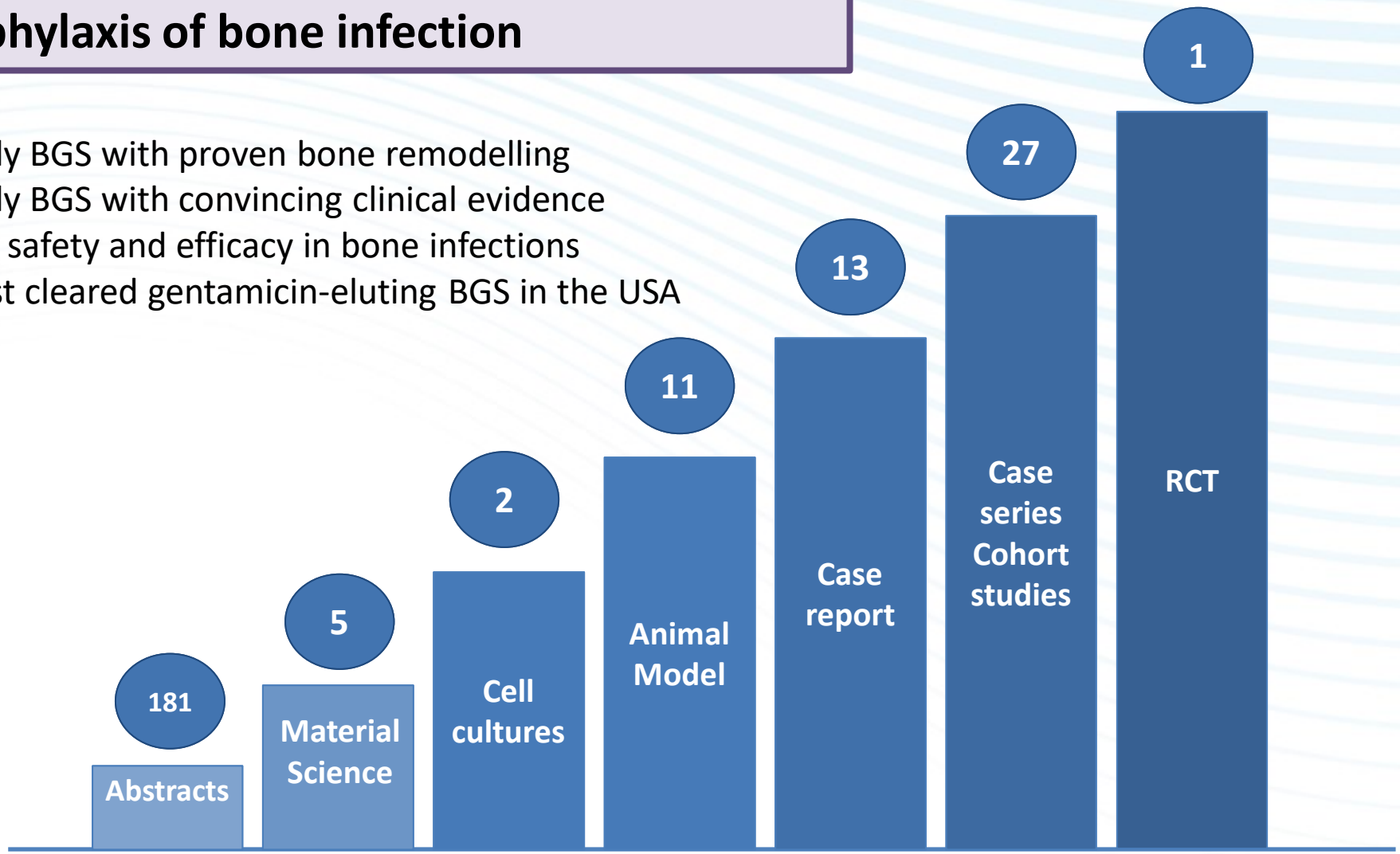


CERAMENT G is a safe and effective treatment of infected bone injuries, superior to the PMMA-beads treatment algorithm, allowing a one-stage procedure

1. Fergusson et al, Radiographic and Histological Analysis of a Synthetic Bone Graft Substitute Eluting Gentamicin in the Treatment of Chronic Osteomyelitis; Journal of bone and joint infection, 2019 vol 4
2. McNally MA, Small JO, Tofighi HG, Mollan RA. Two-stage management of chronic osteomyelitis of the long bones. The Belfast technique. J Bone Joint Surg Br. 1993 May;75(3):375-80.
3. Meta-analysis of published data from 7 studies on PMMA-beads as part of treatment of osteomyelitis, submitted to FDA as part of CERAMENT G application

Strong and convincing clinical evidence in key indications for management and prophylaxis of bone infection

- Only BGS with proven bone remodelling
- Only BGS with convincing clinical evidence for safety and efficacy in bone infections
- First cleared gentamicin-eluting BGS in the USA



Reference: Clinical Evaluation Reports 2021

BONESUPPORT™

BONESUPPORT Capital Market Day September 1st 2022

CERAMENT®

Clinical Experience

Prof Anand Pillai

Manchester University Hospitals

Scenario 1

Fracture Related Infections (FRI)

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Augmented debridement for implant related chronic osteomyelitis with an absorbable, gentamycin loaded calcium sulfate/hydroxyapatite biocomposite

Efstathios Drampalos*, Hasan Raza Mohammad, Anand Pillai

Department of Orthopaedics, Orthoplastic Unit, Wythenshawe Hospital, Manchester NHS Univeristy Foundation, NHS Trust, UK

ARTICLE INFO

Keywords:
Implant related osteomyelitis
Augmented debridement
Absorbable
Gentamycin loaded calcium sulphate/
hydroxyapatite biocomposite

ABSTRACT

We report outcomes from 52 patients with chronic osteomyelitis from implant infection treated with a single stage protocol including debridement augmented with application of CERAMENT™/G biocomposite after resection of Cierny-Mader (C-M) stage III and IV chronic osteomyelitis. Mean age was 53 years with a mean follow up of 17 months. Infection was eradicated in 48 (92.3%) patients. There were four (7.7%) recurrences. Eighteen patients (35%) had a flap. Staphylococci (51%) and Enterococci (15%) were the commonest microorganisms. Local antibiotic augmentation (CERAMENT™/G biocomposite) with dead space management is effective in the treatment of implant related chronic osteomyelitis.

Level of evidence: Prognostic Level IV.

1. Introduction

Chronic osteomyelitis in orthopaedic surgery is a limb threatening pathology.[1] Different factors can contribute to chronicity. The presence of implants (i.e. plates, screws, intramedullary nails) and devascularised or dead bone contributes to chronicity. The pathogens with their ability of producing a protective biofilm and reduction of their metabolism compromise the host's potential to eliminate infection. The host's physiological status, smoking, obesity or systemic diseases (diabetes mellitus, peripheral vascular disease) are also related to inadequate response to infection.[1]

Surgical treatment with repeated debridement, fixation in stages and soft tissue coverage has been the classical treatment over the past decades.[2] Antibiotic-impregnated acrylic beads and antibiotic-loaded polymethylmethacrylate (PMMA) cement may be used for dead space sterilization and management[3] but need removal and increase the number of operative stages. Furthermore, failure to remove can lead to secondary infection due to retained foreign material.[2] Calcium sulphate (CAS) carriers loaded with antibiotics are often for bone defects after excision of infected bone but bone formation does not always happen, and pathological fractures have been reported in up to 10% of patients in some studies.[3,4]

Recently, CAS crystals and hydroxyapatite (HA) particles have been combined in a liquid, injectable product called CERAMENT™ Fig. 1.[5] This promising product has also been loaded with antibiotics (175 mg gentamycin in 10 mls CAS/HA: Cerament G; 66 mg vancomycin in 10 mls CAS/HA: CERAMENT V; Bonesupport, Lund, Sweden). The rational is that after injection of the biocomposite into a bone void both active resorption and passive dissolution begin and what left is a HA scaffold for new bone formation. Literature regarding CERAMENT™ as a void filler is restricted.[6] Even fewer reports exist for the use of CERAMENT™ in the treatment of osteomyelitis in animal models or humans.[7] In a series of 100 patients with chronic osteomyelitis, McNally et al. report 96% eradication of infection with a single-stage protocol including debridement, dead space management with CERAMENT G, culture-specific systemic antibiotics, primary skin closure and stabilization if needed.[7]

We present a series of 52 patients all with implant related chronic osteomyelitis treated in a single stage surgical protocol, with removal of the metalwork, debridement augmented by CERAMENT G, culture-based antibiotics, appropriate soft tissue cover and stabilization. This is a single center, single surgeon study.

2. Methods

This is a review of prospectively collected data from 52 patients with chronic osteomyelitis from implant infection. Informed consent was taken from all patients included in the study. The retrospective

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E-mail address: edrampalos@gmail.com (E. Drampalos).

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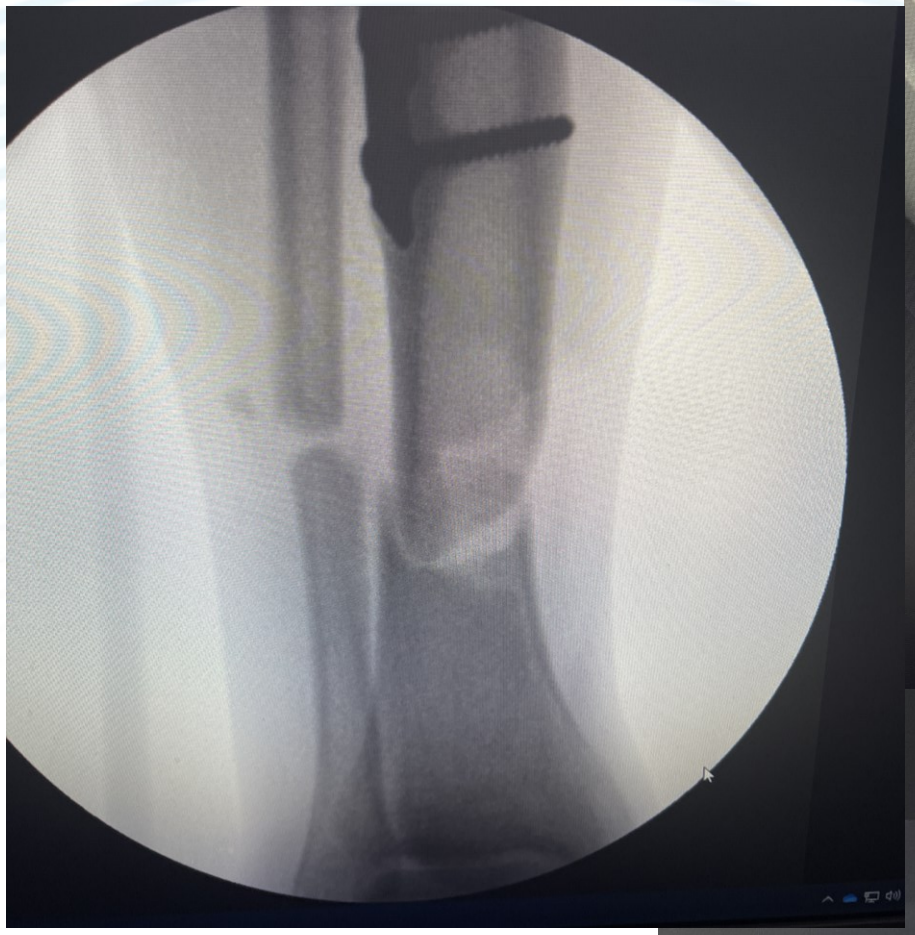
HB LATERAL

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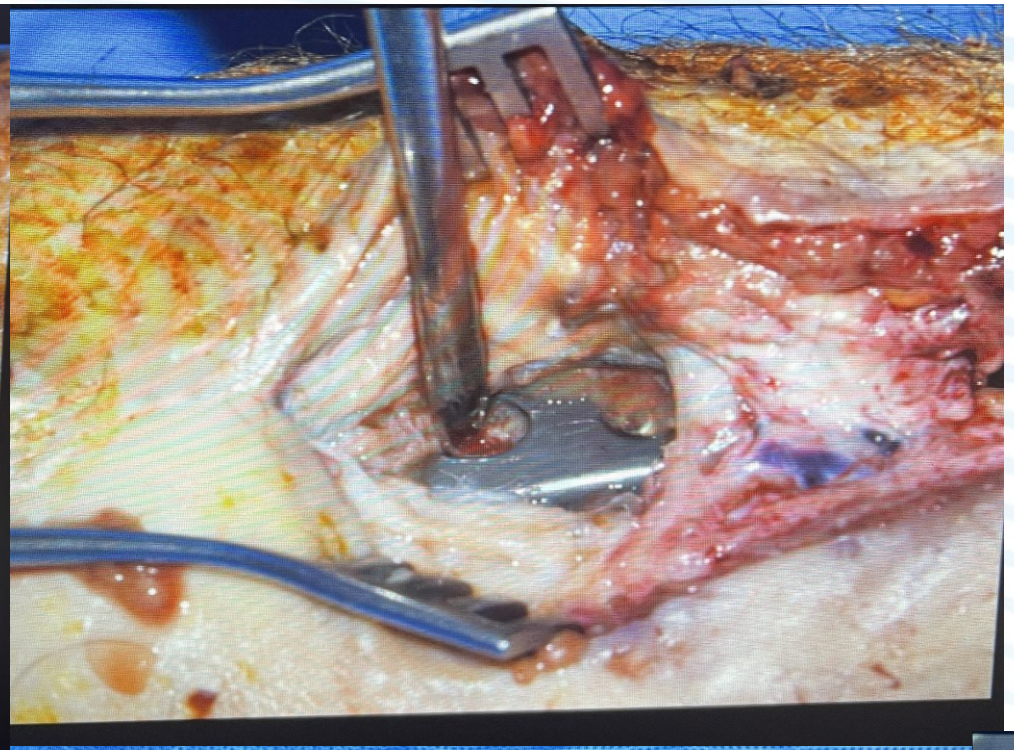

