Capital Markets Day 2026

May 26, 2026

Stockholm

DISCLAIMER

This presentation contains forward-looking statements regarding Bonesupport Holding AB (publ) ("BONESUPPORT"), including, but not limited to, statements about future operations, financial performance, market conditions, growth strategies, product development, regulatory approvals, and other projections. These statements are based on current expectations, estimates, and assumptions and involve risks and uncertainties that could cause actual results to differ materially from those expressed or implied. Statements contained in this presentation regarding past trends or activities should not be taken as a representation that such trends or activities will continue in the future.

Forward-looking statements are subject to risks and uncertainties, including, but not limited to, changes in economic conditions, market demand, competitive factors, regulatory developments, and other factors described in BONESUPPORT's annual report. BONESUPPORT undertakes no obligation to update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise, except as required by applicable law. You are cautioned not to place undue reliance on forward-looking statements. Actual results may differ materially from those anticipated.

BONESUPPORT Capital Markets Day, May 26th, 2026

Agenda

13.00-13.30	Strategy update - Strategy | Unmet needs | Competition | Moat
13.30-14.00	A segment based approach - Market segments & value propositions - Market potential - Segment deep dives – Arthroplasty & Spine
14.00-14.45	Clinical update
14.45-15.00	Q&A
15.00-15.30	Coffee break & Product demonstrations
15.30-16.30	Clinical experience - Arthroplasty & Periprosthetic Joint Infection (PJI) - Trauma & Fracture Related Infection (FRI)
16.30-16.45	Value creating technology & operating model
16.45-17.00	Wrap up & Q&A

Speaker list

Moderator:
- Charlotte Stjerngren, CORD

Company representatives
- Torbjörn Sköld, CEO
- Håkan Johansson, CFO
- Annelie Aava-Vikner, EVP Marketing
- Dr. Michael Diefenbeck, Chief Medical Officer

Surgeons
- Dr. Meller, Orthopedic Surgeon, Charité University Hospital, Berlin, Germany
- Dr. Matuszewski, Orthopedic Surgeon, University of Kentucky, Lexington, US

Additional BONESUPPORT on-site for product demonstrations:
- Candice Maxwell, Director Medical Education
- Karin Kings, Director Medical Education
- Pia Walby, Director Product Management

Capital Markets Day 2026

Strategy update

Strategy | Unmet needs | Competition | Moat

Torbjörn Sköld, CEO

BONESUPPORT Capital Markets Day 2026 in context - Purpose

- Capital Markets Day 2018 focused on:
  - New strategy and sales outlook
  - Reorganized European sales team
  - Regulatory pathways

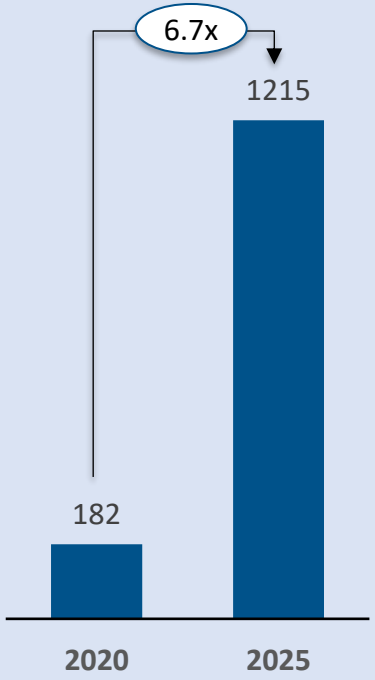
- Capital Markets Day 2022 focused on:
  - Medical education
  - Booster program
  - CPO and IDN contracts

- Capital Markets Day 2023 focused on:
  - New indication: Spine
  - CERAMENT G US
  - CERAMENT V US
  - Clinical update

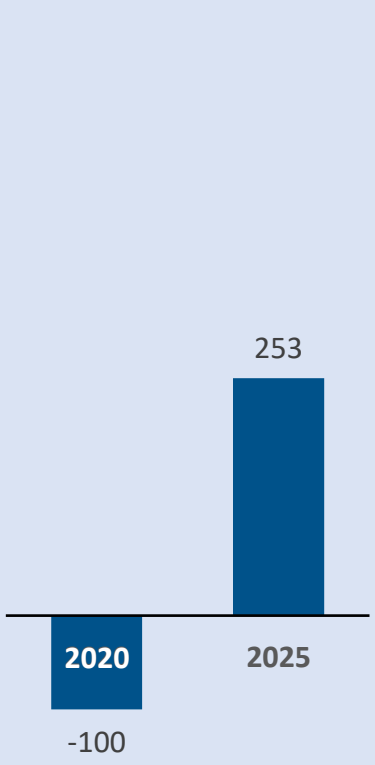
- **Focus for today's Capital Markets Day 2026:**
  - Strategy update – Segment specific execution unlocks potential
  - Upward adjustment of market opportunity
  - Clinical update – Arthroplasty and Spine multicentre studies on antibiotic eluting CERAMENT to start in 2027
  - Spine – Unmet need and regulatory (FDA) submission no later than 2031

BONESUPPORT has grown and transformed — from early-stage science to a proven, cash-generative business with substantial growth ahead

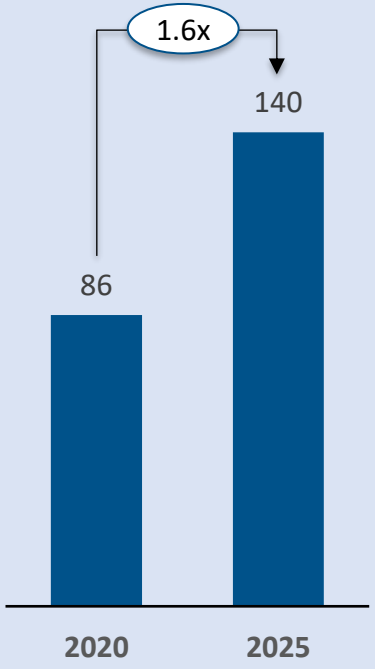
Revenue, SEK m



Cash flow, SEK m



Employees, no



From...	...to
▪ Interesting science	▪ Undisputable clinical data
▪ Limited brand awareness	▪ Market mover
▪ Negligible penetration	▪ Early in our growth journey

Our strategy remains right – and has delivered

BONESUPPORT Strategy (2018)

- Three strategic pillars

Innovation | **Evidence** | **Commercial Platform**

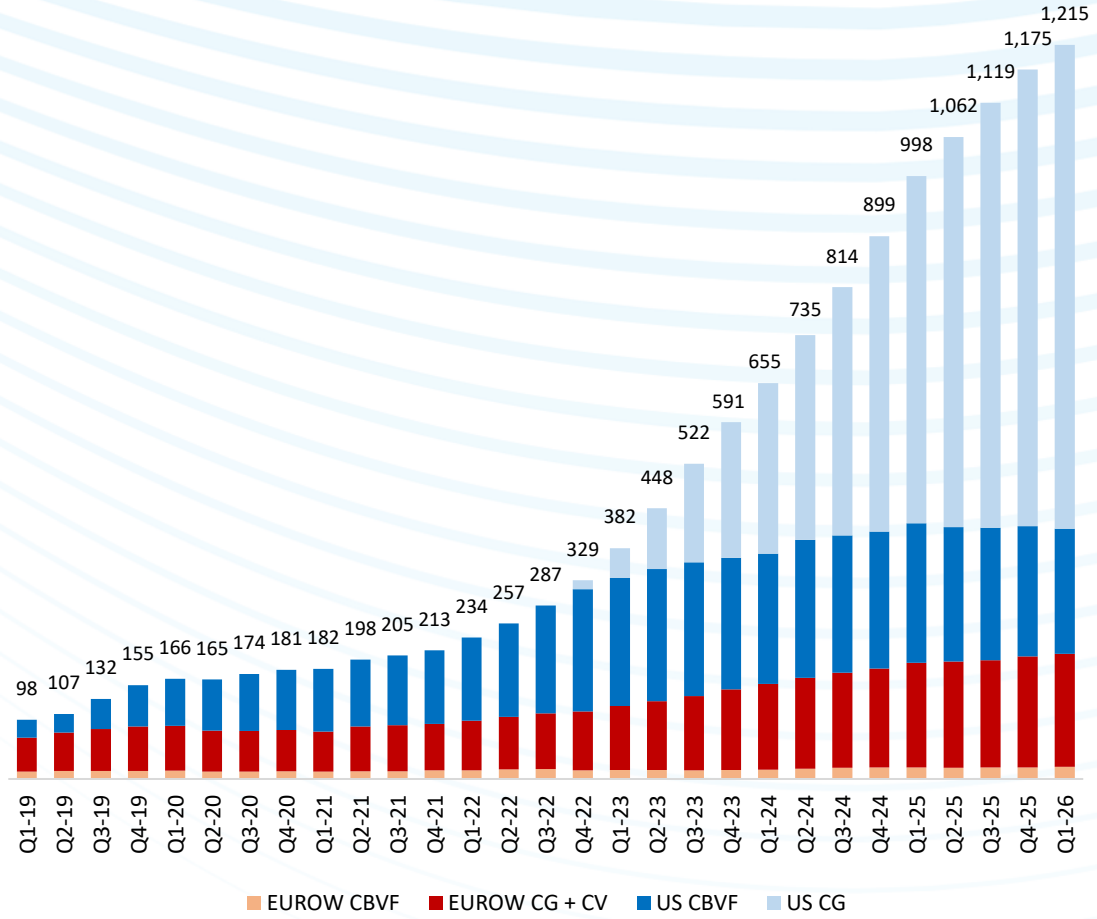
- The strategy introduced in 2018 remains right
- We execute according to plan
- The results follow

Next evolution – become segment specific to fully unlock BONESUPPORT's potential

Foot & Ankle | Trauma | Arthroplasty | Spine

BONESUPPORT Revenue 2019-2025

- LTM by quarter by segment SEK m



Bone infections are among the most complex, costly and consequential complications in orthopaedics with increasing incidence[1]

FOOT & ANKLE

1 in 5

diabetic foot infections[2,3]

progresses to bone infection — the leading cause of non-traumatic amputation

TRAUMA

>30%

Fracture related infection (FRI) incidence

after open fracture fixation[4]

ARTHROPLASTY

$150–200K

in treatment cost per PJI patient[5]

with 5-year mortality rivalling many cancers[6]

"Telling an orthopedic patient that they have an infection is like giving them a diagnosis of cancer"
- Late Richard Rothman, MD, PhD (1999)[7]

1) Hackett DJ Jr et al. The Economic Significance of Orthopedic Infections. J Am Acad Orthop Surg. 2015;23(Suppl):S1–S7.
2) Lipsky BA et al. 2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections. Diabetes Care. 2012;35(10):2864–2869.
3) Lavery LA et al. Risk factors for foot infections in individuals with diabetes. Diabetes Care. 2006;29(6):1288–1293
4) Metsemakers WJ et al. Fracture-related infections: Current status and perspectives from the International Society of Antimicrobial Chemotherapy. Int J Antimicrob Agents. 2020;56(2):106024.
5) Kapadia BH et al. Periprosthetic joint infection. Lancet. 2016;387(10016):386–394.
8) Kurtz SM, Lau EC, Son MS, Chang ET, Zimmerli W, Parvizi J. Are We Winning or Losing the Battle With Periprosthetic Joint Infection: Trends in Periprosthetic Joint Infection and Mortality Risk for the Medicare Population. J Arthroplasty. 2018;33(10):3238–3245.
7) Parvizi J, Gehrke T. International Consensus Meeting 2025: Did We Need Another One? The Journal of Arthroplasty. 2025;41:S4–S5

Note: Data presented for Capital Markets Day purposes. Epidemiology figures based on published US estimates. All figures indicative.

The unmet clinical needs share the same failure pattern across three indications

Bone defect + infection + no single solution: the result is multi-stage care, high recurrence and avoidable cost

FOOT & ANKLE

Diabetic foot osteomyelitis

Without CERAMENT G/V: prolonged IV antibiotics, recurrence at 3 months, second debridement, amputation at 6 months.

94%

limb salvage rate with CERAMENT G vs amputation as standard outcome[1]

Care pathway cost[4]

~~$500K–700K lifetime~~ → ~$35K–50K

Saving: $80K–120K per patient

Same root cause across all three — bone defect, infection, no combined solution

TRAUMA

Fracture related infections

Without CERAMENT G/V: hardware removal, PMMA beads, 4 surgical episodes over 18 months, non-union risk remains

96%

bony union at 12 months, no infection vs 4 surgeries and chronic pain[2]

Care pathway cost[5]

~~$180K–250K~~ → ~$35K–50K

Saving: >$150K per patient

Standard of care consistently delivers multi-stage treatment, high recurrence, and avoidable cost

ARTHROPLASTY

Periprosthetic joint infections

Without CERAMENT G/V: two-stage revision, 10 weeks non-weight-bearing, reinfection within 18 months, long-term care.

100%

infection eradication, single-stage[3]

Care pathway cost[6,7]

~~$150K–200K~~ → ~$45K–65K

Saving: $90K–140K per patient

CERAMENT addresses all three simultaneously — in a single surgical episode

1) Vasukutty et al. The Diabetic Foot Journal. 2022
2) Henry JA et al. Cureus. 2023;15(5):e39103
3) Khakzad T, Meller S, Hardt S, Leopold VJ, Mödl L, Perka C, Mueller M, Winkler T. Cementless one-stage hip revision arthroplasty with an injectable antibiotic bone graft substitute: a pilot study. Bone & Joint Open. 2025;6(9):1146–1155. doi:10.1302/2633-1462.69.BJO-2025-0086.R1
4) MacKenzie EJ, Jones AS, Bosse MJ et al. Health-care costs associated with amputation or reconstruction of a limb-threatening injury. J Bone Joint Surg Am. 2007;89(8):1685–1692. doi:10.2106/JBJS.F.01350
5) Metsemakers WJ et al. Costs of fracture-related infection: the impact on direct hospital costs and healthcare utilisation. Eur J Trauma Emerg Surg. 2024;50(4):1701–1707. doi:10.1007/s00068-024-02497-9
6) Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. J Arthroplasty. 2012;27(8 Suppl):61–65. doi:10.1016/j.arth.2012.02.022
7) Kapadia BH et al. Periprosthetic joint infection. Lancet. 2016;387(10016):386–394. doi:10.1016/S0140-6736(14)61798-0

Note: Data presented for Capital Markets Day purposes. Epidemiology figures based on published US estimates. All figures indicative and illustrative.

Three disease cascades — tens of millions of patients — each an inevitable pathway to bone infection

These are not rare events. They are the predictable downstream consequences of conditions affecting tens of millions of patients globally.

FOOT & ANKLE

38M

Americans with type 2 diabetes[1]. Diabetes is a global epidemic

Diabetic foot ulcer

1 in 4 diabetics affected in their lifetime[2]

Amputation

20% of DFUs progress — #1 cause of non-traumatic amputation[3]

Tens of millions of patients at the top of each cascade — a substantial, growing, underserved population

TRAUMA

54M

Americans with osteoporosis or low bone mass[4]
Ageing population with fragile bones

Open / high-energy fracture

2M+ fragility fractures annually in the US[5]

Fracture related infection

Up to 30% of Gustilo III fractures develop infection[6]

Each cascade is driven by conditions (diabetes, osteoporosis, osteoarthritis) that are rising globally

ARTHROPLASTY

2M

hip & knee replacements per year in the US[7]

Revision surgery & bone loss

PJI is a top-3 cause of arthroplasty revision[8]

Periprosthetic joint infection

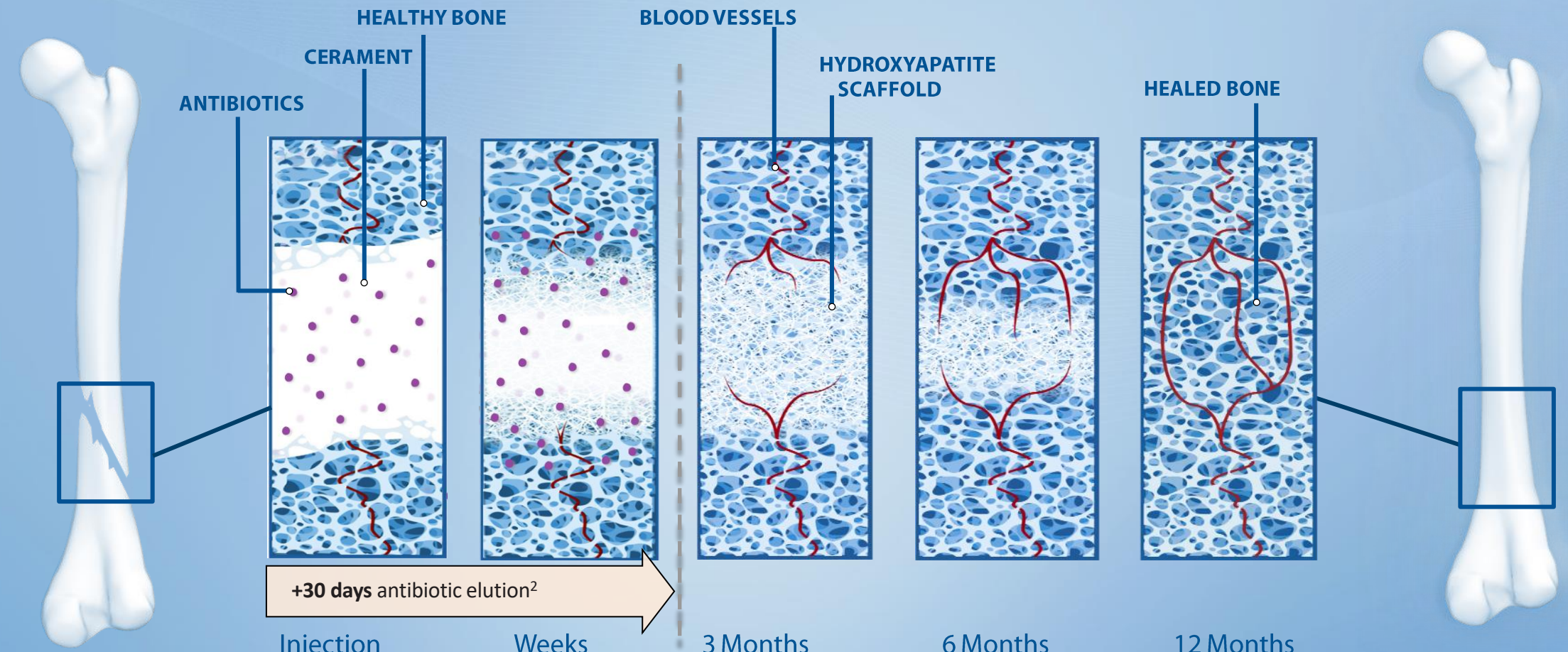
1–2% of all arthroplasties — 5-yr mortality rivals cancer[9]

The bottom of every cascade is the same structural treatment failure — and the same unmet need

1) Centers for Disease Control and Prevention. National Diabetes Statistics Report. 2024. Available at: cdc.gov/diabetes/php/data-research
2) Armstrong DG et al. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376(24):2367–2375. doi:10.1056/NEJMra1615439
3) Brownrigg JRW et al. Current Status and Principles for the Treatment and Prevention of Diabetic Foot Ulcers in the Cardiovascular Patient Population: A Scientific Statement From the American Heart Association. Circulation. 2023;148(24):1958–1974. doi:10.1161/CIR.0000000000001192
4) Wright NC et al. The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. J Bone Miner Res. 2014;29(11):2520–2526. doi:10.1002/jbmr.2269
5) Bone Health and Osteoporosis Foundation (BHOF). Osteoporosis Fast Facts. Available at: bonehealthandosteoporosis.org
6) Metsemakers WJ et al. Fracture-related infections: current status and perspectives from the International Society of Antimicrobial Chemotherapy. Int J Antimicrob Agents. 2020;56(2):106024. doi:10.1016/j.ijantimicag.2020.106024
7) Shichman I et al. Projections and epidemiology of primary hip and knee arthroplasty in Medicare patients to 2040–2060. JBJS Open Access. 2023;8(1):e22.00112. doi:10.2106/JBJS.OA.22.00112
8) Aftab MHS et al. Periprosthetic joint infection: a multifaceted burden undermining arthroplasty success. Orthopedic Reviews. 2025;17. doi:10.52965/001c.138205
9) Kurtz SM, Lau EC, Son MS, Chang ET, Zimmerli W, Parvizi J. Are we winning or losing the battle with periprosthetic joint infection: trends in periprosthetic joint infection and mortality risk for the Medicare population. J Arthroplasty. 2018;33(10):3238–3245. doi:10.1016/j.arth.2018.05.042

Note: Data presented for Capital Markets Day purposes. Epidemiology figures based on published US estimates. All figures indicative.

CERAMENT® - Promotes and protects natural healing



CERAMENT Bi-phasic mode of action

- CERAMENT is injectable, upon implantation, completely filling voids and cavities
- Antibiotic elution protects the healing during the most critical phase
- CERAMENT has transformed into a porous scaffold of micron-sized hydroxyapatite
- Bone-forming cells (Osteoblasts) migrate onto the scaffold which is resorbed as bone is formed

CERAMENT is fully resorbed and replaced with healthy natural bone

CERAMENT heals fractures as effectively as autograft, eliminating the need for bone transplants[1]

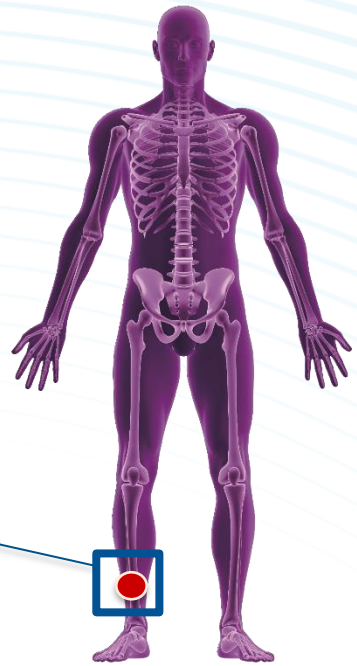
[1] Autologous Iliac Bone Graft Compared with Biphasic Hydroxyapatite and Calcium Sulfate Cement for the treatment of Bone Defects in Tibial Plateau Fractures. J Bone Joint Surg Am. 2019;00:1-15

[2] CERAMENT G (Gentamicin) and CERAMENT V (Vancomycin)

CERAMENT® versus systemic antibiotics

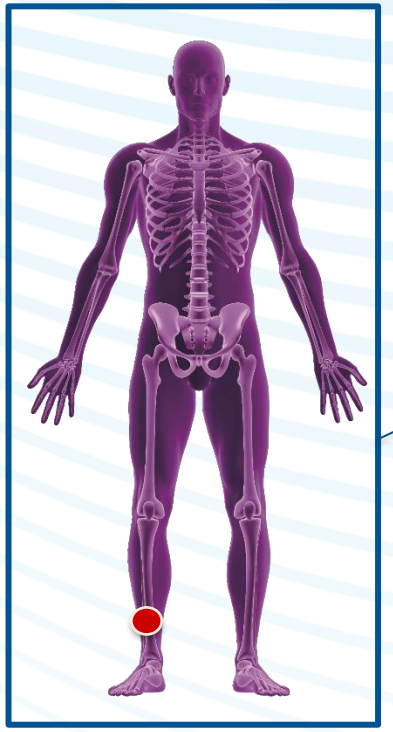
Local concentration:
90 mg/l

System concentration:
Below detection limits[1,2]



Site of infection

Antibiotic exposure



System concentration:
15-20 mg/l[3]

CERAMENT G and V:

- One procedure treatment
- High local concentration with no risk of systemic toxicity
- Predictable local elution up to 30 days over Minimal Inhibitory Concentration (MIC)
- Reduced risk of bacterial resistance

Systemic antibiotics :

- 4-12 months intravenous or oral systemic antibiotic treatment
- Common side effects
  - Nephrotoxicity and ototoxixity
  - Diarrhea and nausea.
  - Pseudomembranesous colitis
  - Risk of Bacterial resistance development

[1] Stravinskas M, Vancomycin elution from a biphasic ceramic bone substitute Bone Joint Res. 2019 Feb; 8(2): 49–54;
[2] McNally MA, Lidgren L. 'Pharmacokinetics of gentamicin eluted from a regenerating bone graft substitute - In vitro and clinical release studies. *Bone Joint Res* 2016;5:427–435.
[3] Fraimow. 'Systemic Antimicrobial Therapy in Osteomyelitis.' Semin Plast Surg. 2009; 23(2): 90–99. 4. Spellberg & Lipsky. 'Systemic Antibiotic Therapy for Chronic Osteomyelitis in Adults.' Clinical Infectious Diseases 2012;54(3):393–407.

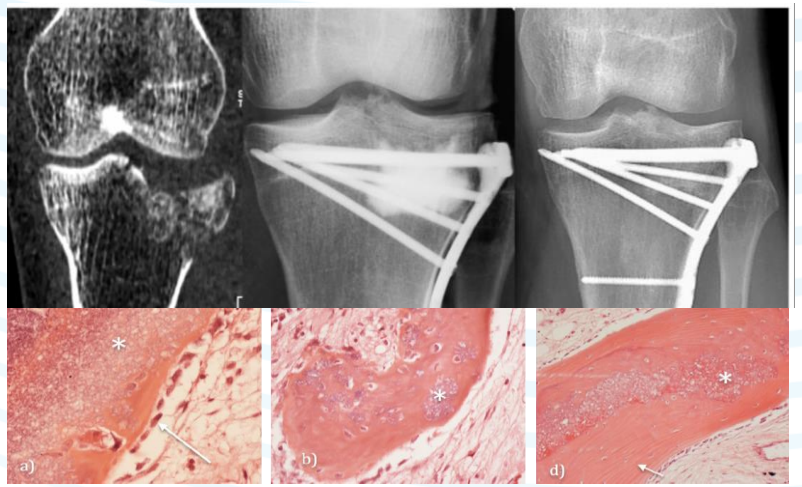
CERAMENT® G unique composition provides antibiotic elution and bone remodeling

- **CERAMENT G**
  - Purpose engineered ceramic bio-composite
  - Same mineral composition as natural bone
  - Mimics natural healing
  - Resorbs at pace of bone healing
- Full bone remodeling in 6-12 months
- Gentamicin at high local concentration levels significantly above minimal inhibitory concentration (MIC), with no shown systemic side effect

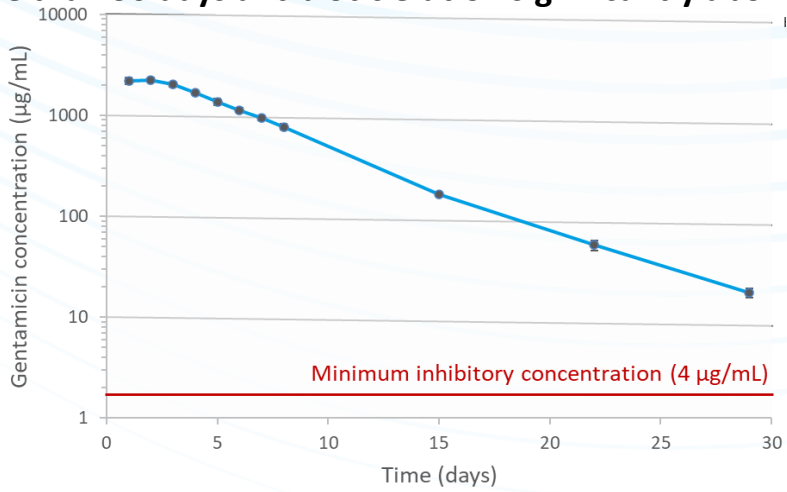
Clinical evidence (peer-reviewed, published clinical studies) **showing:**