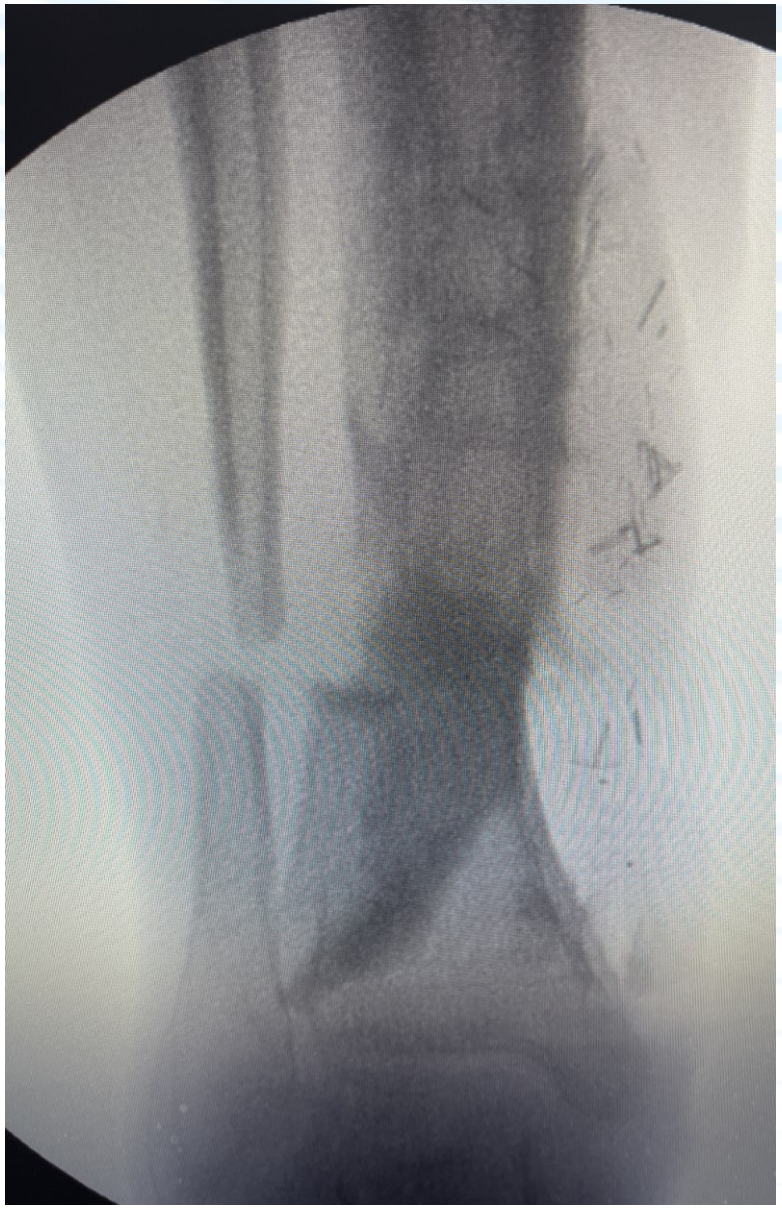


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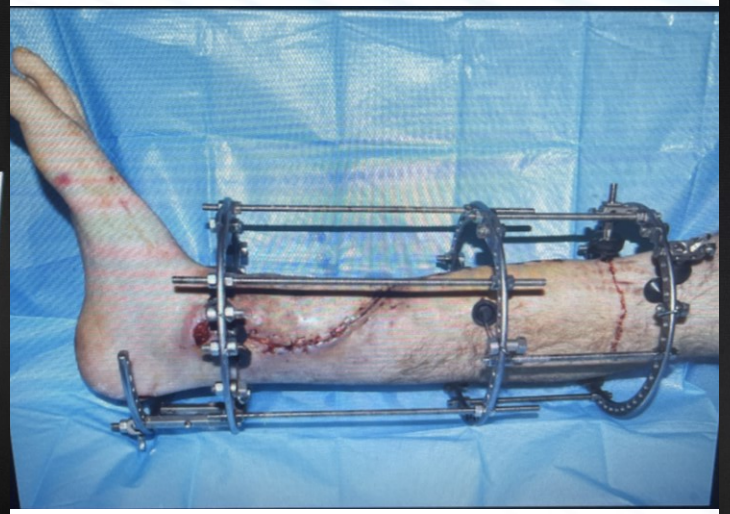


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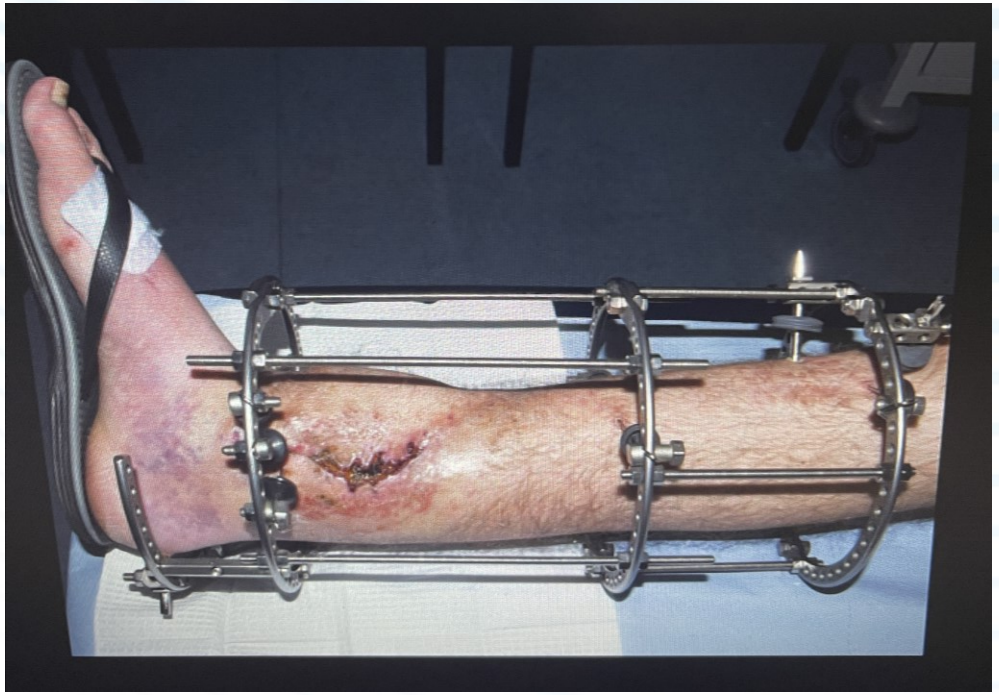

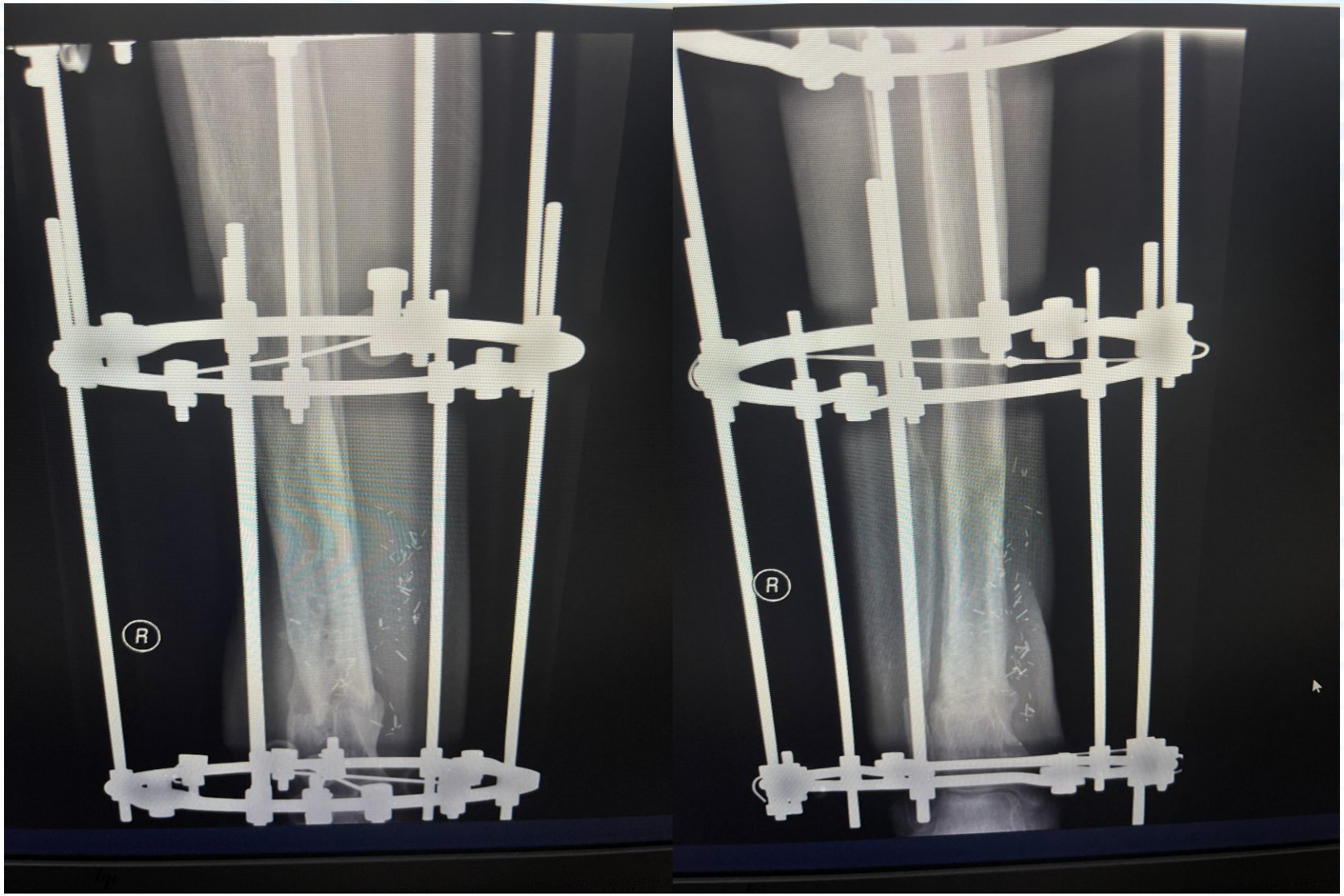
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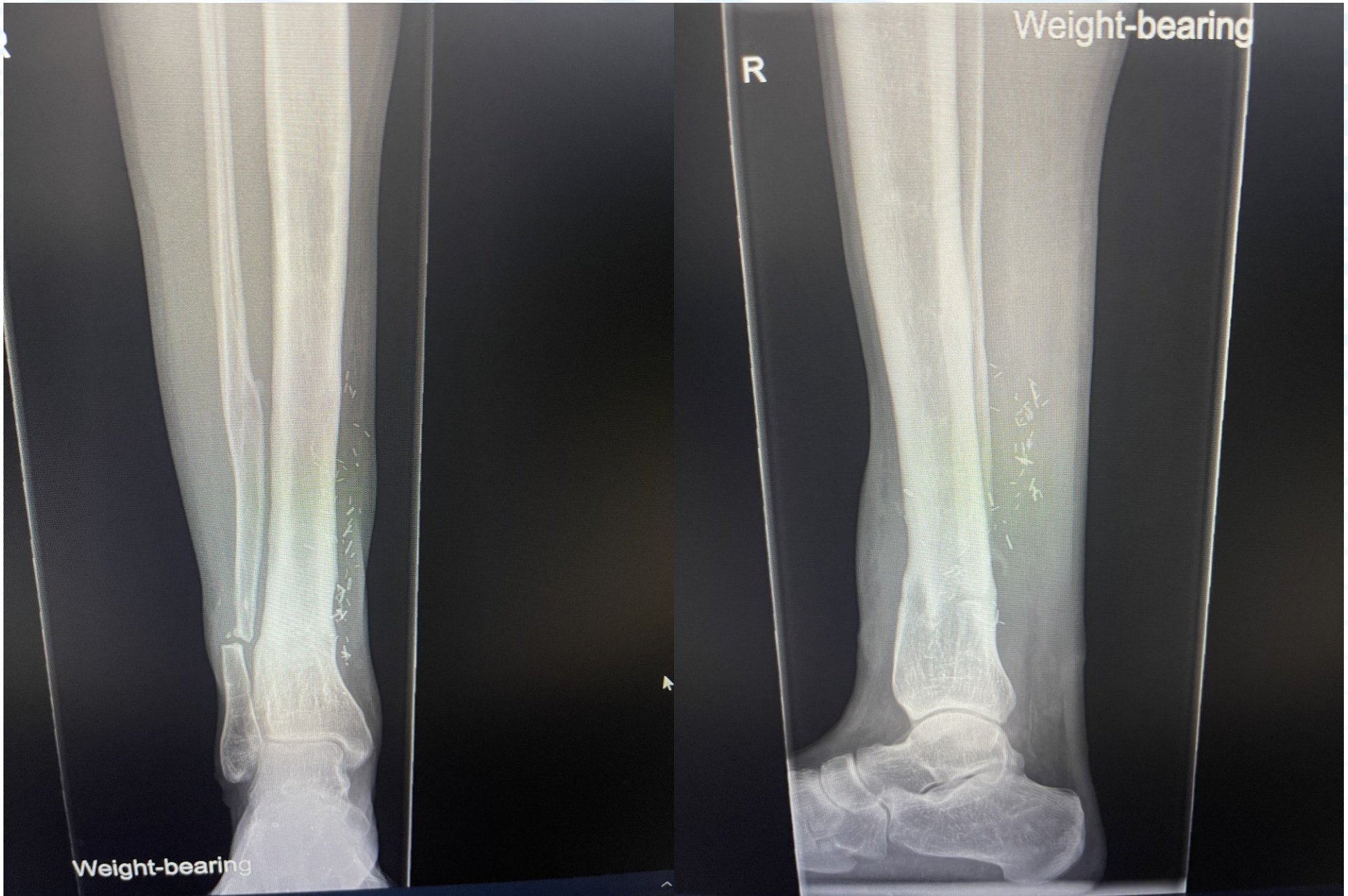
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Weight-bearing