- **96% infection elimination**[1]
- **94% Diabetic foot limb salvage rate**[2]
- **74% reduction in open fracture trauma amputation rate**[3]

Clinically proven bone remodeling [4,5]



More than 30 days antibiotic elution significantly above MIC



[1] McNally et al. Single-stage treatment of chronic osteomyelitis with a new absorbable, gentamicin-loaded, calcium sulphate, Bone Joint J 2016;98-B:1289–96.
[2] NL Vasukutty et al. Limb salvage surgery in diabetic foot infection: encouraging early results with a local antibiotic carrier The Diabetic Foot Journal Vol 25 No 2 2022
[3] Henry et al. Long-Term Follow-Up of Open Gustilo-Anderson IIIB Fractures Treated With an Adjuvant Local Antibiotic Hydroxyapatite Bio-Composite, Cureus 15(5): e39103. DOI 10.7759/cureus.39103
[4] Hofmann A, Gorbulev S, Guehring T, et al. Autologous Iliac Bone Graft Compared with Biphasic HA and Calcium Sulfate Cement for the Treatment of Bone Defects in Tibial Plateau Fractures: A Prospective, Randomized,. *J Bone Joint Surg Am*. 2020;102(3):179-193.
[5] J Ferguson et al. A comparison of clinical and radiological outcomes between two different biodegradable local antibiotic carriers used in the single-stage surgical management of long bone osteomyelitis, Journal of Bone and Joint Infection.2019; 4(2): 76-84

Current standard of care is largely based on organic bone grafts and systemic antibiotics – all with respective gaps

Three treatment categories dominate the landscape — each addresses part of the challenge, none addresses all of it

01 AUTOGRAFT[2]

Patient's own bone

WHAT IT DOES WELL

- ✓ Biological bone healing
- ✓ Established surgical technique
- ✓ Histocompatibility

WHERE IT FALLS SHORT

- ✗ No infection control
- ✗ Supply limits
- ✗ Infection risk
- ✗ Scar / pain[3]

THE GAP

Heals the void — but leaves infection untreated

02 ALLOGRAFT[4]

Donated bone transplant

WHAT IT DOES WELL

- ✓ Biological bone healing
- ✓ Established surgical technique

WHERE IT FALLS SHORT

- ✗ No infection control
- ✗ Disease risk
- ✗ Limited success rate[5]
- ✗ Variable quality

03 SYSTEMIC ANTIBIOTICS

Intravenous · Oral

WHAT IT DOES WELL

- ✓ Broad spectrum coverage
- ✓ Well-established protocols
- ✓ Non-surgical administration

WHERE IT FALLS SHORT

- ✗ Cannot reach site at therapeutic conc.
- ✗ Long treatment; toxicity risk
- ✗ Compliance
- ✗ Antibiotic stewardship

THE GAP

Fights infection — but can't reach the site or heal the bone

CERAMENT G/V[1]

Designed to close all gaps simultaneously

- **Bone regeneration**

  Resorbs at the pace of natural healing — full bone remodelling in 6–12 months

- **Local antibiotic delivery**

  Sustained antibiotic elution >30 days, well above MIC — with no systemic toxicity

[1] Nilsson M, Wang JS, Wielanek L, Tanner KE, Lidgren L: Biodegradation and biocompatability of a calcium sulphatehydroxyapatite bone substitute. Journal of Bone and Joint Surgery-British Volume 86B:120-125, 2004
[2] Myerhoff et al. Autogenous bone graft: Donor sites and techniques. J. Bone Joint Surg Am. 2011; 93: 2227-36
[3] Dmitriou et al. Complications following autologous bone graft harvesting from the iliac crest and using the RIA: A systematic review. Injury, 2011 (42) S3-S15 3. Silber et al. Donor site morbidity after anterior iliac crest bone harvest for single-level anterior cervical discectomy and fusion. Spine 2003;28(2):134–9
[4] http://www.surgeryencyclopedia.com/A-Ce/Bone-Grafting.html
[5] Zheng et al. Mechanism of bone allograft failure. J Bone Joint Surg Br 2002 vol. 84-B no. SUPP III 234

Within synthetic bone grafts there are multiple opportunities, combinations and approaches – all categories available for decades

	$CaSO_4$	Biphasic	$CaPO_4$	Bioglass	PMMA
Biodegradable	☑ Rapid (weeks)	☑ Controlled	☑ Slow / variable	☑ Very slow	☒ None
Intrinsic antimicrobial	☒	☒	☒	☑	☒
Antibiotic carriage	☑	☑	☑ (+BNPs)	☒	☑
Drug elution	Complete, rapid	More sustained	Sustained	N/A	Burst, incomplete
Mechanical strength	☑	☑ ☑	☑ ☑ Brittle	☑ Brittle	☑☑☑ (non-integrating)
Risk of leakage	High	Lower	Low	Very low	None
Bone regeneration	☑	☑ ☑ Conductive	☑ ☑ Conductive	☑ Bioactive	☒
Typical use	Dead space Short, high dose abx	Infection, bone regeneration	Bone defects and infection	Cavitary infection	Staged surgery

Source: Table presented by Matt Scarborough at Oxford Bone Infection Conference April 13, 2026

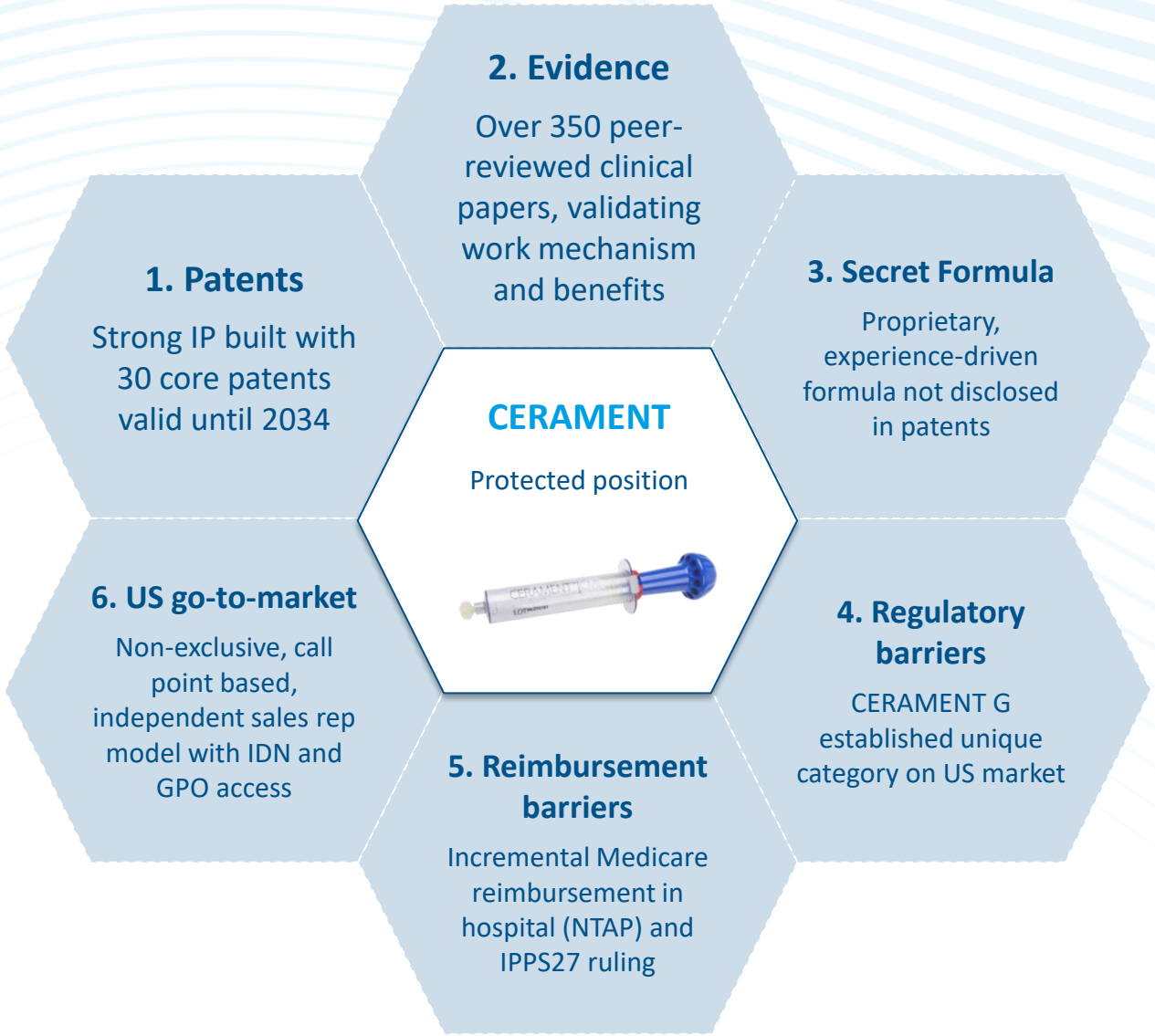
Calcium sulphat – Very quick resorbtion[1,2]
- No or very limited bone regrowth[3]
- Risk for recurring fractures in incidence of 10%[5]
- Unpredictable antibiotic elution[1,2]
- Risk for hypercalcemia[1]

Hydroxyapatite (Calcium phosphate) - very slow resorption[3].
- Very slow or limited bone regrowth. X-rays after 4 years shows largely unchanged "block" of material in bone void
- Sensitive to ambient temperature
- Unpredictable antibiotic elution[1] – Only surface release. Increased risk of returning infections and multi resistance development
- Limited In vivo studies available

PMMA ("Bone cement") – No resorption
- No bone regrowth
- Unpredictable antibiotic elution with high variability[4]
- High risk for recurring infections
- Requires multiple surgeries (bead-string)

[1] J Ferguson et al. Ceramic Biocomposites as Biodegradable Antibiotic Carriers in the Treatment of Bone Infections, JBJI; 2017; 2(1): 38-51.
[2] G. E Maale, MD et al Local Elution Profiles of a Highly Purified Calcium Sulfate Pellet at Physiologic PH, Loaded with Vancomycin and Tobramycin, in the Treatment of Infected Total Joints Abstract at Western Orthopaedic Association 75th Annual Meeting Honolulu, Hawaii2011
[3] Malin Nilsson et al. The composite of hydroxyapatite and calcium sulphate: a review of preclinical evaluation and clinical applications Expert Rev. Med. Devices 10(5), 675–684 (2013)
[4] K Anagnostakos et al, Elution of gentamicin and vancomycin from polymethylmethacrylate beads and hip spacers in vivo Acta Orthop. 2009 Apr 29; 80(2): 193–197
[5] Chang W, Colangeli M, Colangeli S, et al. Adult osteomyelitis: debridement versus, debridement plus Osteoset T pellets. Acta Orthop Belg. 2007;73:238–243. Ferguson JY, Dudareva M, Riley ND, Stubbs D, Atkins BL, McNally MA. The use of a biodegradable antibiotic-loaded calcium sulphate carrier containing tobramycin for the treatment of chronic osteomyelitis: a series of 195 cases. Bone Joint Lett J. 2014;96-B:829–836

The CERAMENT moat consists of six interlocking barriers that are expensive, slow and complex to replicate



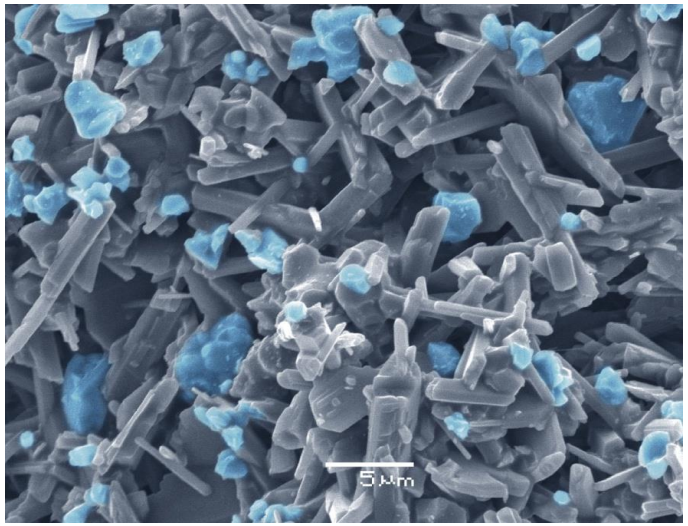
- Each barrier is both **distinct and interlocking** with CERAMENT protected at the center
- The **barriers compound** —each year that passes makes them harder to replicate
- The **barriers aren't equal in durability** - patents and NTAPs expire while evidence, GTM model and regulatory barriers have become stronger over time

Moat 3: Secret formula – why is difficult to replicate CERAMENT?

By combining advanced material science, years of bone biology research and manufacturing experiences and over 350 validating clinical studies, Bonesupport has developed a proprietary synthetic bone graft material that mimics natural healing, and which functions to manage bone infections

The right components, formula and modifications

CERAMENT comprises of modified variants of hydroxyapatite and calcium sulphate. The formulation is engineered using a patented process and in house know-how to ensure injectability, consistent setting times, biocompatibility, osteoconductivity and full reproducibility. The ratio and modifications of components in CERAMENT is the result of years of research



Scanning Electron Microscope (SEM) photo of CERAMENT BVF showing the actual physical microstructure of the material

…enabling…

The right elution and bone remodeling

Consistent, reliable and therapeutic antibiotic elution is enabled by the composition and properties of CERAMENT. As CERAMENT resorbs, the antibiotic molecules are released. This mechanism of action is consistent and reproducible no matter application form of CERAMENT.
Material resorption rates matches the rate of natural bone ingrowth, enabling effective bone remodelling.