Scenario 2

Diabetic Foot Osteomyelitis (DFO)

The Foot 34 (2018) 40–44

Contents lists available at ScienceDirect

The Foot

journal homepage: www.elsevier.com/locate/foot

Original Article

Single stage treatment of diabetic calcaneal osteomyelitis with an absorbable gentamicin-loaded calcium sulphate/hydroxyapatite biocomposite: The Silo technique

Efstathios Drampalos*, Hasan Raza Mohammad, Chris Kosmidis, Moez Balal, Jason Wong, Anand Pillai

Trauma and Orthopaedics Department, Wythenshawe Hospital, Manchester, United Kingdom


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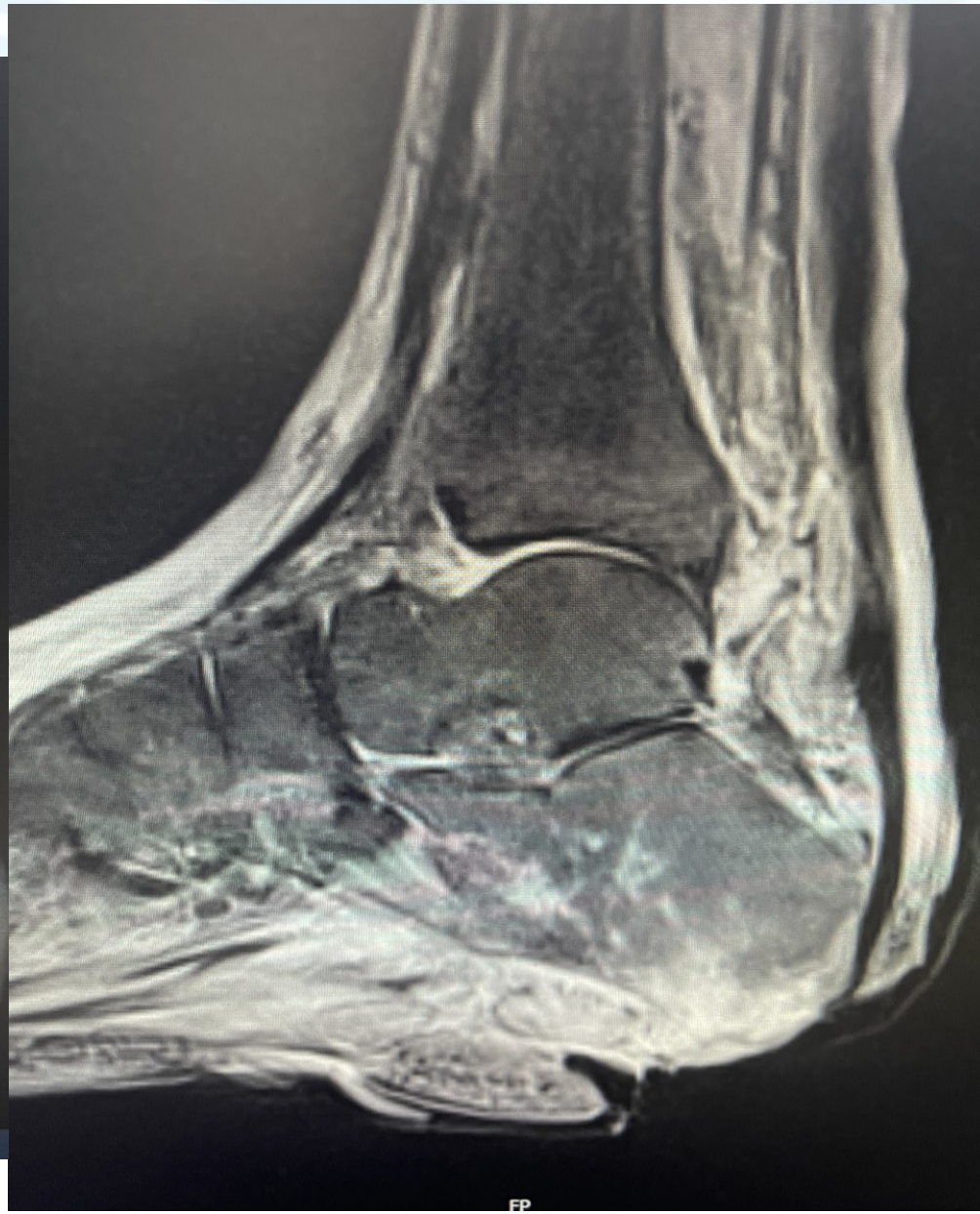
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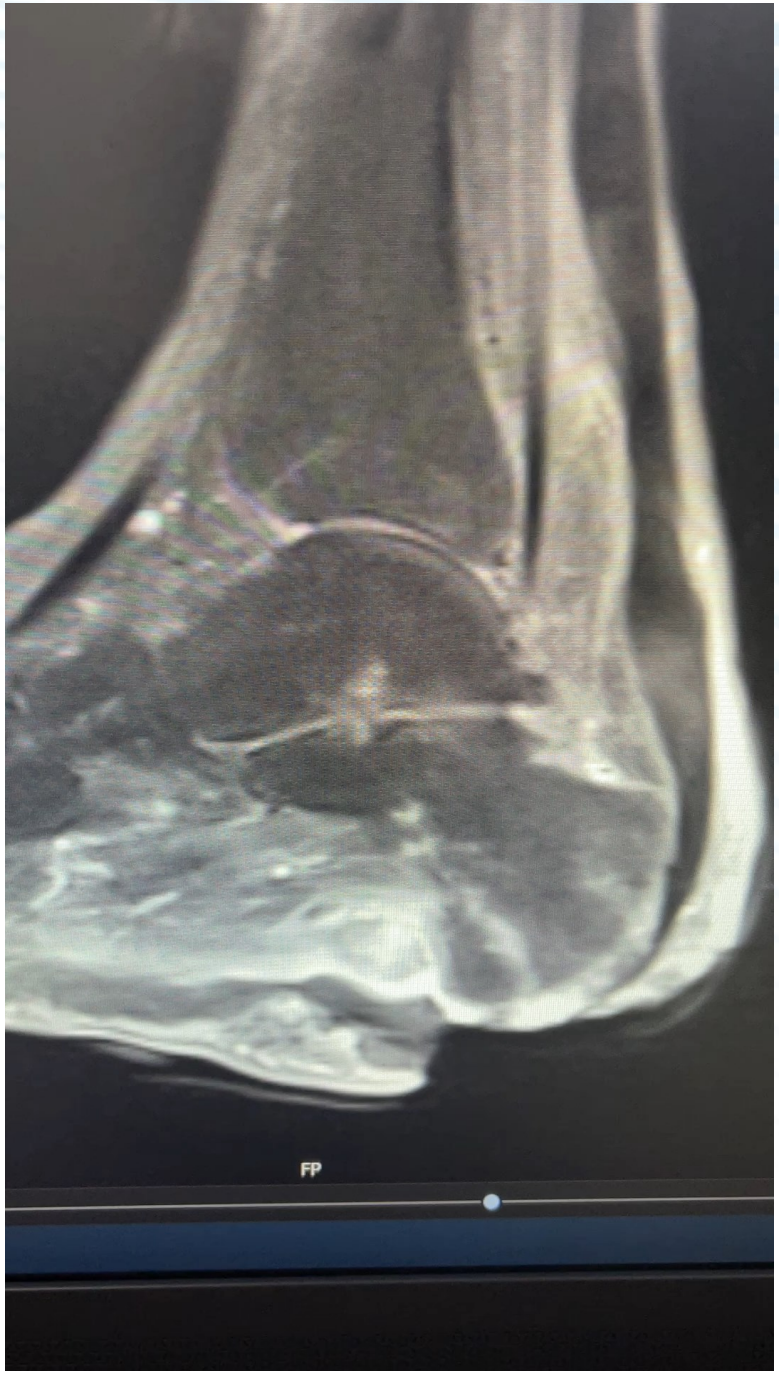
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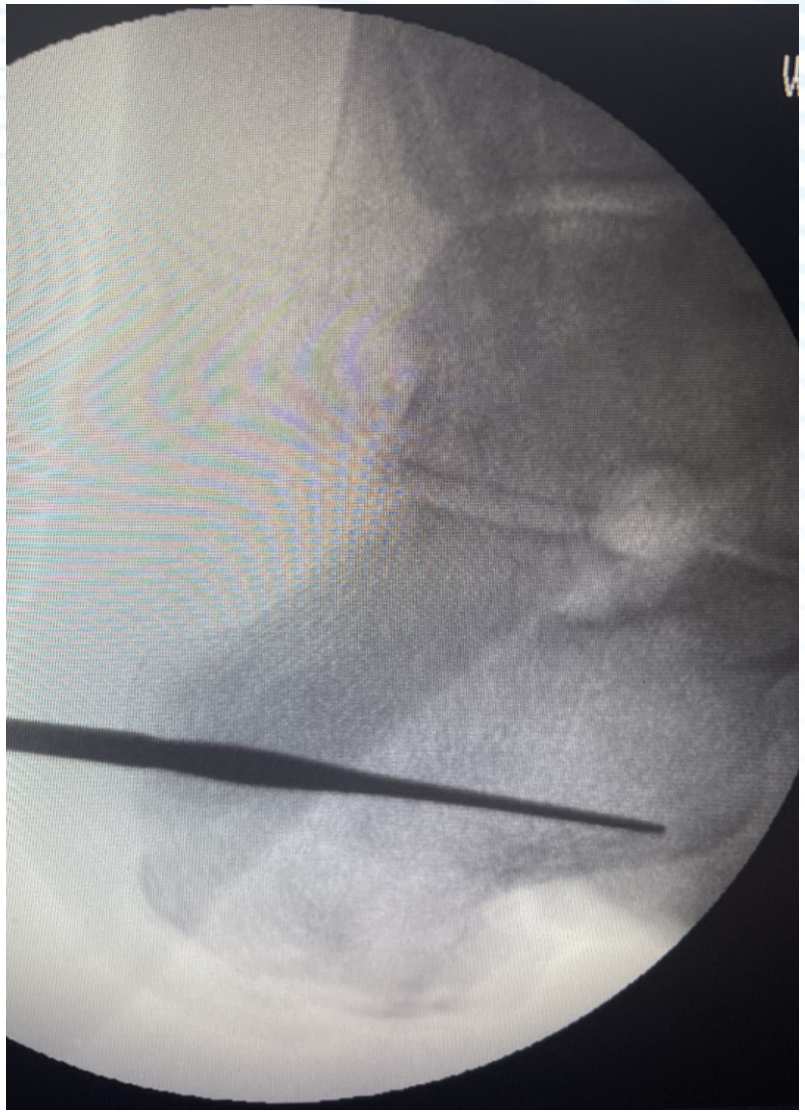