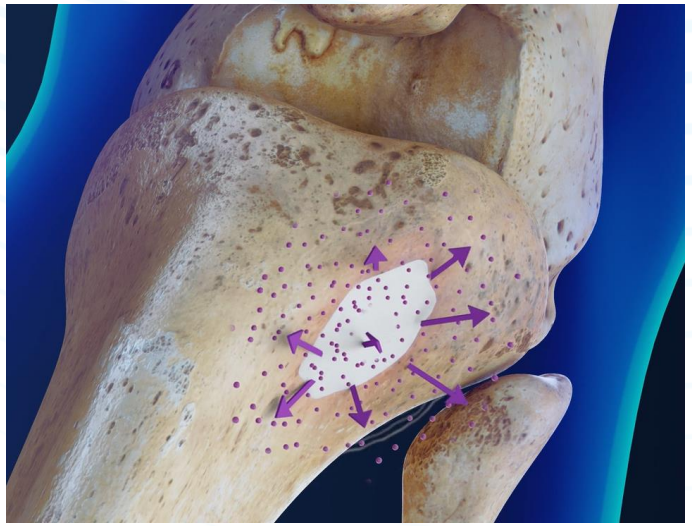


Illustration of CERAMENT injected into a bone void, showing elution of antibiotic as CERAMENT is absorbed

Moat 4: Regulatory barriers

- The FDA product categories
  - Synthetic bone void fillers
  - Resorbable calcium salt bone void filler

  ….both fall under the classification **21 CFR 888.3045**.

- The category **holds about 400 approved products**, with on average 10-20 new approvals per year, using a 510(k) to match the **General Controls** for the category

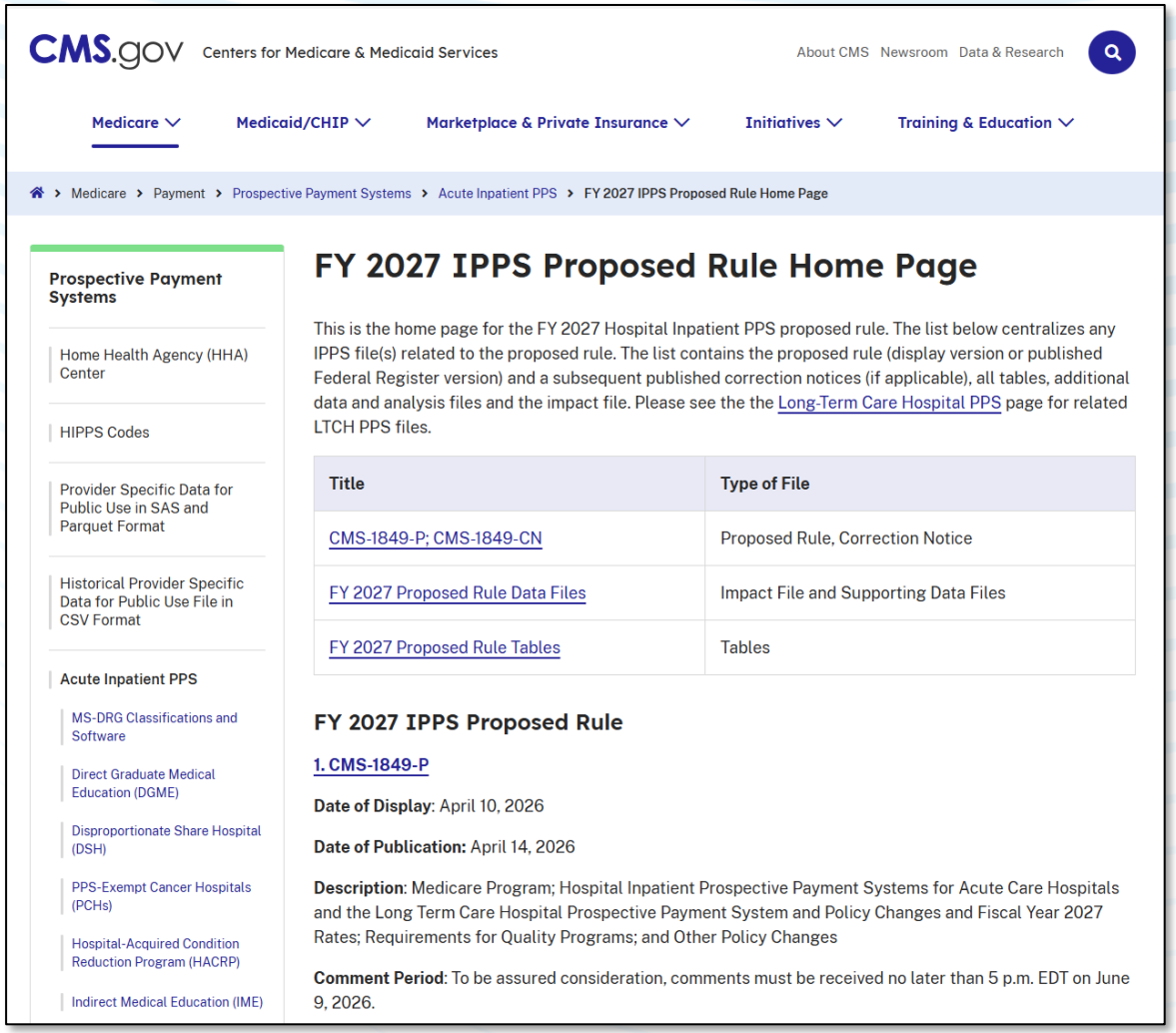
- The product category “Resorbable calcium salt bone void filler containing a single approved aminoglycoside antibacterial” with classification **21 CFR 888.3046** was introduced in 2022 following FDA approval of CERAMENT G.

- The category **holds 1 approved product,** and can only be entered through matching of all of the **Special Controls**

- CERAMENT G is the first ever DeNovo market authorization for a combination device
- The approval of CERAMENT G is built on 17 000 data points, which outcomes has defined the tailored Special Controls:
  - Clinical data on new bone formation and product resorption in clinically relevant time frame
  - Clinical data on antibiotic serum levels
  - Special requirements on product, drug substance and drug constituent components
  - Performance data and stability data on every batch
  - Batch elution kinetics studies matching clinical performance testing studies
  - Additional Special Controls for manufacturing

Moat 5: Reimbursement – The CMS FY 27 IPPS proposed rule increases payments to support the standard use of CERAMENT G

- The proposed DRG reassignment involves cases of **fracture-related infections, diabetic foot osteomyelitis and periprosthetic joint infections**.
- A **unique code for CERAMENT G** will trigger reassignment to higher payment rates, i.e., no other bone void filler will qualify[1].
- Fee schedules of other public insurers as well as commercial insurers are **expected to be influenced** as many utilize Medicare-like reimbursement structures based on the Medicare Severity Diagnosis Related Group (MS-DRG) system.



Picture from CMS.gov on FY 2027 IPPS Proposed Rule Home Page (accessed May 17, 2026)

[1] BONESUPPORT will request CMS for a unique code for CERAMENT V to also trigger reassignment.

Payments based on CMS principles are projected to increase USD 5,000 to 11,000 on average as determined by the Diagnosis Related Group (DRG)

- From October 1, 2026, the US Centers for Medicare and Medicaid Services (CMS) proposes to increase reimbursements for bone infection surgeries where CERAMENT G is used.
- Cases where CERAMENT G is used are to be reassigned to higher DRGs, i.e., higher payment rates. This applies to inpatient surgeries.
- The final ruling is expected by August 1, 2026.

For this DRG set, the case mix adjusted average payment increase with the use of CERAMENT G would be ~$7,900.

Example: The common DRG for fracture-related infection (FRI) cases

DRG	DRG TITLE	FY2026 Final Payment	FY2027 Proposed Payment*	Change for FY2027 (from October 1, 2026)
492	LOWER EXTREMITY AND HUMERUS PROCEDURES EXCEPT HIP, FOOT, FEMUR WITH MCC **OR INSERTION OF ANTIBIOTIC-ELUTING BONE VOID FILLER**	$ 26,717.32	$ 27,705.27	**All CERAMENT G cases will be assigned here**
493	LOWER EXTREMITY AND HUMERUS PROCEDURES EXCEPT HIP, FOOT, FEMUR WITH CC	$ 18,454.57	$ 19,245.53	Cases with CERAMENT G will no longer be assigned here.
494	LOWER EXTREMITY AND HUMERUS PROCEDURES EXCEPT HIP, FOOT, FEMUR WITHOUT CC/MCC	$ 14,600.80	$ 15,305.67	Cases with CERAMENT G will no longer be assigned here.

Note: Changes to DRG title are in bold. Antibiotic-eluting bone void filler refers to CERAMENT G.

[1)] Proposed payments are updated annually and depend on the reported cost of treating a case in each DRG

Capital Markets Day 2026

A Segment Based Approach

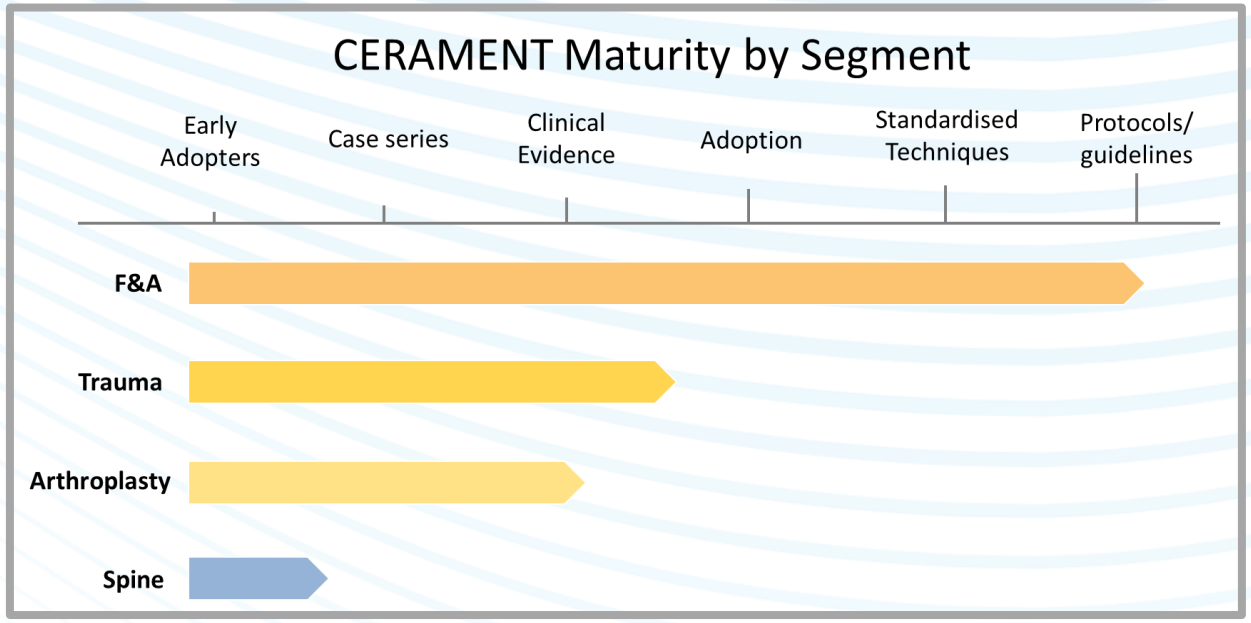
Market Segments | Value Propositions | Market Data & Research

Annelie Aava Vikner, EVP Marketing

The CERAMENT Segment Strategy – Applied

One Platform. Scalable Growth. Multiple Segments.

- Targeting segment & sub segments with high unmet-need & value
- Same core technology → Bone healing + Infection control → Multiple applications
- Proven superior clinical and economic outcomes, and scale through standardized procedures and segment-specific adoption to maximize value
- Expanding from surgical treatment into prevention across large, adjacent markets



Segment-Specific Value Creation

Clinical and Economic Value with CERAMENT

Foot & Ankle (DFO)

Strategic lever:
Emerging leadership
Strongest evidence & clear value story

Clinical value
Limb salvage

Infection eradication (90–96%)

Preserved mobility / QoL /Survival impact

Economic value
Avoid amputation → lifetime cost reduction

Fewer reoperations & complications

Reduced long-term care burden

Trauma

Strategic lever:
Scaling & Expansion
Volume driver: underpenetrated, strong prevention story

Clinical value
Fracture healing + bone regeneration

Infection **prevention + eradication**

High limb salvage and functional recovery

Economic value
Prevents fracture-related infection (very high system cost)

Enables single-stage treatment → fewer OR events

Faster recovery → reduced length of stay

Arthroplasty

Strategic lever:
Strong growth driver
High economic impact per case

Clinical value
Infection control in PJI (critical driver)

Enables single-stage revision

Restores function and implant stability

Economic value
Avoids costly multi-stage revisions

Reduces implant failure and reoperations

High DRG leverage / premium procedures

Spine

Strategic lever:
Future Platform Expansion
Long-term growth + adjacency expansion

Clinical value
Support fusion and bone formation

Infection control

Economic value
Reduces revision surgery

Lower complication-related costs

Examples of segment specific CERAMENT surgical procedures and application techniques

Diabetic Foot Osteomyelitis (DFO)
Fore -, Mid-, Hind-foot

Limb salvage with preserved mobility and function

Transmetatarsal Amputation Procedure,
Dr. N Vasakutty
Silo Technique Professor Pillai

Trauma - Open/Closed Fractures, Fracture Related Infections related to previous Trauma, Non-Union

Restore Bone. Control Infection. Preserve the Limb

Tibial Osteomyelitis procedure
Professor McNally
Dr. S Sandilands Tibia Surgical
Procedure for IM Nailing with 2-CAN