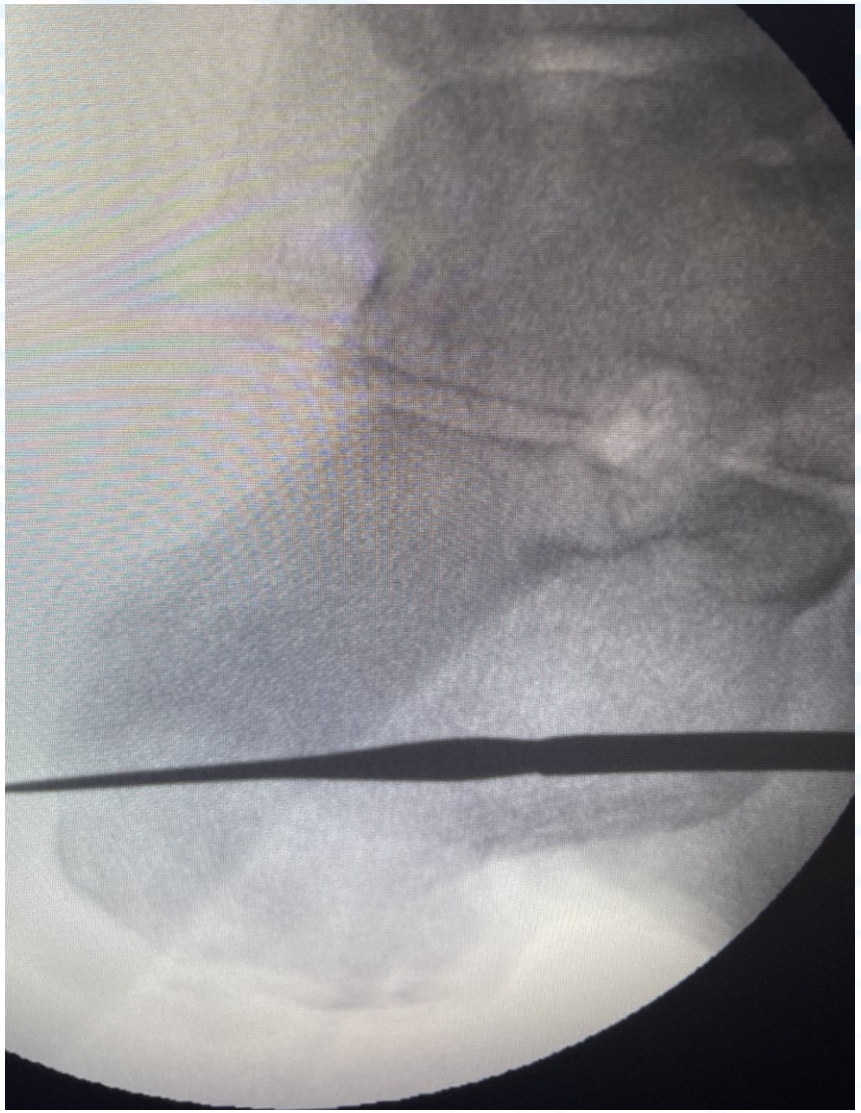

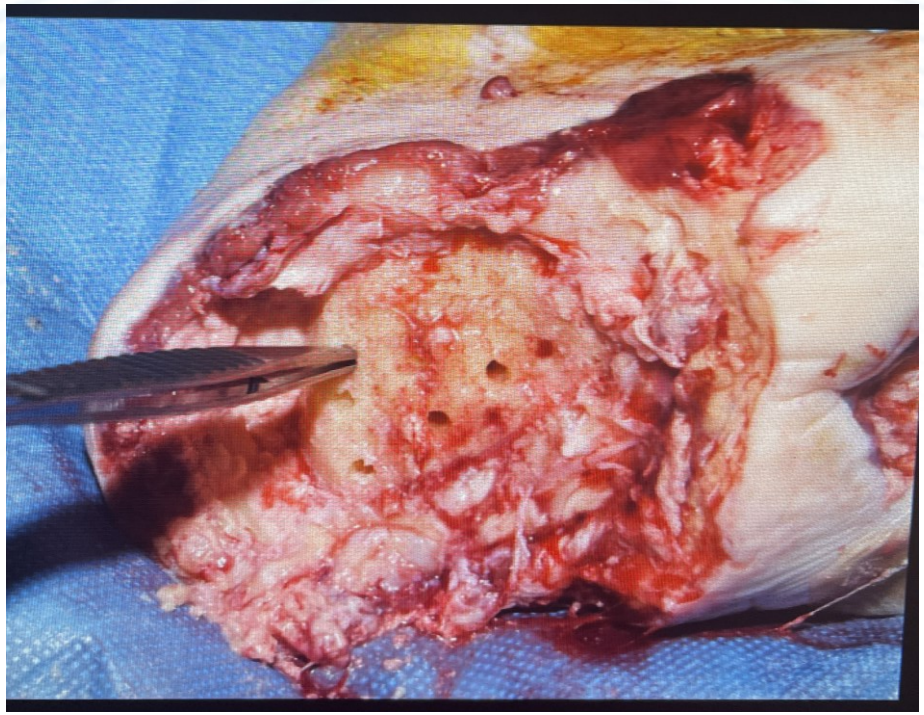

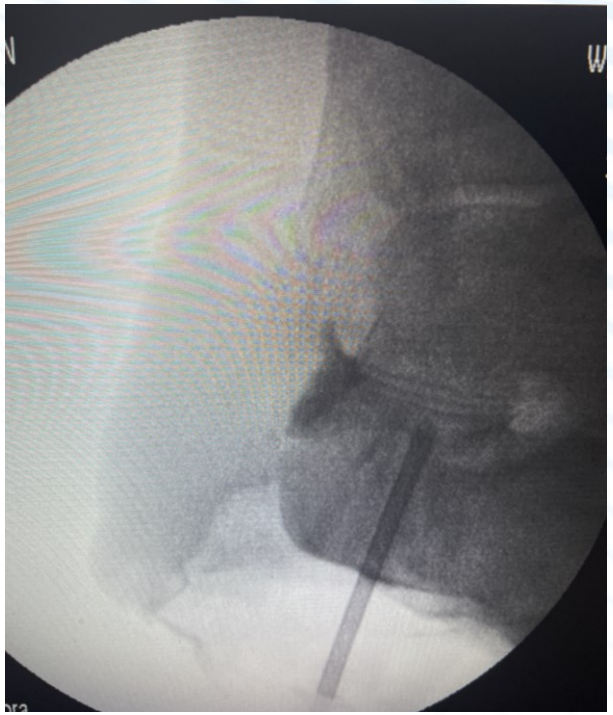

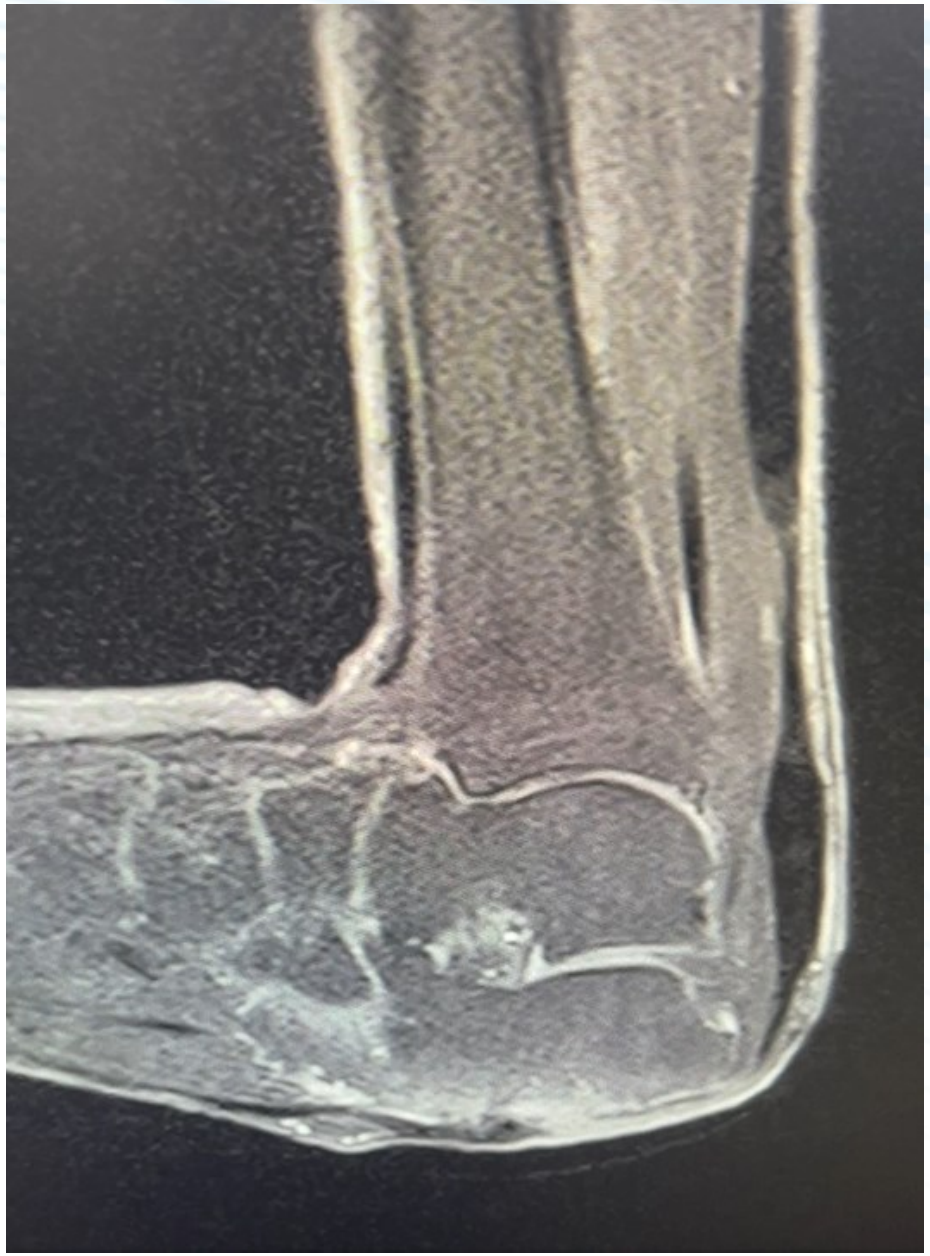


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Scenario 3
Open Fractures

Contents lists available at ScienceDirect

Journal of Orthopaedics

journal homepage: www.elsevier.com

The use of adjuvant local antibiotic hydroxyapatite bio-composite in the management of open Gustilo Anderson type IIIB fractures. A prospective review

Noman Jahangir [a, *], Noman Niazi [a], Ahmed Aljawadi [b], Adam Reid [c], Jason Wong [c], Efstathios Drampalos [a], Anand Pillai [a]

[a] Trauma and Orthopaedics, Manchester Foundation Trust, Southmoor Rd, Wythenshawe, Manchester, M23 9LT, UK
[b] Manchester Foundation Trust, Southmoor Rd, Wythenshawe, Manchester, M23 9LT, UK
[c] Plastic Surgery, Manchester Foundation Trust, Southmoor Rd, Wythenshawe, Manchester, M23 9LT, UK

PROOF

Journal of Orthopaedics 18 (2020) 261–266

Contents lists available at ScienceDirect

Journal of Orthopaedics

journal homepage: www.elsevier.com/locate/jor

Original Article

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**

Ahmed Aljawadi[a,*], Amirul Islam[a], Noman Jahangir[a], Noman Niazi[a], Zak Ferguson[a], Benjamin Sephton[a], Mohammed Elmajee[b], Adam Reid[c], Jason Wong[c], Anand Pillai[a]

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[b] ST4 Spine Department, Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, B31 2AP, UK
[c] Plastic Surgery, Manchester Foundation Trust, Southmoor Rd, Wythenshawe, Manchester, M23 9LT, UK