CERAMENT BVF Injected Under Fluoroscopy - Tibial Plateau CERTIFY

Arthroplasty
PJI & Revision Arthroplasty

Eradicate/Prevent Infection.
Restore the Joint. Return to Life

CeraHip Single stage procedure PJI,
Dr Meller

Spine
Posterior Open surgery

Achieve Fusion. Prevent Complications. Restore Stability

Scoliosis Fusion
CERAMENT BVF

Market segments presented at Capital Markets Day Nov 2023

Based on 2022 market data. Market share based on 2023 sales

TAM communicated at CMD 2023

Revision rate: 4,7%

Main segment	**Trauma 226 k**	**Revision Arth. 71 k**	**F&A, Diabetic Foot Issues 67 k**	**Tumor/ Bone lesions 20 k**	**Tot: 384k**	**Spine 750 k**
Subsegments	Open/ Closed 147 / 79					Thoracic/Cervical/ Lumbal 75 k/ 113 k/ 562k
Infection incidence	15-52% / 2%	10%-25%		6%		2% - 6%
Infected procedure (A_x)	27 k/ 1 k		18 k	1 k	**Tot: 54 k**	38 k
Prevention (A_x)	52 k		23 k	1 k	**94 k**	280 k
Clinical evidence (Published)	y strong	Coming (2025)	Several, Very Strong	Good		
Penetration US (Market Shares)	**Very low <2% Approval for CERAMENT G only in March 2024**	**Low <3% Just about to start. No clinical studies published yet**	**Low 5-7% Strong US advocates, developing techniques/ applications**	**Low 5-7%**		
Market share trend	Very strong (Just started)	Very strong (Just started)	Very strong	Strong		

From Capital Markets Day 2023

Out of 1 500 k spine procedures/ year, 750 use bone grafts

"57% of Orthopedic Spinal Surgeons are highly concerned about infection"

Bonesupport market survey 2024

Major revisions to Market Segment Model, US

Up- revision of relevant procedure in Revision Arthroplasty

- Previous Market Segment Model (Capital Markets Day 2023) underestimated number of procedures, as only very challenging cases with large bone loss was accounted for in TAM
- Number of revisions has grown very strongly over the last 6-10 years due to arthroplasty procedures being done earlier on patients
- Infection rates has grown significantly, from 33,9% in 2017 to 51,8% in knee, as reason for revision[1]. Infection is now ranked the most common reason for revision[1]
- Access to reliable data sources confirming large volume of arthroplasty revisions (revision procedures have increased around 50% between 2019 to 2023)
- Market segment “Revision arthroplasty” was estimated at 71 k cases p.a. in 2022, and is now (2025) estimated at 120 k cases[2] ,

Use of local antibiotics to treat and prevent infection in common orthopedic procedures

- Previous Market Segment Model (Capital Markets Day 2023) had estimations on use of local antibiotics triangulated from various sources. As “off-label” alternative, the data and details on use of local antibiotics was scarce
- Original estimation on local antibiotics use was based on off-label mixing of antibiotics and synthetic bone grafts, and did not sufficiently take into accounts the widespread use of mixing antibiotics into autograft or allograft, or the use of bone graft in combination with antibiotic powder
- Publications on use of local antibiotics[3,4] have followed in the footstep of the pivotal VANC-study by the influential METRC group, showing local antibiotic use in over 30% of trauma cases (38,8% in Open Trauma and 26,6% in Closed Trauma)
- Extensive market research has been commissioned by BONESUPPORT with findings showing significantly higher use of local antibiotics than previous assumed (mostly related to the use of antibiotic powder and PMMA+antibiotics)

Removal of Tumor & Lesions from "key segments"

- A small (20 k procedures) market segment with flat development. The segment has a loyal customer base for CERAMENT, but it is not a core focus for the future development of the business

1. AJRR 2025 Annual Report. Rosemont, IL: American Academy of Orthopaedic Surgeons; 2025
2. 32 k is an adjustment based on more accurate data and the remaining difference is related to strong market growth between 2022-2025
3. Marchand LS, Sprague S, O’Hara NN, Li CS, O’Toole RV, Joshi M, et al.; PREP-IT Investigators.Local administration of vancomycin powder in orthopaedic fracture surgery: current practice and trends.OTA International. 2023;6(1):e223
4. O’Toole RV, Joshi M, Carlini AR, Murray CK, Allen LE, Scharfstein DO, et al.; METRC.Effect of intrawound vancomycin powder in operatively treated fractures: a randomized clinical trial.JAMA Surgery. 2021;156(6):e207259

Market segment US 2025

Serviceable Addressable Market (SAM)

Definition: Procedures / indications where bone grafts (organic or synthetic) are used[1] within defined focus

	Extremities key segments				Spinal	
Main Market segment	**Foot & Ankle, Diabetic Foot 80k**	**Trauma 240 k**	**Revision Arthroplasty 120 k**	**Total (incl Other) : 460k**	**Spine 770 k**	
Infection incidence	20% - 30%	2% -35%[1]	35% - 40%[2]	**Total est. (incl Other) 115 k**	2%- 6%	**Total est.: 30 k**
Use of local antibiotics	30% - 50%[5]	30% -35%[3]	40% - 50%[4,5]	**Total est. (incl Other) 190 k**	30%-40%[4,5]	**Total est.: 250 k**
CERAMENT Market Penetration (CERAMENT Market Share)	**9-11%** Early market entry focus, due to available clinical evidence	**2-4 %** Approval for CERAMENT G only since March 2024.	**3-5 %** Recent focus following arrival of favorable clinical evidence		**< 1 %** Market launch in Dec 2025 Only CBVF	

1. Open trauma represents app 65% of the procedures (and Closed trauma 35%) of the procedures requiring bone grafts. The infection incidence with closed trauma in general is 1-2%. For the Closed trauma severe enough to require bone grafts, the infection incidence is 2-6%, dependent on tissue injury and patient comorbidities. Open trauma infection incidence matches the severity on GA categorization, and ranges from 5% to over 40%, depending on patient specific parameters.
2. AJRR 2025 Annual Report. Rosemont, IL: American Academy of Orthopaedic Surgeons; 2025. In total 69800 infected revisions are made annually. In the model above this has been converted to app 63000 infected procedures requiring bone grafts, eliminating low grade infection solved with only systemic antibiotics.
3. Marchand LS, Sprague S, O'Hara NN, Li CS, O'Toole RV, Joshi M, et al.; PREP-IT Investigators. Local administration of vancomycin powder in orthopaedic fracture surgery: current practice and trends. OTA International. 2023;6(1):e223
4. Bonesupport commissioned research
5. Bonesupport estimate + Various industry reports

Preceding Market segment US 2025

Definition: From which indications and etiology does the Serviceable Addressable Market come from. Part of the Preceding Market Segment can become a potential for CERAMENT in the future

Preceding Market Segment

Total Addressable Market (TAM)

	Diabetic foot ulcers: 1 600 k p.a	Surgical Trauma procedures[1]: 1 200 k p.a	Primary arthroplasty procedures[2]: 2 000 k p.a	Spine 1500 k
	Infection incidence with diabetic foot 50-60% leading to bone infection in 30% of cases.	Whereof low energy trauma for osteoporotic patients: app 420 k procedures p.a.	Use of local antibiotic in powder formulation or as part of PMMA application	
Use of local antibiotics	No data available	No data available	Up to 40%[3]	No data available

Serviceable Addressable Market (SAM)

	Foot & Ankle, Diabetic Foot 80k	Trauma 240 k	Revision Arthroplasty 120 k	Total (incl Other) : 460k	Spine procedures requiring bone grafts 770 k	
Main Market segment						
Infection incidence	20% - 30%	2% -35%	35% - 40%	Total est.(incl Other) 115 k	2%- 6%	App: 30 k
Use of local antibiotics	30% - 50%	30% -35%	40% - 50%	Total est. (incl Other) 190 k	30%-40%[4,5]	App: 250 k
CERAMENT Market Penetration TASM	**9-11%**	**2-4 %**	**3-5 %**			

1. Jarman et al. The National Burden of Orthopedic Injury: Cross-Sectional Estimates for Trauma System Planning and Optimization. Journal of Surgical Research. 2020 May
2. Jones et al. Trends in Medicare Arthroplasty Procedure Volume: Projecting From 2025 to 2040. Journal of Arthroplasty. 2025
3. Bonesupport commissioned research
4. Bonesupport commissioned research
5. Bonesupport estimate + Various industry reports

Market Dynamics, US

Market segment
Procedure volume
2025

F&A, Diabetic Foot Issues
80 k

Estimated US market procedure volume growth rate (2025-2030): +5,5%

- High infection rate due to prevalence of infected diabetic ulcers. Use of bone grafts and effective infection management is significantly under penetrated.
- Regular foot and ankle surgery makes up 50% of segment
- Full potential of Diabetic foot infection is estimated at 100 k procedure / year
- CERAMENT is used for bone repair, avoiding amputation and minimizing amputation

Trauma
240 k

Estimated US market procedure volume growth rate (2025-2030): +1.5%

- Closed trauma is 65% of procedure volume. Open trauma is 35% of procedure volume
- Bone grafts used shortly after acute phase and in reconstructive phase
- The larger the injury and presence of comorbidities, the higher risk of infection
- Segment growth drivers are: ageing population with higher prevalence of osteoporosis, and a slightly increasing trend in use of bone grafts
- CERAMENT is used in conjunction with hardware implants. Many different applications relevant.

Revision Arth.
120 k

Estimated US market procedure volume growth rate (2025-2030): +6.0%

- Fast growing segment linked to demographics and primary arthroplasties being done at younger ages and infection related revisions
- Fastest growing segment is prevention and management of infection with patients undergoing revisions. Infection is the most common reason for needing revision
- CERAMENT is used to repair bone injuries/ loss caused by the revision or debridement following the revision.
- CERAMENT is used in combination with a replaced prothesis or in effort to retain the implant (DAIR procedure). Many different applications relevant.

Capital Markets Day 2026

Segment Deep Dives

Arthroplasty | Spine

Annelie Aava Vikner, EVP Marketing

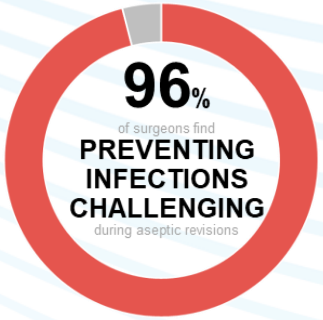
Market insight suggest very strong need and potential for CERAMENT G in the US arthroplasty market (1/2)

BONESUPPORT invests regularly in specific qualitative and quantitative market research to build market insights. Since public data for the space of orthobiologics is limited the market research generated insight, serves as important input to strategy development and execution planning.

Market Research Arthroplasty, INSHEH#426. n=100, 25-minute online surveys with orthopedic surgeons in the US in regards of current practices, trends, and perceptions related to the use of local antibiotics in primary arthroplasty, aseptic revision arthroplasty, and PJI

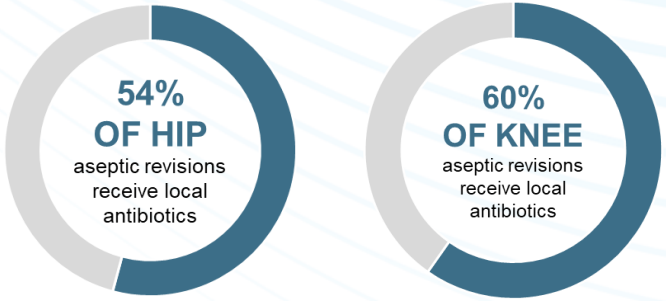
- **96%** of orthopedic surgeons find **infection prevention challenging** in aseptic (non-infected) arthroplasty revisions

  Top challenging factors:
  - High-risk comorbidities (diabetes, high BMI etc)
  - Prior surgeries
  - Large bone defects



Data from the AJRR 2025 annual registry[1], show that the most common reason for revision arthroplasty was infection. 52% of the knee revisions and 21% of the hip revisions were due to infection, followed by mechanical complications and instability

- High usage of local antibiotics in regular aseptic (non-infected) arthroplasty revisions due to strong concerns on development of infection
- **54%** (hip) respective **60%** (knee) of the revision arthroplasties receive some form of local antibiotics application
- **PMMA** and **antibiotic powder** were most common application forms



- Of all the surgeons in the survey **82%** found CERAMENT G **appealing to highly appealing**, for integration in treatment protocols

1. AJRR 2025 Annual Report. Rosemont, IL: American Academy of Orthopaedic Surgeons; 2025.

Market insight suggest very strong need and potential for CERAMENT G in the US arthroplasty market (2/2)

Market Research Arthroplasty, INSHEH#426. n=100, 25-minute online surveys with orthopedic surgeons in the US in regards of current practices, trends, and perceptions related to the use of local antibiotics in primary arthroplasty, aseptic revision arthroplasty, and PJI

Primary Arthroplasties:

- Infection incidence is low (1-2%) and the clinical data and protocols for use of local antibiotics is underdeveloped
- In clinical praxis local antibiotics is used in primary arthroplasties for patients with high-risk comorbidities, poor soft tissue quality or other risk factors
- In the survey, surgeons responded that local antibiotics is used in ~40% of the cases

Market Research PJI, INSP#924
n=100, 25-minute online surveys with orthopedic surgeons in the US and EU responsible for the treatment of PJI. Results were supplemented by 1.5 hour in person roundtable discussion with selected orthopedic surgeons

- **Antibiotic stewardship is important for surgeons and a growing concern**
- Use of local antibiotics is seen as critically important. Current administration is through antibiotic loaded PMMA (78%), as spacer or beads, and/or antibiotic powder (64%) and/or antibiotics mixed with bone grafts, synthetic or organic, (35%)
- **Micro-defects in bone is an issue** which can occur in routine surgeries, fractures, primaries and revisions, which opens up significant use for CERAMENT G even if there are not large defects

Highlights:

- The biggest challenges with Prosthetic Joint Infections are (in order): recurrence of infection, bone loss and implant biofilm
- 93% of surgeons express that PJI is a challenging condition
- 84% of surgeons express lack of available technology and techniques that would enable the transition to 1-stage procedure

Spine – current status

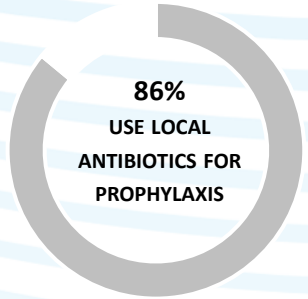
- Clearance obtained for CERAMENT BVF for use in interbody fusion in spine
- Pre-clinical CERAMENT BVF studies, application methods
- Understanding the customers and the spine market – validating clinical unmet need through market research, interviews & KOL engagement
- Targeted CERAMENT BVF launch ongoing
- CERAMENT G and CERAMENT V plan established and initiated