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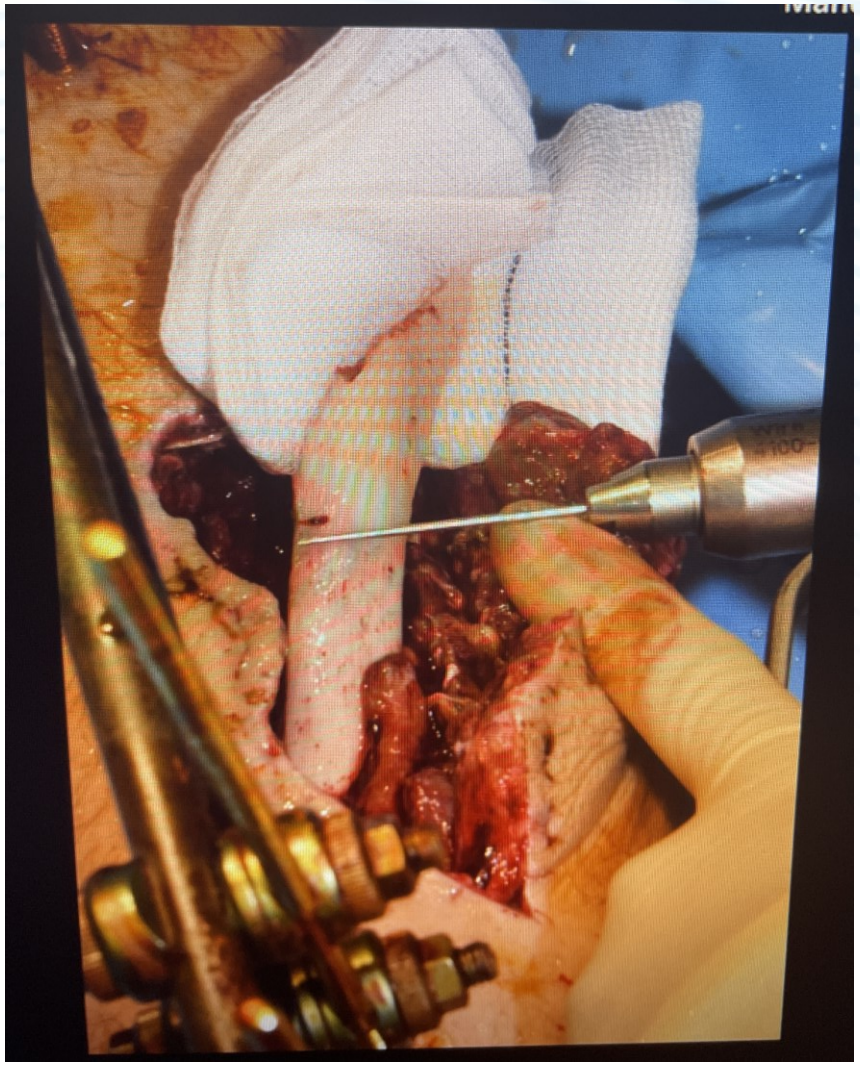