Market insight supports strong clinical and market rationale for antibiotic eluting CERAMENT in spinal procedures

Survey included 50 Orthopedic spine surgeons and Neurosurgeons in the US, Double-blinded self-administered online survey taking 15 minutes to complete to investigate current practices, trends, and perceptions related to procedure types and the use of local antibiotics in spine surgery

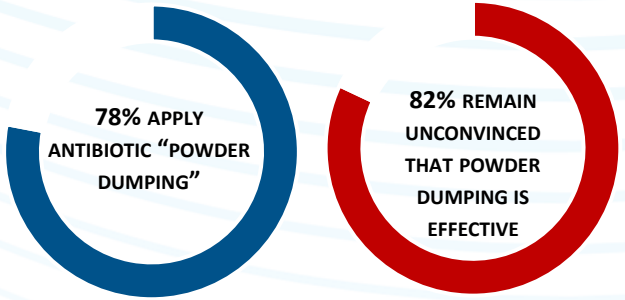
Infection and reinfection prevention are major unmet needs in spine surgery

- ~75% of surgeons already use local antibiotics for surgical treatment and 86% for prophylaxis in at least some patient
- High-risk patients (diabetes, obesity, smoking, multi-level surgery) drive usage



Current standard (antibiotic "dumping") is widely used but suboptimal

- While 82% of surgeons consider the approach suboptimal
- ~78% apply antibiotics as powder without controlled delivery
- *Limited duration and unpredictable distribution of antibiotics*



Majority 78 % expressed need for a bone graft substitute with extended local antibiotic delivery capability

SPINE MARKET STRATEGY – Antibiotic Eluting CERAMENT

Lead Indication Focus: Posterolateral fusion (PLF)
Pre-clinical: Building foundational spine data across the full CERAMENT portfolio
Ongoing*:* Pilot studies to guide model selection and study design
Next: Pivotal study models for FDA PreSub and clinical evaluation
Timing: 2026-2027

Clinical Strategy: Clinical program in design phase, adaptable to pre-clinical outcomes
Focus on generating strong efficacy and safety data supporting fusion/bone healing and implant protection

Clinical studies:
- Single center case series (~20pts) CERAMENT BVF PLF
- Multi-center PLF study (~300-400 pts) on Antibiotic eluting CERAMENT versus standard of care

Estimated costs: 80-90 MSEK
Timing: 2027-2030

Regulatory Pathway Strategy: Likely DeNovo pathway given novel spine indication and claims
Timing: 2030/2031

- High unmet need for an on-label solution
- First to market with bone healing + infection control
- Builds on proven CERAMENT platform and clinical track record
- Scalable expansion opportunity

Capital Markets Day 2026

Clinical Update

Michael Diefenbeck, Chief Medical Officer

Segmentation / market segments

Market segmentation is the strategic process of dividing a broad target market into smaller, distinct groups (segments) of [users] patients who share similar characteristics [needs, behaviors, or interests.].

BONESUPPORT

Foot & Ankle

Trauma

Arthroplasty

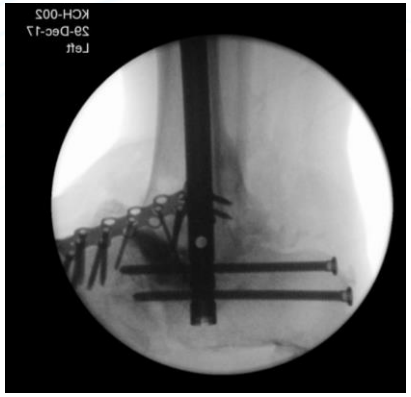
Spine

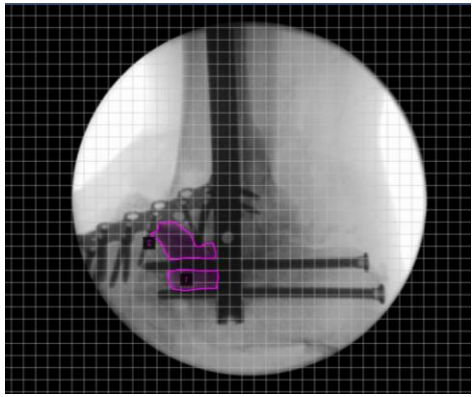
Foot & Ankle: Diabetic Foot Osteomyelitis (DFO)

Illustrative example

- Male diabetic patient in the age group 51-60 years, with a diabetic foot osteomyelitis (DFO)
- Charcot deformity of the midfoot

Foot & Ankle: Diabetic Foot Osteomyelitis (DFO)





Intra-op

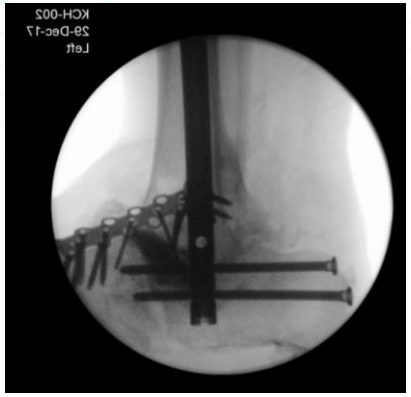
Illustrative example continued

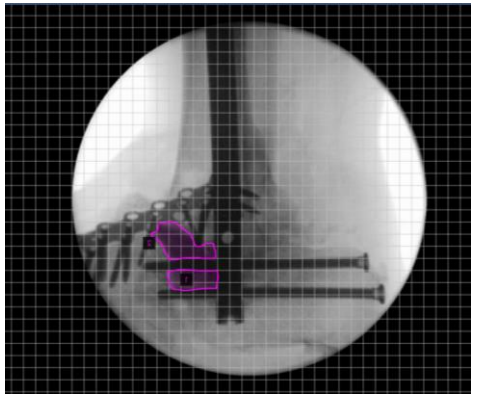
- A Charcot deformity correction was performed through bone osteotomies and wedge resections and the correction was maintained with internal fixation devices (retrograde hindfoot nail and plate/screw construct).
- The debrided bone void was filled with 10cc CERAMENT V.

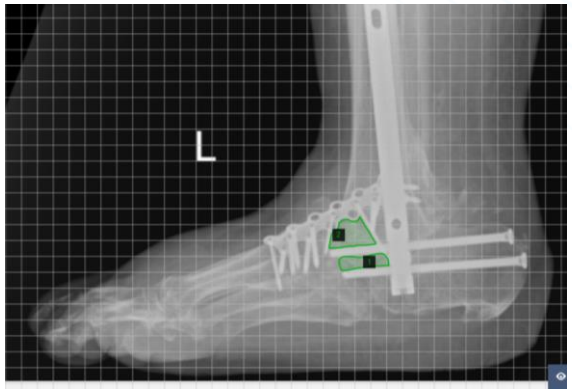
Foot & Ankle: Diabetic Foot Osteomyelitis (DFO)

BONESUPPORT

Foot & Ankle







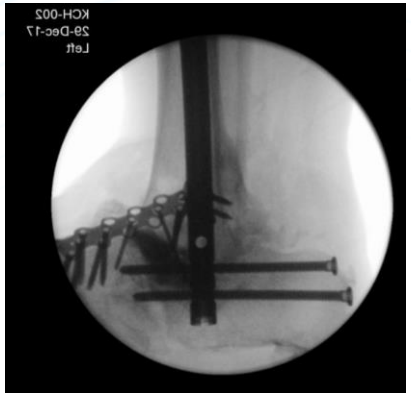
Intra-op

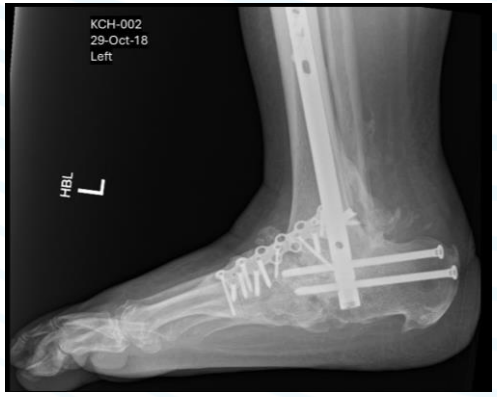
6 months follow-up

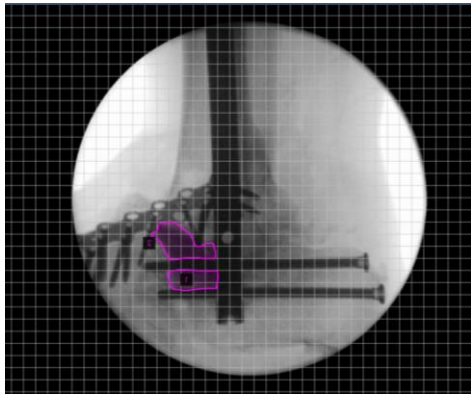
Foot & Ankle: Diabetic Foot Osteomyelitis (DFO)

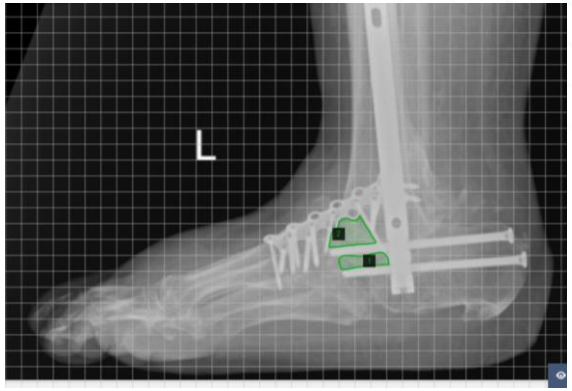
BONESUPPORT

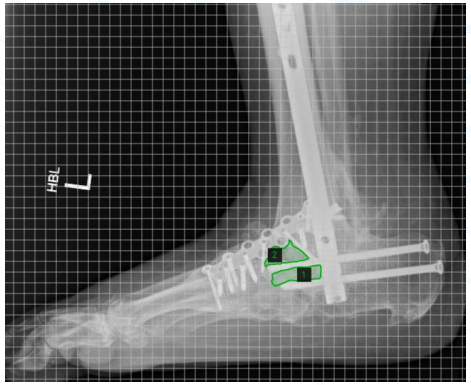
Foot & Ankle











Intra-op

6 months follow-up

9 months follow-up

Foot & Ankle: Diabetic Foot Osteomyelitis (DFO)

BONESUPPORT

Foot & Ankle

J. Bone Joint Infect., 10, 199–206, 2025
https://doi.org/10.5194/jbji-10-199-2025

JBJI Journal of Bone and Joint Infection Open Access

CLOSE-UP – a favourable protocol for limb-sparing surgery of diabetic foot osteomyelitis

Anton Alexander Nolte Peterlin[1,2], Louise Kruse Jensen[1], Emil Gleipner-Andersen[2], and Hans Gottlieb[2]

[1]Experimental Pathology, Department of Veterinary and Animal Sciences, University of Copenhagen, 1870 Frederiksberg, Denmark
[2]Department of Orthopaedic Surgery, Herlev Hospital, 2730 Herlev, Denmark

Correspondence: Anton Alexander Nolte Peterlin (anton.peterlin@sund.ku.dk)

Received: 28 February 2025 – Revised: 25 April 2025 – Accepted: 15 May 2025 – Published: 16 June 2025

Abstract. Introduction: Diabetic foot osteomyelitis (DFO) is a severe complication of diabetic foot ulcers, leading to high morbidity, mortality, and major limb amputation risk. While limb-sparing surgery is well established, optimal wound closure and intraosseous antibiotic strategies remain under-explored and under-reported. This study evaluates a single-stage limb-sparing surgical approach incorporating primary closure and local intraosseous antibiotic therapy. **Methods**: This retrospective study included 97 DFO patients (2017–2024) treated using the CLOSE-UP (Conservative surgery, Local antibiotics, Oral versus intravenous antibiotics – OVIVA, Samples, Effective limb preservation, and closUre Primary) protocol, developed to standardize DFO surgery. The one-stage procedure involved bone sampling, local debridement or minor amputation (distal to the tarsometatarsal joint), antibiotic-loaded calcium sulfate–hydroxyapatite biocomposite application, and primary wound closure. Postoperatively, patients followed the OVIVA antimicrobial protocol: 1 week of intravenous (IV) therapy and 5 weeks of oral (empiric penicillin–cloxacillin) therapy. The primary outcome was treatment failure within 1 year, with a minimum follow-up of 12 months. **Results**: Clinical failure occurred in 13 patients (13.4 %), with only 4 patients (4.1 %) requiring major amputation. Peripheral arterial disease was present in 24 patients (24.7 %) and was the only variable significantly associated with clinical failure (odds ratios: 10.21; $P < 0.01$). The 1-year and 3-year mortality rates were 14.4 % and 35.9 %, respectively. **Conclusions**: The CLOSE-UP protocol demonstrated favourable outcomes. Given the high risk of mortality and limb loss in DFO, this structured approach has the potential to improve mobility, shorten rehabilitation, lower costs, and enhance quality of life. Further research, particularly randomized controlled trials, should focus on optimizing wound closure to improve long-term limb preservation and survival.