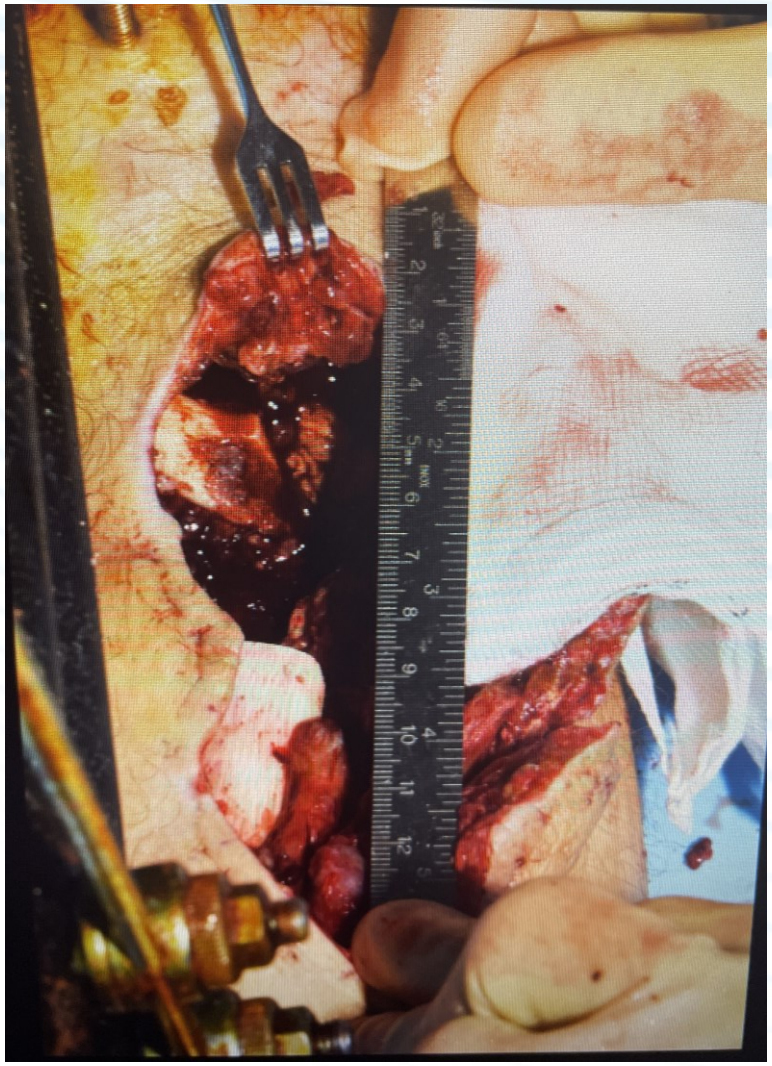

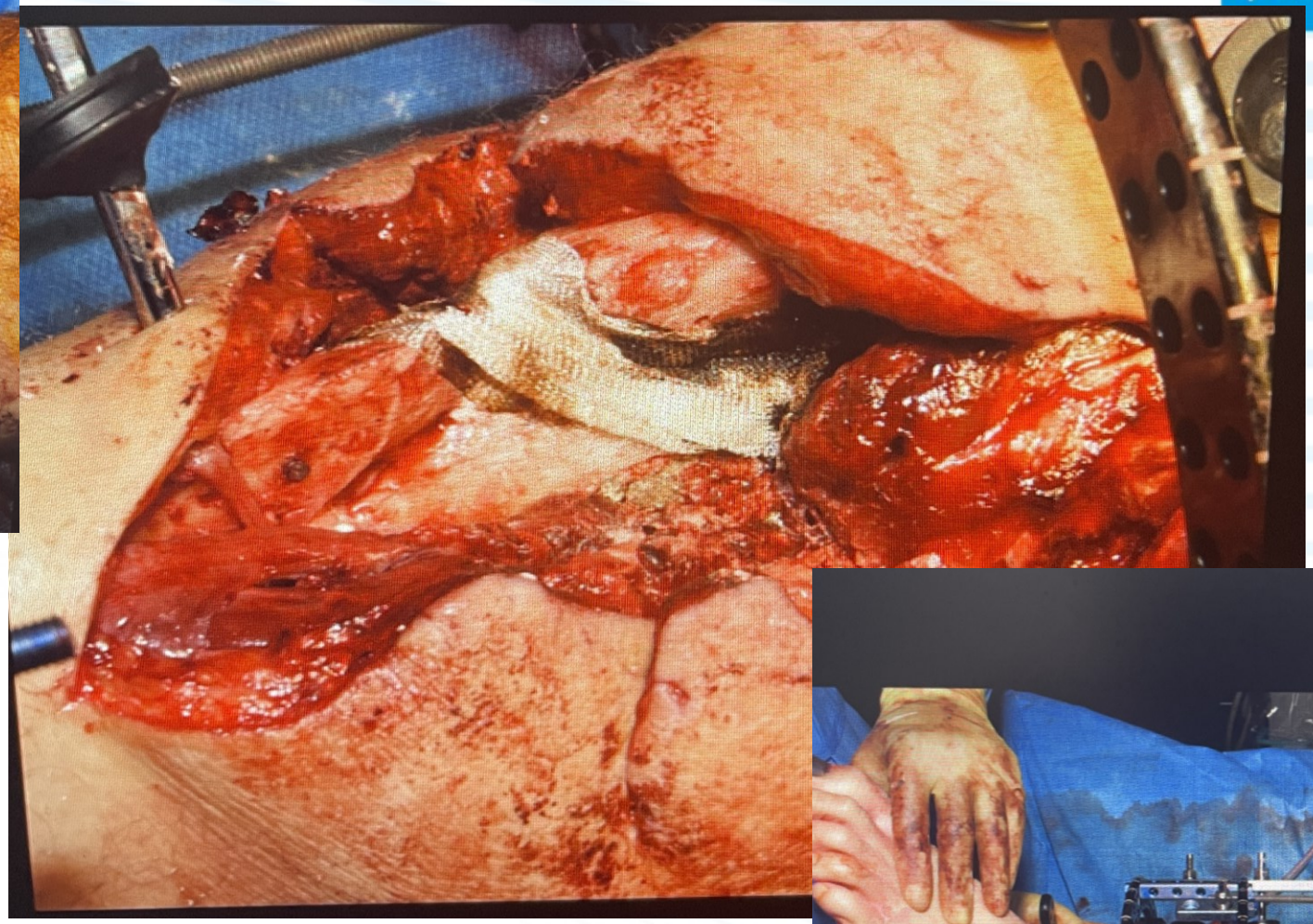

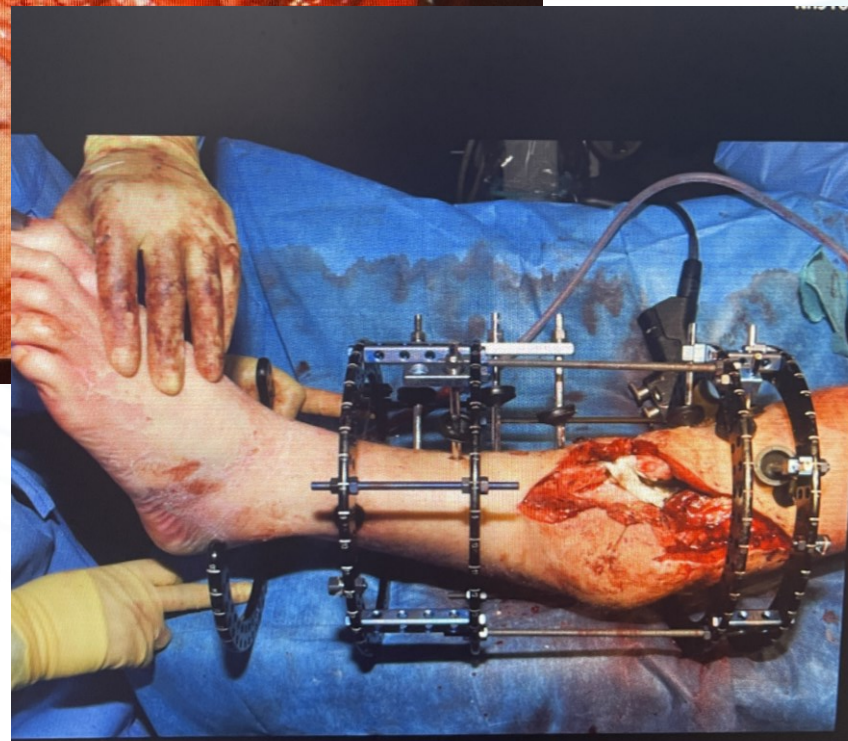

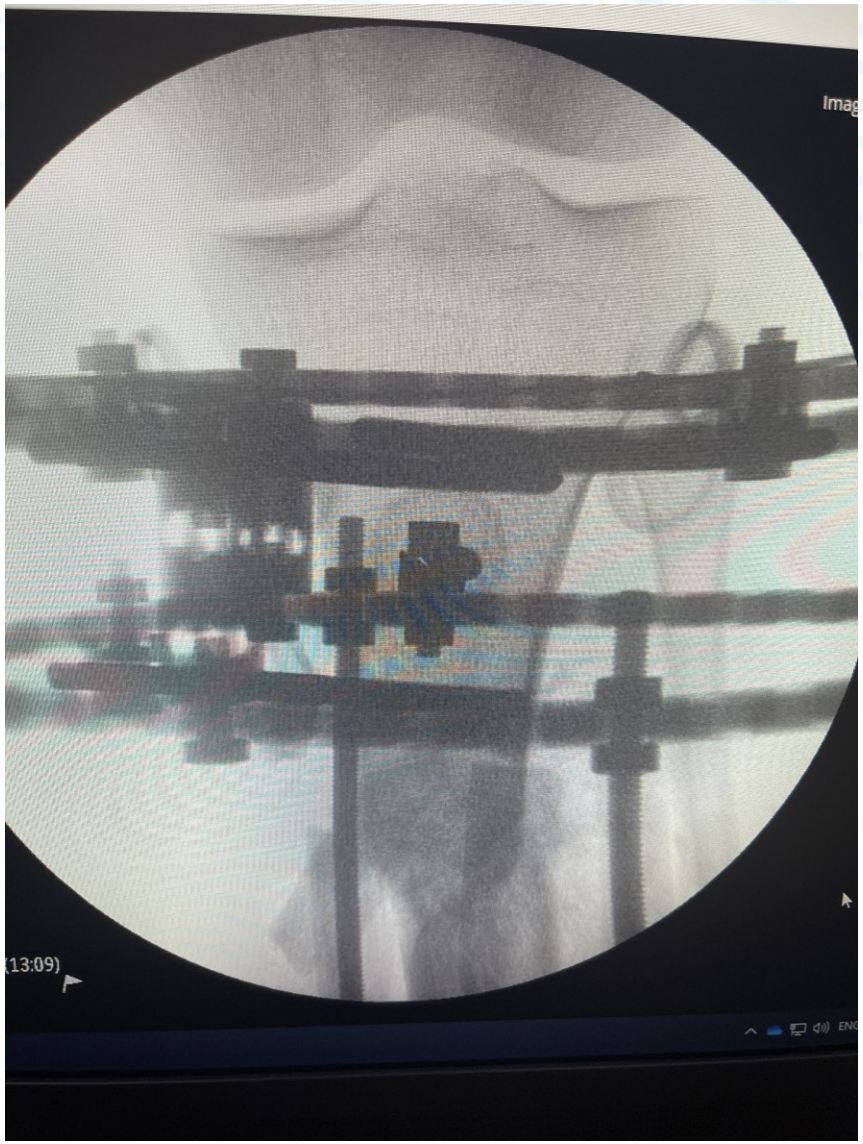

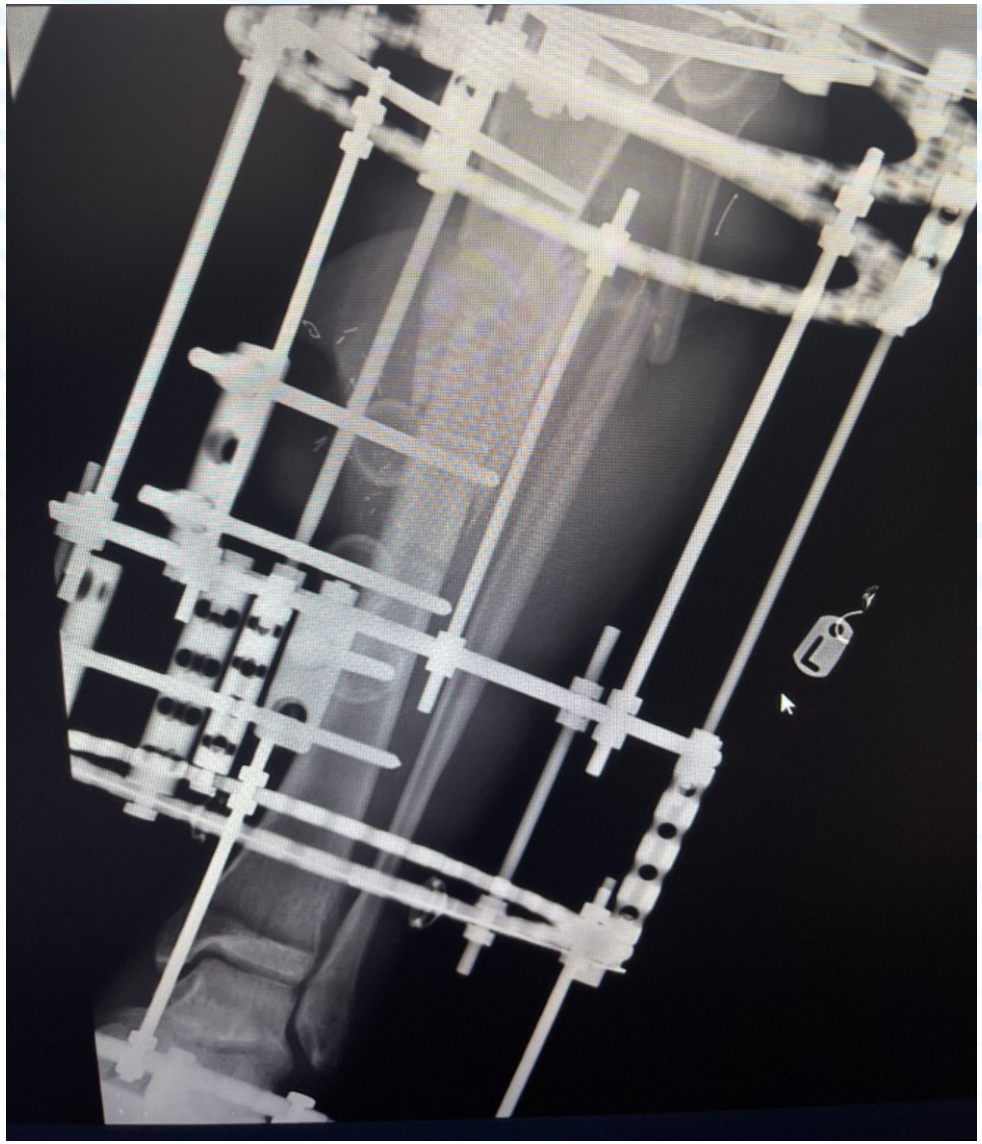

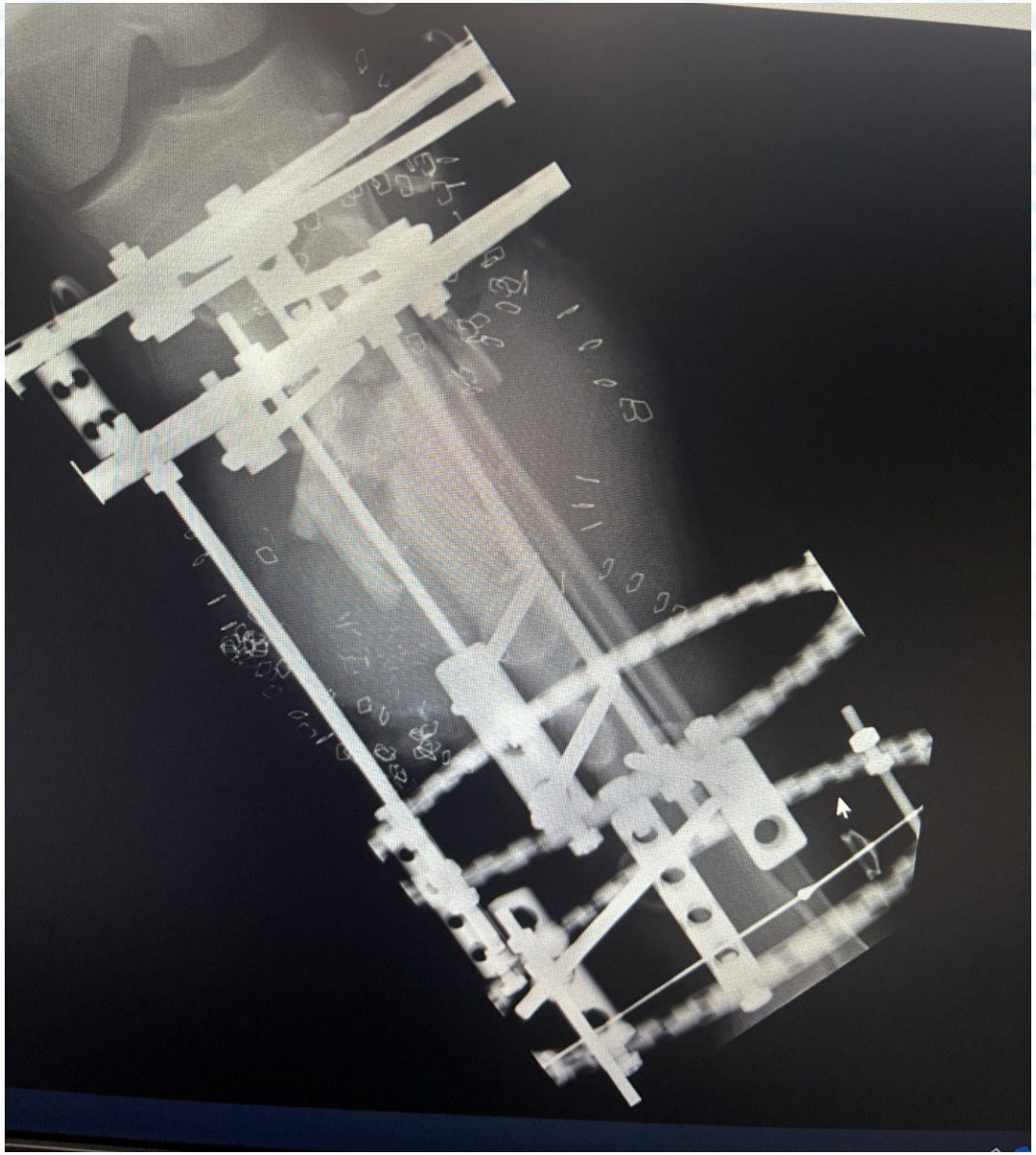

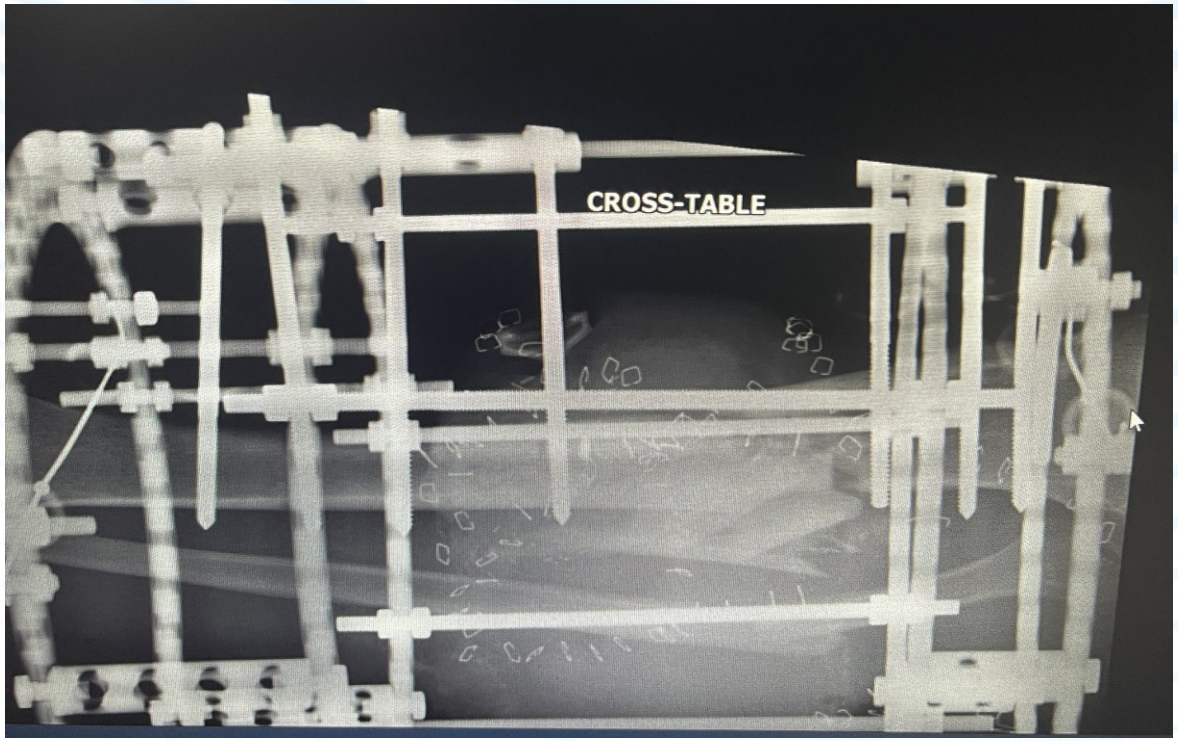
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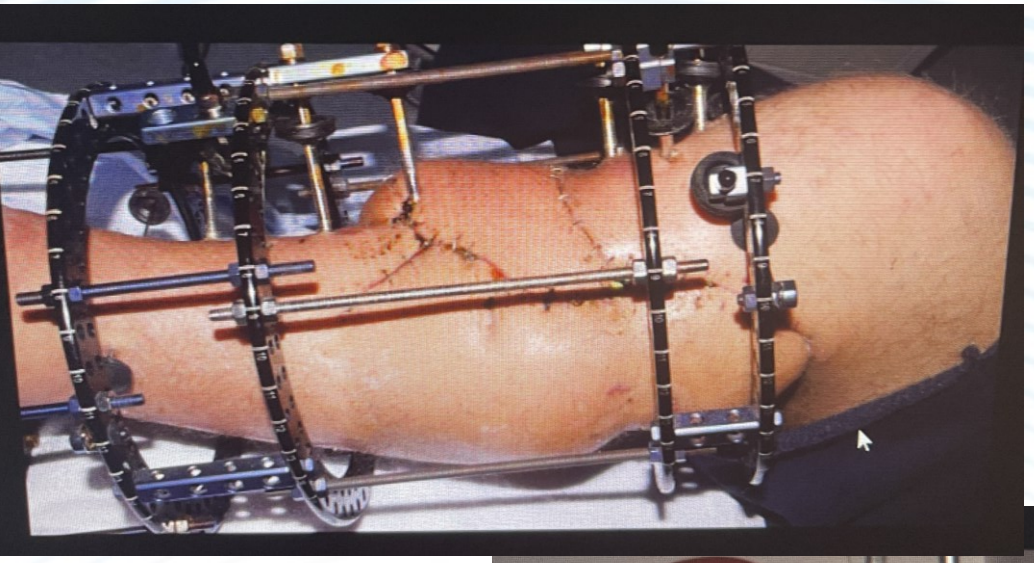
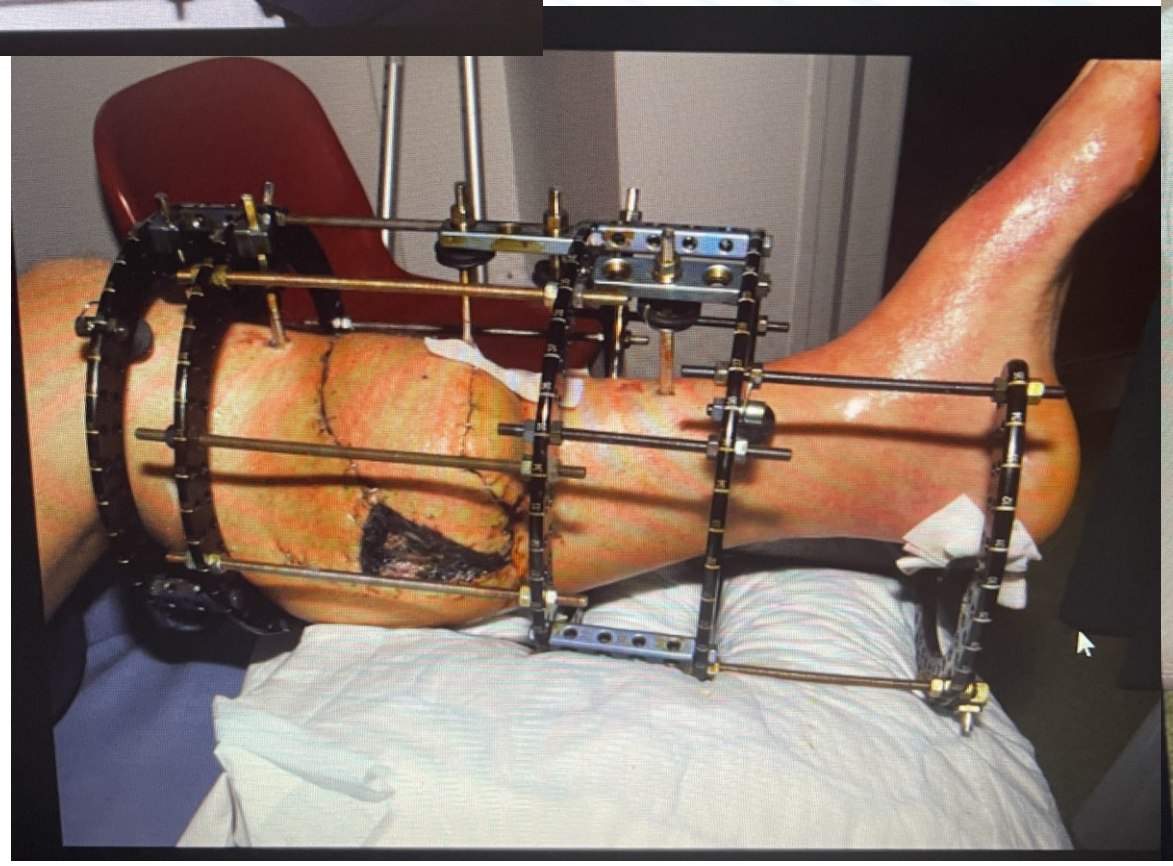
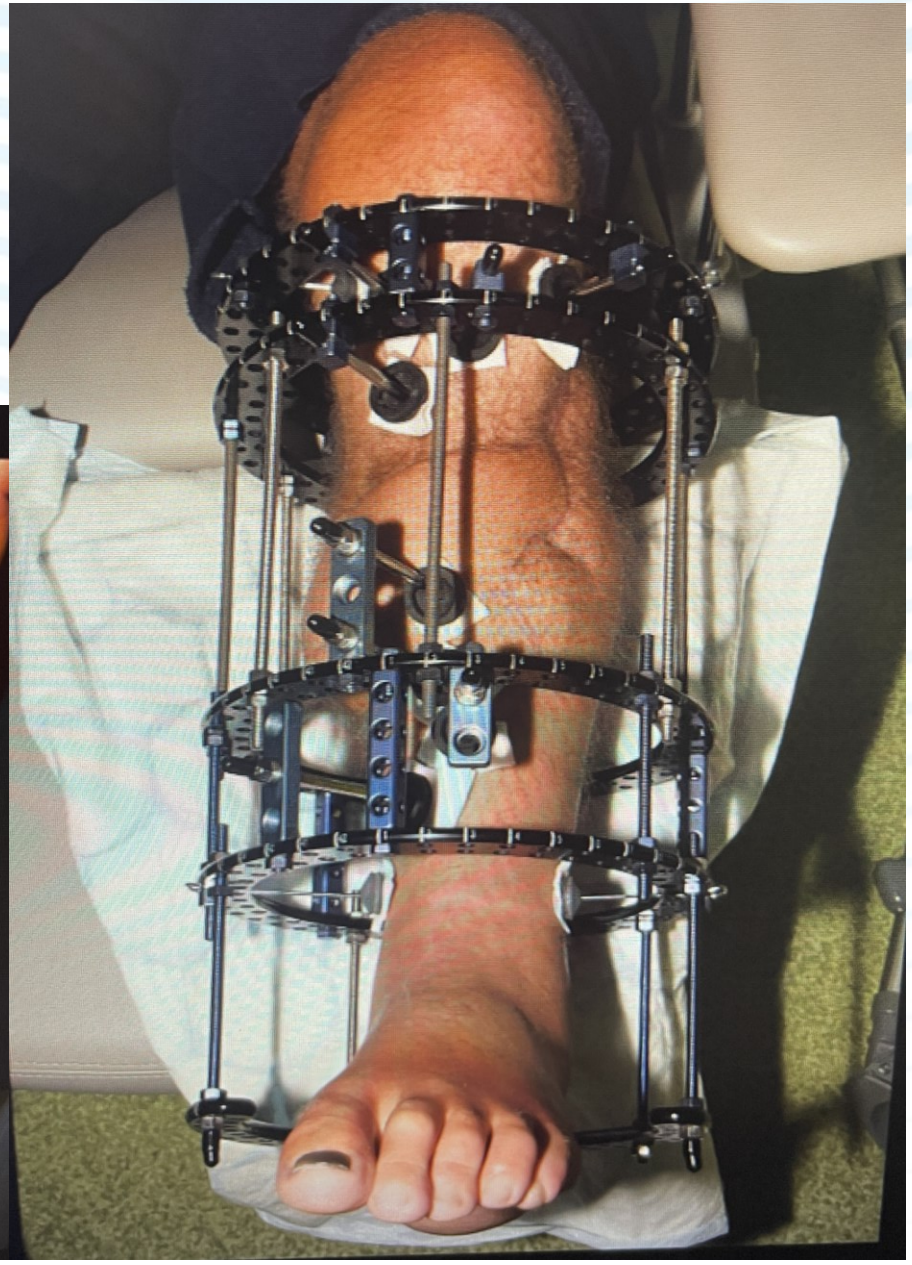







96.5%
35.20%
45%

BONESUPPORT
Capital Market Day
September 1st, 2022

CERAMENT®

Clinical Experience