Foot & Ankle: Diabetic Foot Osteomyelitis (DFO)

BONESUPPORT

Foot & Ankle

J. Bone Joint Infect., 10, 199–206, 2025
https://doi.org/10.5194/jbji-10-199-2025

JBJI Journal of Bone and Joint Infection Open Access

CLOSE-UP – a favourable protocol for limb-sparing surgery of diabetic foot osteomyelitis

Anton Alexander Nolte Peterlin[1,2], Louise Kruse Jensen[1], Emil Gleipner-Andersen[2], and Hans Gottlieb[2]

[1]Experimental Pathology, Department of Veterinary and Animal Sciences, University of Copenhagen, 1870 Frederiksberg, Denmark
[2]Department of Orthopaedic Surgery, Herlev Hospital, 2730 Herlev, Denmark

Correspondence: Anton Alexander Nolte Peterlin (anton.peterlin@sund.ku.dk)

Received: 28 February 2025 – Revised: 25 April 2025 – Accepted: 15 May 2025 – Published: 16 June 2025

Abstract. Introduction: Diabetic foot osteomyelitis (DFO) is a severe complication of diabetic foot ulcers, leading to high morbidity, mortality, and major limb amputation risk. While limb-sparing surgery is well established, optimal wound closure and intraosseous antibiotic strategies remain under-explored and under-reported. This study evaluates a single-stage limb-sparing surgical approach incorporating primary closure and local intraosseous antibiotic therapy. **Methods**: This retrospective study included 97 DFO patients (2017–2024) treated using the CLOSE-UP (Conservative surgery, Local antibiotics, Oral versus intravenous antibiotics – OVIVA, Samples, Effective limb preservation, and closUre Primary) protocol, developed to standardize DFO surgery. The one-stage procedure involved bone sampling, local debridement or minor amputation (distal to the tarsometatarsal joint), antibiotic-loaded calcium sulfate–hydroxyapatite biocomposite application, and primary wound closure. Postoperatively, patients followed the OVIVA antimicrobial protocol: 1 week of intravenous (IV) therapy and 5 weeks of oral (empiric penicillin–cloxacillin) therapy. The primary outcome was treatment failure within 1 year, with a minimum follow-up of 12 months. **Results**: Clinical failure occurred in 13 patients (13.4 %), with only 4 patients (4.1 %) requiring major amputation. Peripheral arterial disease was present in 24 patients (24.7 %) and was the only variable significantly associated with clinical failure (odds ratios: 10.21; $P < 0.01$). The 1-year and 3-year mortality rates were 14.4 % and 35.9 %, respectively. **Conclusions**: The CLOSE-UP protocol demonstrated favourable outcomes. Given the high risk of mortality and limb loss in DFO, this structured approach has the potential to improve mobility, shorten rehabilitation, lower costs, and enhance quality of life. Further research, particularly randomized controlled trials, should focus on optimizing wound closure to improve long-term limb preservation and survival.

Highlights:

- One-stage procedure with local debridement or minor amputation, CERAMENT G or V and primary wound closure in 97 pat.
- OVIVA protocol: 1 week of IV and 5 weeks of oral therapy
- Clinical failure occurred in 13 patients (13.4 %), with only 4 patients (4.1 %) requiring major amputation.
- Benchmark: Amputation rate up to 24%[1]

- Defined protocol with CERAMENT leads to favourable results

[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

Foot & Ankle: Diabetic Foot Osteomyelitis (DFO)

BONESUPPORT

Foot & Ankle

Metaoy *et al. Clinical Diabetes and Endocrinology* (2024) 10:51
https://doi.org/10.1186/s40842-024-00200-w

Clinical Diabetes and Endocrinology

RESEARCH ARTICLE Open Access

Adjuvant local antibiotic therapy in the management of diabetic foot osteomyelitis

Sara Metaoy[1,2*], Iulia Rusu[1] and Anand Pillai[1,2]

Abstract

Background The management of diabetic foot osteomyelitis (DFO) is complex. The targeted use of adjuvant local antibiotics, in the form of biocomposite bone void filler, in DFO, can enhance patient outcomes while minimising the adverse effects associated with systemic antibiotic therapy and its shortcomings.

Methods We reviewed a series of 105 consecutive patients who underwent surgical management for diabetic foot osteomyelitis. In the NLAB group, (no adjuvant local antibiotic use), 49 patients, received the current standard of care treatment with no use of adjunctive local antibiotic therapy. In group LAB, (adjuvant use of local antibiotics), 56 patients received additional adjuvant local antibiotic therapy. Patient outcomes were compared between both groups.

Results Infection healing was demonstrated in 10 (20.41%) patients from group NLAB and 41 (73.21%) from group LAB ($p < 0.0001$). Persistence of infection with no evidence of wound healing, 6 months from surgery, was observed in 15 (30.61%) patients in group NLAB. Among the LAB group, only 4 (7.14%) patients demonstrated infection persistence ($p = 0.00183$). Reinfection was observed in 24 of 49 patients in group NLAB (49%) and in only 11 out of 56 patients in group LAB (20%) ($p = 0.001466$). 7 (6.67%) patients required major amputation with 6 (12.24%) belonging to group NLAB. Only 1 (1.78%) patient in group LAB underwent major amputation. A higher 5-year mortality rate was noted within patients in group NLAB, 27 (55.1%). The mortality rate in group LAB was (12.5%).

Conclusion The adjuvant use of antibiotic loaded bio-composite bone void filler locally was associated with increased infection clearance rates regarding diabetic foot osteomyelitis when compared with the standard care of treatment while achieving lower rates of infection persistence and recurrence. It also has the potential to reduce amputation and mortality rates with further research.

Foot & Ankle: Diabetic Foot Osteomyelitis (DFO)

BONESUPPORT

Foot & Ankle

Metaoy *et al. Clinical Diabetes and Endocrinology* (2024) 10:51
https://doi.org/10.1186/s40842-024-00200-w

Clinical Diabetes and Endocrinology

RESEARCH ARTICLE Open Access

Adjuvant local antibiotic therapy in the management of diabetic foot osteomyelitis

Sara Metaoy[1,2*], Iulia Rusu[1] and Anand Pillai[1,2]

Abstract

Background The management of diabetic foot osteomyelitis (DFO) is complex. The targeted use of adjuvant local antibiotics, in the form of biocomposite bone void filler, in DFO, can enhance patient outcomes while minimising the adverse effects associated with systemic antibiotic therapy and its shortcomings.

Methods We reviewed a series of 105 consecutive patients who underwent surgical management for diabetic foot osteomyelitis. In the NLAB group, (no adjuvant local antibiotic use), 49 patients, received the current standard of care treatment with no use of adjunctive local antibiotic therapy. In group LAB, (adjuvant use of local antibiotics), 56 patients received additional adjuvant local antibiotic therapy. Patient outcomes were compared between both groups.

Results Infection healing was demonstrated in 10 (20.41%) patients from group NLAB and 41 (73.21%) from group LAB ($p < 0.0001$). Persistence of infection with no evidence of wound healing, 6 months from surgery, was observed in 15 (30.61%) patients in group NLAB. Among the LAB group, only 4 (7.14%) patients demonstrated infection persistence ($p = 0.00183$). Reinfection was observed in 24 of 49 patients in group NLAB (49%) and in only 11 out of 56 patients in group LAB (20%) ($p = 0.001466$). 7 (6.67%) patients required major amputation with 6 (12.24%) belonging to group NLAB. Only 1 (1.78%) patient in group LAB underwent major amputation. A higher 5-year mortality rate was noted within patients in group NLAB, 27 (55.1%). The mortality rate in group LAB was (12.5%).

Conclusion The adjuvant use of antibiotic loaded bio-composite bone void filler locally was associated with increased infection clearance rates regarding diabetic foot osteomyelitis when compared with the standard care of treatment while achieving lower rates of infection persistence and recurrence. It also has the potential to reduce amputation and mortality rates with further research.

Highlights:

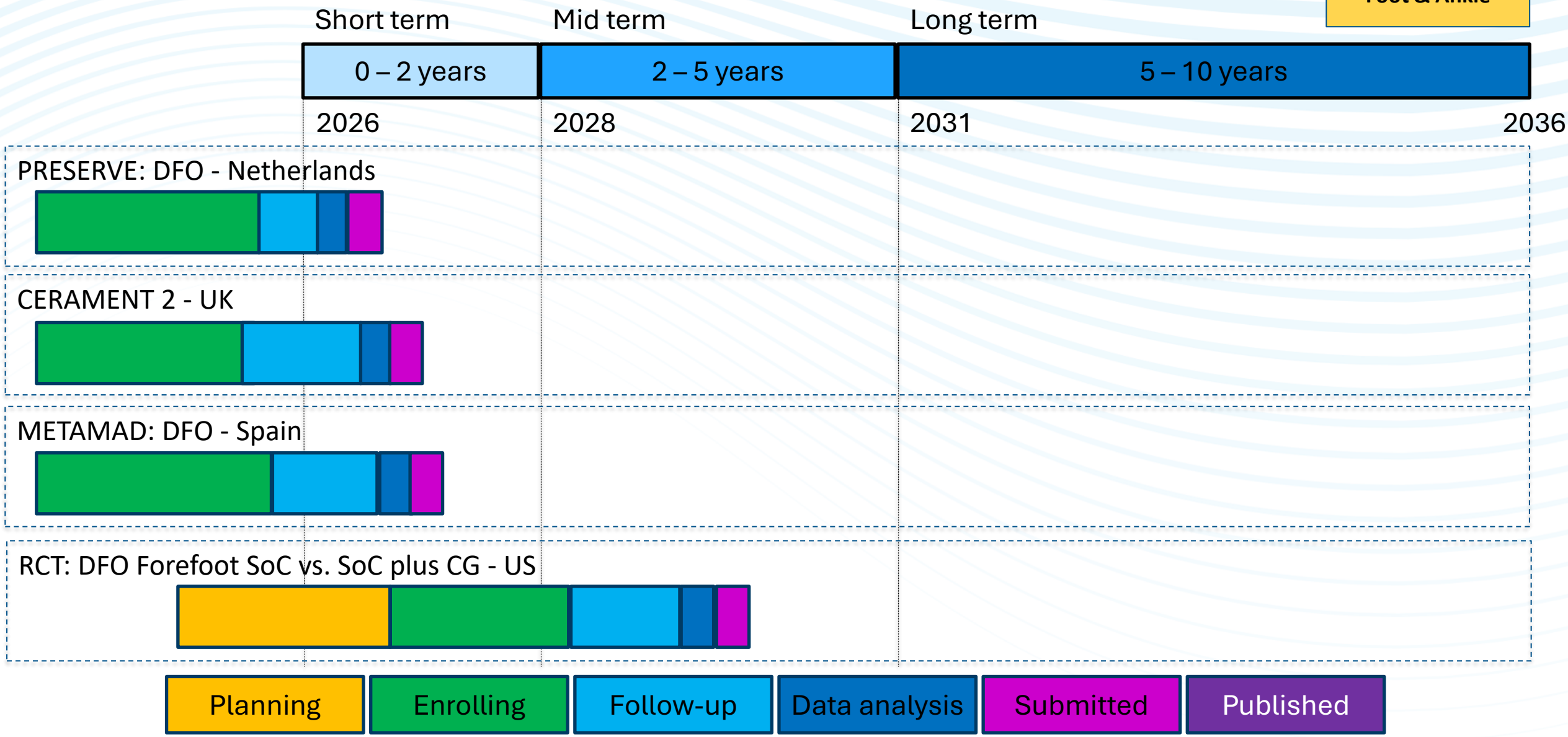
- 105 patients. All receiving surgical treatment, CERAMENT G or CERAMENT V (LAB) vs. conventional surgical treatment with no local antibiotic delivery (NLAB)
- Reinfection Rate: 19.6% in LAB vs. 48.9% in NLAB group
- Major Amputation rate: 1.8% in LAB vs. 12.3% in NLAB group
- Benchmark: Amputation rate up to 24%[1]

- Defined protocol with CERAMENT leads to favorable results in direct comparison to NLAB

[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

Foot & Ankle: Evidence pipeline

Foot & Ankle

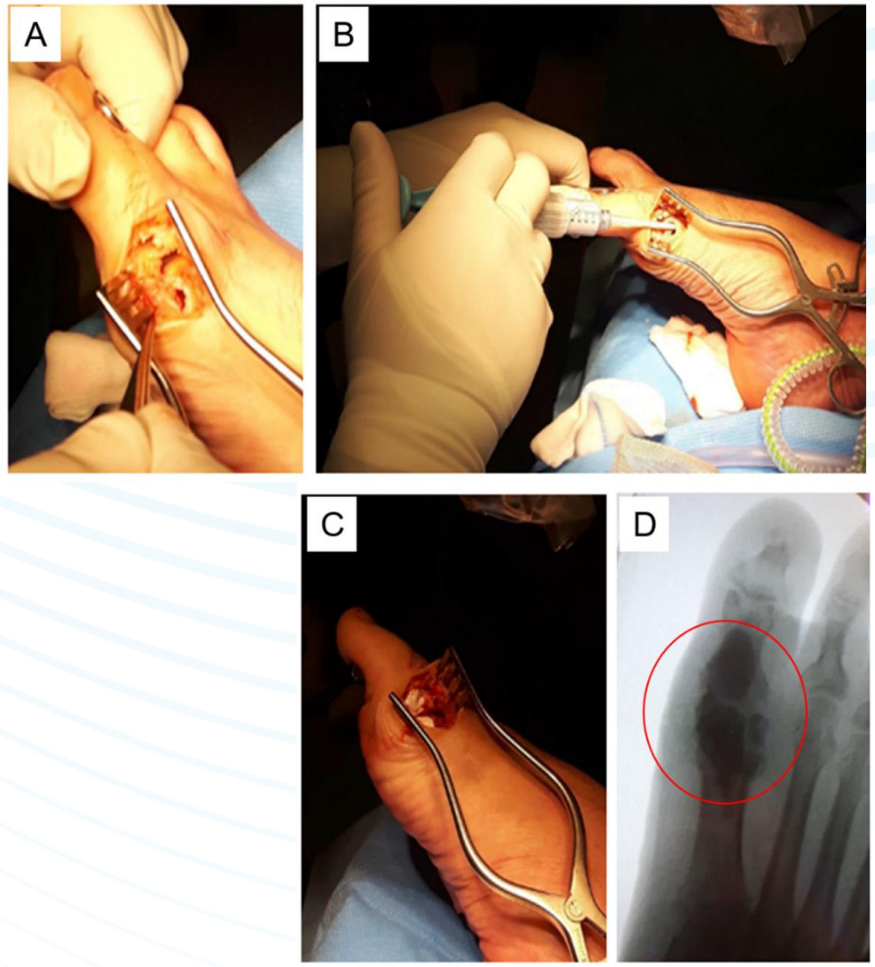


PRESERVE: Diabetic Foot Osteomyelitis (DFO)