Prof Anand Pillai

Manchester University Hospitals

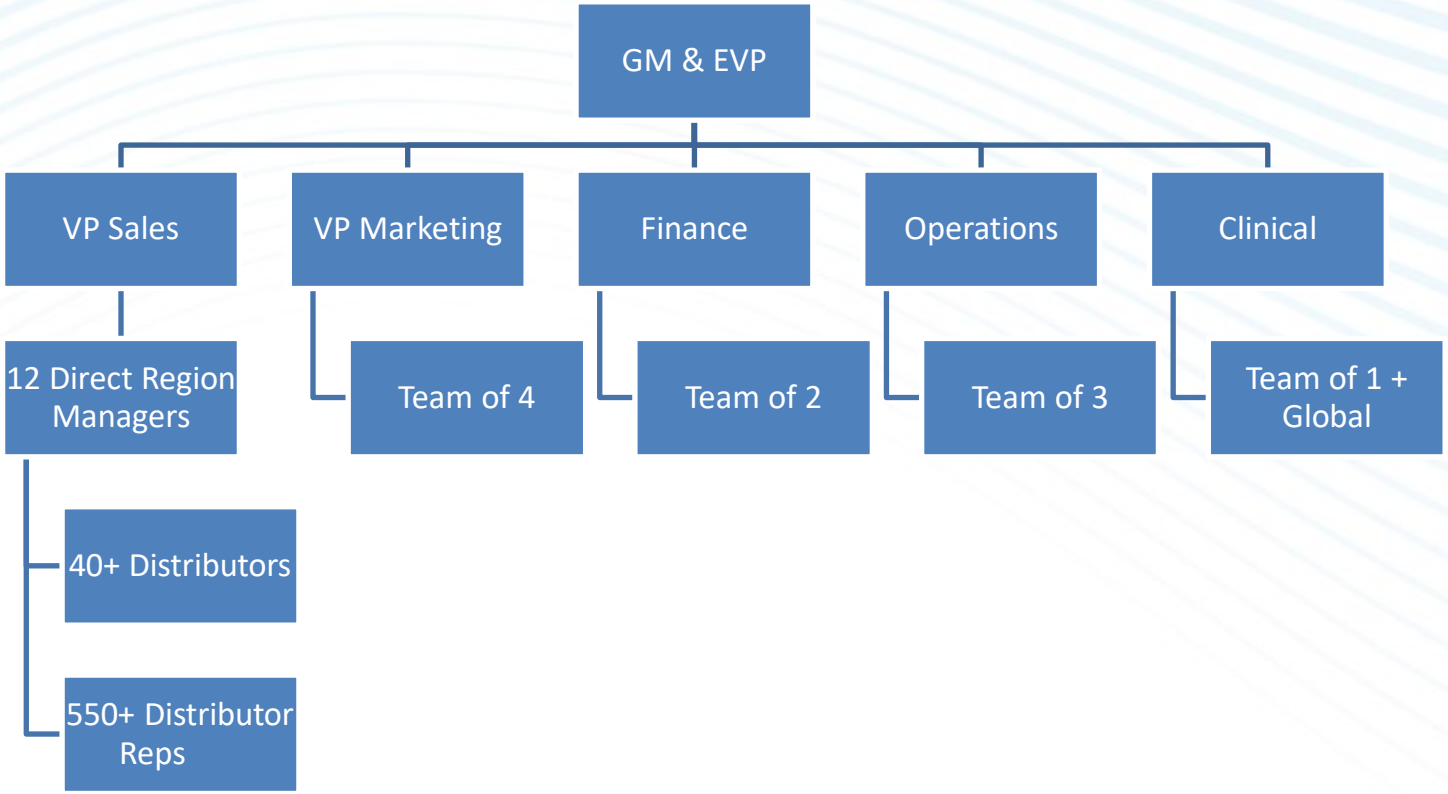
BONESUPPORT Capital Market Day September 1st, 2022

CERAMENT G launch US

Mike Roth, General Manager &
Executive Vice President North America

Strong sales team ready to expand

U.S. Commercial Organization



Distribution Partner

OrthoPediatrics

Non-exclusive Distribution for CERAMENT BONE VOID FILLER

Network of 250+ pediatric hospitals

CERAMENT G expected to accelerate strong underlying growth

- Strong sales growth in USA since independence (Q4 2018), despite negative impact from COVID

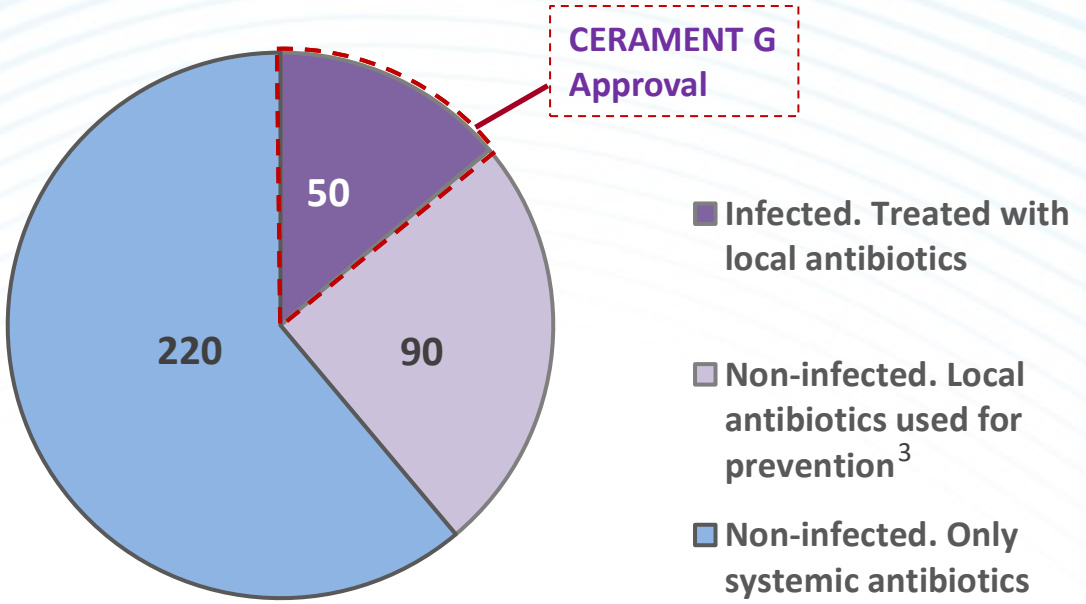
	2022 June 2022	Growth vs LTM June 2021	Growth vs LTM June 2019
Sales LTM	87.2 mSEK	40%	216%

- Strong sales momentum
- High Gross Margin (93.5%)
- Scalable platform

- Performance driven by increase in direct Region Managers (from 8 – 12), expanded distribution and focus on high potential accounts (Mayo, Cleveland Clinic, HSS, Sinai)
- Significant progress on national contracts awarded from several top GPOs and IDNs
- CERAMENT G awarded New Technology Add-On Payment (NTAP) from CMS of $4,920 (effective Oct. 1, 2022)
  - ➢ Supports premium pricing with limited discounting
- Strong unmet market need and pent-up demand for CERAMENT G
  - ➢ First and Only injectable antibiotic eluting bone graft

US bone graft market:

360 k surgical procedures per year in the US with bone grafts used to manage bone injuries



360 k surgical **procedures** per year

- 48% fracture/ trauma etiology[2] for infected cases
- All current use of bone grafts + local antibiotics in the US, are off-label use / unauthorized use
- Market leading treatment of bone infection and prevention of infection is PMMA-beads (off-label use) followed by autograft mixed with antibiotics

CERAMENT G addressing a 780[1] mUSD market opportunity

First and only FDA approved bone graft with antibiotic elution

1. **280 mUSD Bone infection and (future potential) 500 mUSD for prevention. Measured in CERAMENT G value (procedures x anticipated price)**
2. Gustilo RB, Mendoza RM, Williams DN. Problems in management of type III (severe) open fractures: a new classification of type III open fractures. *J Trauma.* 1984;24:742–746.
3. Local antibiotics is combined with the bone graft in 30% of the non-infected cases to prevent a bone infection. BONESUPPORT data on file: Inspired Health Market Research 2020

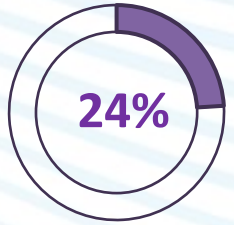
CERAMENT G fills an obvious unmet market need

1. **The Problem**: *Bone infections are difficult to treat*
    1. Patients are complex
    2. Lack of innovation in treatment options
    3. High reinfection rates, low patient QOL

2. **The Need**: *Better dead space management*
    1. Multistage procedures
    2. Improvised treatment options
    3. Lack of safety/efficacy evidence

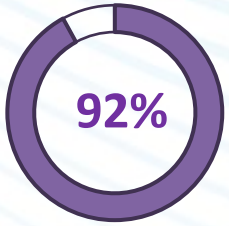
3. **The Solution: CERAMENT G**
    1. Dual mode of action
    2. Enables single-stage approach
    3. Clinically supported

REINFECTION RATE



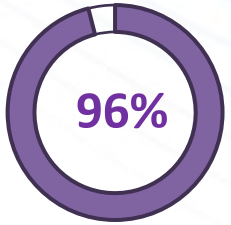
On average **24%** of US bone infection cases result in reinfection[1]

TREATMENT PREFERENCE

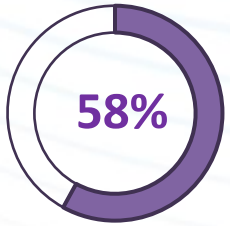


92% would prefer a single-stage-procedure[1]

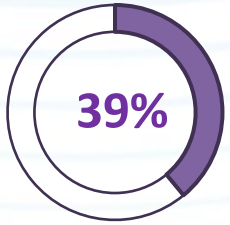
CERAMENT G OUTCOMES



96% Success rate in eradication of infection[2]



58% Reduction in readmissions[3]



39% Reduction in length of stay[3]

1. US market insight – Commissioned Inspired Health Market research
2. McNally et al. 'Single-stage treatment of chronic osteomyelitis with a new absorbable, gentamicin-loaded, calcium sulphate/ hydroxyapatite biocomposite'. *J Bone Joint Infect*. 2016 Sep; 98-B(9):1289-96.
3. Ferguson et al. "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." *J Bone Joint Infect*. 2021 Apr: vol. 6,5 151-163. 28.

Focused sales strategy securing success

- **Quality not quantity – High volume users based on data**
- **Secure early adopters and success with CERAMENT G**
  - Identify & qualify surgeon champions
  - Drive local hospital approvals
  - Focus on Customer Care/onboarding
  - Gather product/clinical feedback
- **Target High Volume Bone Infection sites**
  - Academic and teaching centers
  - Active CERAMENT BONE VOID FILLER users
  - Leverage strong Distribution network (and purchasing/admin relationships) in place
  - Utilize KOLs, Advisory Board and strong surgeon champions in place

Accelerated market access secures future growth

National Account Status

- Weighted (5mL and 10mL) price of CERAMENT G ~ $5,600 USD
- Limited discounting 5% - 15%

Premier — **On Contract**

- 2,501 hospital members

HealthTrust — **On Contract**

- 1,441 hospital members

Government — **On Open Market**

- Submission underway for FSS, DAPA and ECAT contracts
- Plan to secure contracts in Q4/Q1 2023

Vizient — **New Tech Submission...**

- On going conversations exploring options for agreement pathway

Resource Group — **Initial Submission and ongoing discussion...**

- Strategic plan in place for response and updated submission

Reimbursement Status

- Currently bone grafts fall under DRG (bundled pay.)
- CERAMENT G awarded unique ICD-10 and NTAP (through FDA breakthrough designation)
- NTAP effective Oct. 1, 2022
- NTAP provides max payment of $4,920 for CERAMENT G inpatient procedures when hospital costs exceed the DRG payment threshold. Amount will vary based on the facility, payer, costs and the DRG involved.

US Booster Program accelerates market access

Push

Invest in resources that help generate US sales growths > 50%

Develop

Add resources to support the increase in anticipated sales

Anticipated Impact

- Drive aggressive market penetration with NTAP and GPO listing (Healthtrust and Premier)
- Full year 2023 cost of the program is app 8,5 mSEK

Key hirings further develops the business

Push

- **US Medical Advisor(s)**
  - Orthopedic surgeon(s) as "Head of clinical and medical affairs US"
    - Interacting with KOLs
  - Drive antibiotic stewardship agenda
  - Transform standard of care
- **Reimbursement/Billing specialist**
  - Guidance for HCP and clinics on the proper reimbursement from CMS and private insurers
  - Drive market access
- **Medical Education** (2 positions)
  - Training orthopedic surgeons, nurses and distributor sales reps

Develop

- ✓ **Customer Service Rep** to help support incremental increase in volume
- ✓ **Financial Controller** to assist with sales reports to support field sales effort
- ✓ **Marketing Associate** to assist with increased industry meetings, communications, etc.

Incremental 7 FTE to the US organization to drive and develop the business further

Poised to expand…

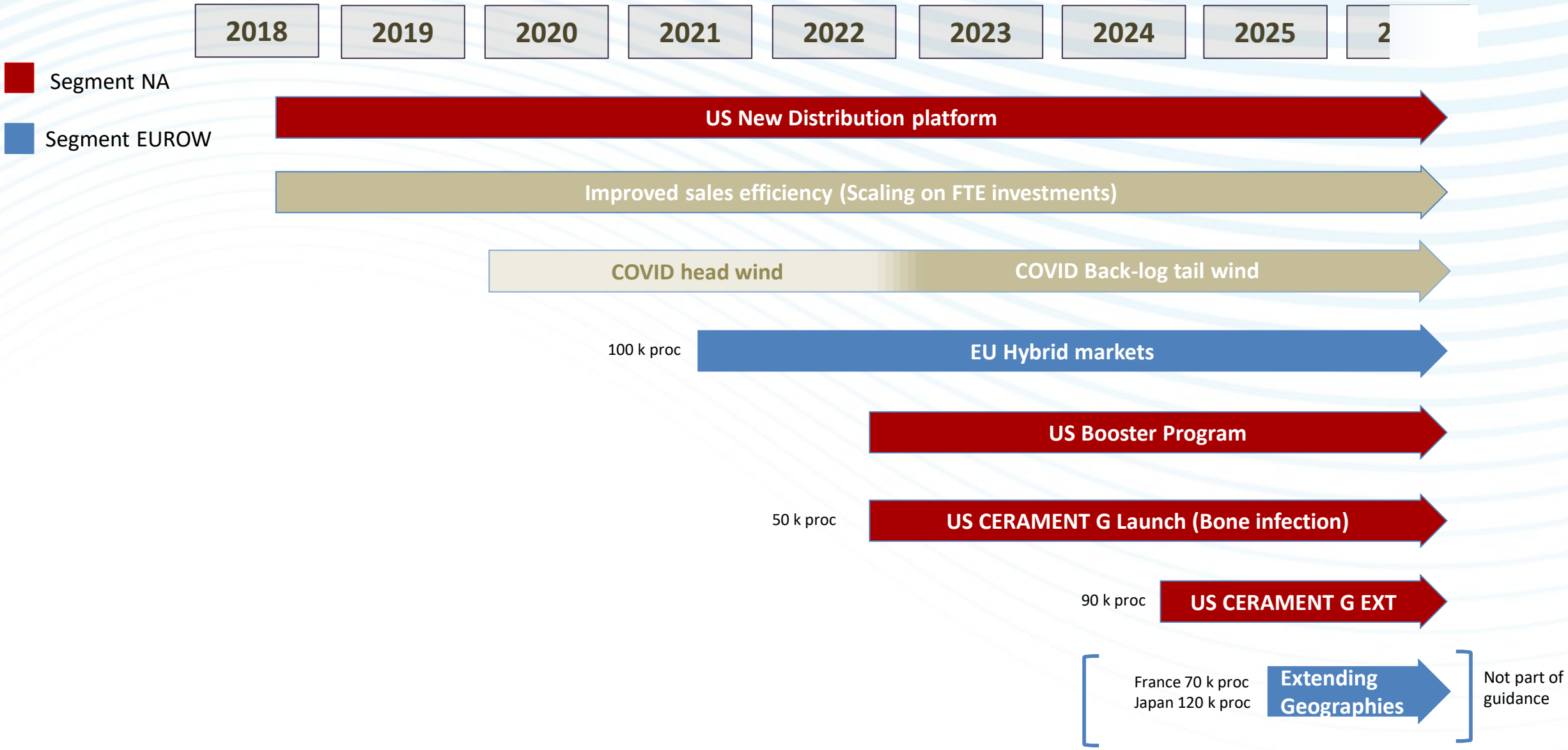
- Well oiled organization
- Strong and growing customer base
- Approvals granted and in motion
- Reimbursement in place
- Booster Program in place

BONESUPPORT Capital Market Day September 1st, 2022

THANK YOU

Future outlook and market guidance

Significant growth vector in favorable post-pandemic environment



First and only of its kind - CERAMENT G US

Superiority of CERAMENT G shown in peer-reviewed clinical studies

US Market penetration rate with CERAMENT BVF since late 2018

CERAMENT G being only product on the market

NTAP of 4920 kUSD for Medicaid patients

Market insight/ market research

GPO presence

Great opportunity to replace the outdated US standard of care

Guidance message

40%[1] sales growth for the next three years (2023-2025)

1. Average and normalized sales growth CAGR from 2023 – 2025

Strong financial position and outlook

Sales growth and profitability

- Leverage from sales growth
- Improved gross margin
- Cost control

+

Efficient use of funds

- Low level of Net Working Capital
- 1 bn SEK in tax losses carried forward
- Low to moderate capex needs

=

Strong cash flow

- Substantial headroom in funding
- Cash at end of Q2-22 was reported to **SEK 172 million**
- Share swap settlement has added **SEK 50 million to cash**