BONESUPPORT

Foot & Ankle

Design: Prospective Case Series
Indication: DFO of forefoot
Patients: **53** subjects, follow-up completed
Treatment: Debridement with CERAMENT G
Hospital: 10 hospitals in the Netherlands



First results presented at OBIC 2026:

- 107 were treated with conservative treatment (systemic antibiotic and wound care) for DFO
- 53 (50%) failed conservative treatment and were included in study
- After 20 weeks of follow up:
  - 8 revision surgeries (15%)
  - No major amputations
  - Wound healing 68% (ulcer healing depends on deformity and wound care)

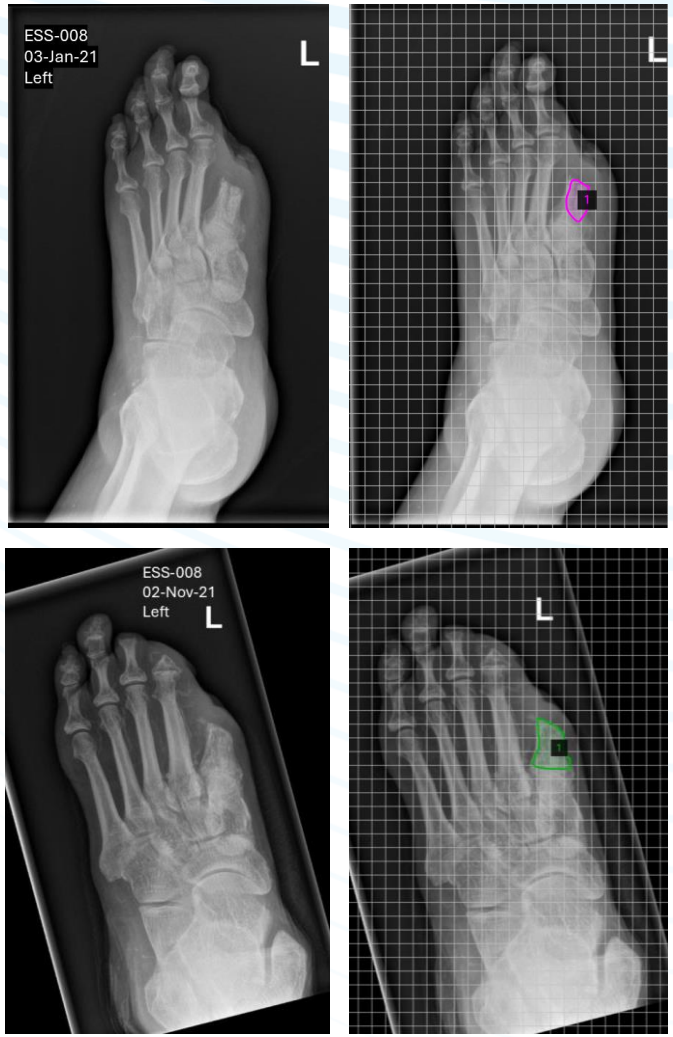
Data analysis

CERAMENT 2: Diabetic Foot Osteomyelitis (DFO)

BONESUPPORT

Foot & Ankle

Design: Prospective Case Series
Indication: DFO of forefoot
Patients: **25** pat. enrolled, 12 months follow-up ongoing
Treatment: Debridement with CERAMENT G
Hospital: Basildon



6-months interim results have been submitted for presentation to EBJIS 2026

Follow-up

METAMAD: Diabetic Foot Osteomyelitis (DFO)

BONESUPPORT

Foot & Ankle

Design: Prospective Case Series
Indication: DFO of forefoot
Patients: **20** enrolled, follow-up started
Treatment: Metatarsal head resection and CERAMENT G
Hospital: Diabetic Foot Unit of the Universidad Complutense de Madrid

Follow-up

RCT: Diabetic Foot Osteomyelitis (DFO)

BONESUPPORT

Foot & Ankle

Design: Randomized Controlled trial (RCT)
Indication: DFO of forefoot
Patients: 100 pat. (50 vs 50)
Treatment: Standard of care vs. Standard of care plus CERAMENT G
Hospital: University of Texas (UTSW and UTSA)
Follow-up: 12 months
Timeline: First-Patient-In in end 2026

Planning

BONESUPPORT

Foot & Ankle

Trauma

Arthroplasty

Spine

Trauma: Fracture Related Infection (FRI)

Trauma

Post-op

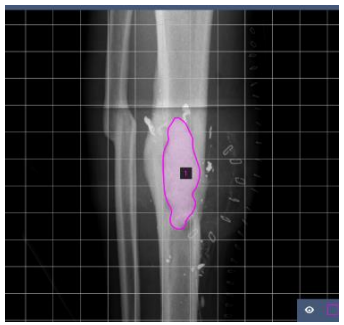
Illustrative example

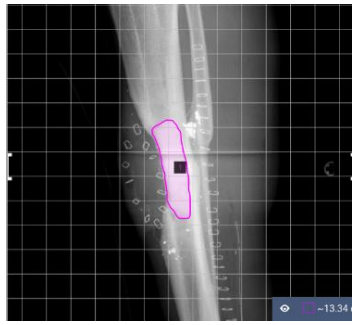
- Male patient in the age group 31-40 years with a fracture-related infection of the right tibia after a gunshot injury and fracture fixation with an intramedullary nail.
- The nail was removed, the bone void debrided, filled with 10cc CERAMENT V and systemic antibiotics started.

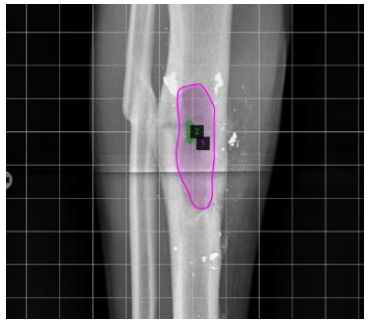
Trauma: Fracture Related Infection (FRI)

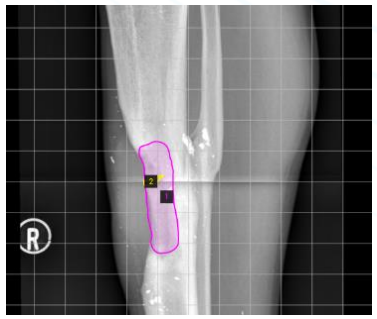
BONESUPPORT

Trauma





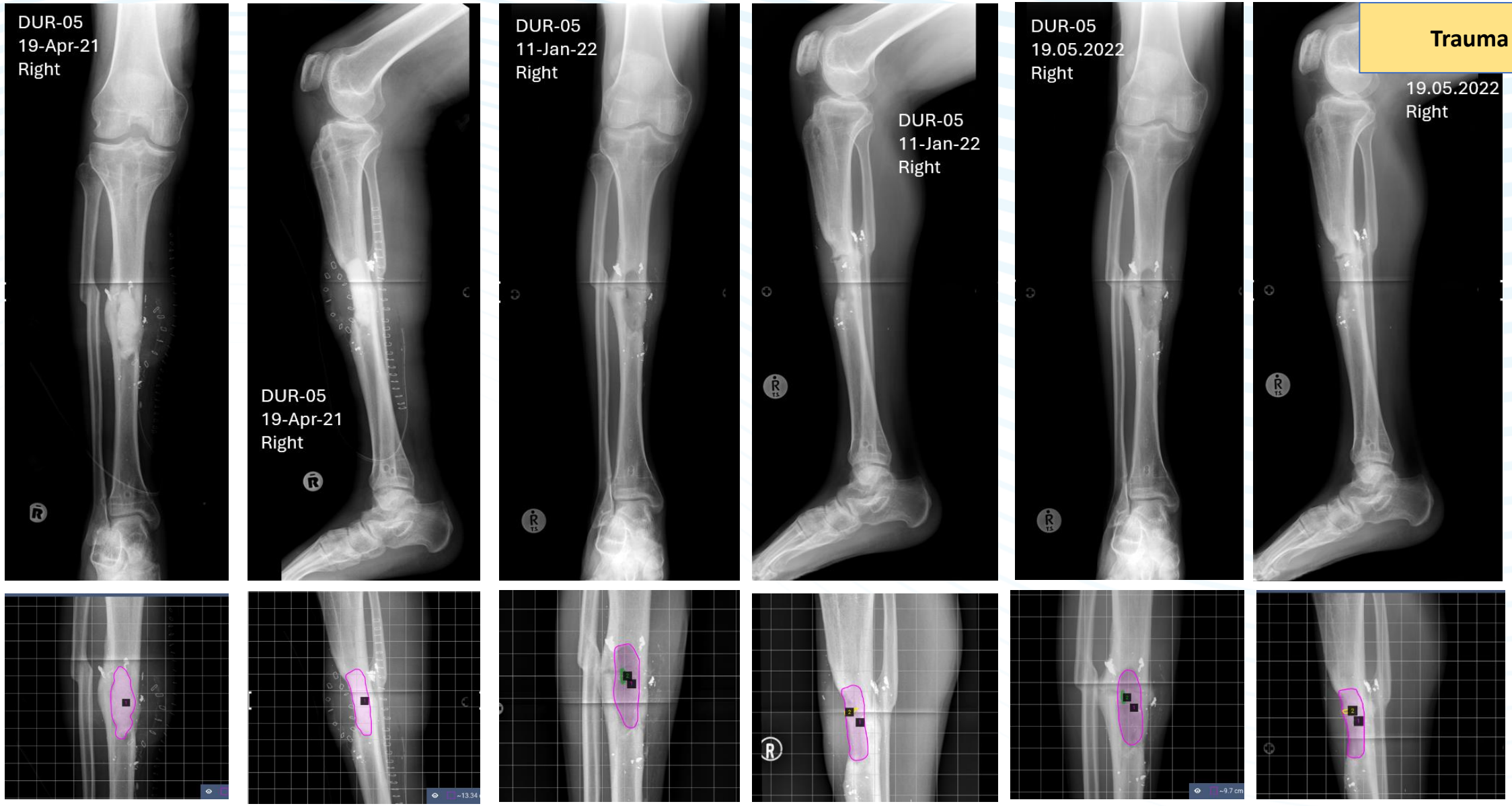




Post-op

8 months follow-up

Trauma: Fracture Related Infection (FRI)



Post-op

8 months follow-up

13 months follow-up

Trauma: Fracture Related Infection (FRI)

BONESUPPORT

Trauma

Clinical/Basic Science Research Article

OPEN

Intramedullary nailing with an absorbable antibiotic bone graft substitute in fracture-related infections and osteomyelitis: a case series

Scott M. Sandilands, DO[a,b,c,*], Akshay V. Daji, MD[a]

Abstract

Objectives: Fracture-related infections (FRI), infected nonunions, and osteomyelitis with bony instability require aggressive treatment involving systemic antibiotics and surgical debridement. Adjuvant local antibiotic therapy delivers higher and sustained concentrations directly to the site of infection while minimizing systemic toxicity. Antibiotic-loaded poly-methyl methacrylate remains a standard option but presents significant limitations, including nonbiodegradability, reduced antibiotic elution over time, and the need for subsequent removal. Cerament G is a bioabsorbable bone void filler composed of calcium sulfate, hydroxyapatite, and gentamicin sulfate. It provides sustained high-dose antibiotic release, promotes osteoconduction, and remodels into bone within 6 to 12 months, eliminating the need for removal. This makes Cerament G a compelling option for the treatment of FRI and osteomyelitis.

Methods: We describe a technique and case series using the Reamer-Irrigator-Aspirator (RIA) system, Cerament G injection via the 2Can device, and, when necessary, intramedullary nailing for the treatment of FRI and osteomyelitis. The technique was applied to 7 patients at a single Level-1 Trauma Center from 2022 to 2024 with FRI or osteomyelitis. Intramedullary nailing was performed in cases of nonunion or bony instability.

Results: The mean age of patients was 35 years, with a mean body mass index of 29.2. Three patients required adjuvant intramedullary nailing for stabilization. All patients were weight bearing as tolerated after surgery. At a mean follow-up of 14.4 months (6–21 months), there were no recurrence of infection, major complications, or amputations.

Conclusion: The combination of Cerament G and the RIA system represents a viable solution for FRI and osteomyelitis providing effective infection control and sustained antibiotic elution. This technique presents a promising alternative to traditional methods, although larger and longer-term studies are needed to confirm its efficacy.

Keywords: intramedullary nailing, absorbable antibiotic eluting bone graft substitute, bone graft substitute, osteomyelitis, fracture-related infections

1. Introduction

The initial treatment for fracture-related infections (FRI) and osteomyelitis (OM) is targeted systemic antibiotic therapy. When this is insufficient, debridement of necrotic bone to remove the infection nidus with local antibiotic therapy delivering high concentrations of antibiotics at the infection site is required. In cases where bony debridement compromises structural stability or in cases of infected nonunions, surgical intervention must address both the infection and bony instability simultaneously. First described in 2002 and now widely utilized, antibiotic coated nails (ACN) are an effective way to stabilize the bone while providing high concentrations of local antibiotics with low systemic toxicity.[1,2] Although prefabricated ACNs are available, most surgeons will create their own ACN using poly-methyl methacrylate (PMMA) mixed with antibiotics based on culture sensitivities coated around intramedullary nails, Ilizarov rods, guide rods, or threaded wires.

Although effective, using PMMA for ACN fabrication has several disadvantages. It is nonbiodegradable and necessitates reoperation for removal. In addition, PMMA and antibiotics can

Trauma: Fracture Related Infection (FRI)

BONESUPPORT

Trauma

Clinical/Basic Science Research Article

OPEN

Intramedullary nailing with an absorbable antibiotic bone graft substitute in fracture-related infections and osteomyelitis: a case series

Scott M. Sandilands, DO[a,b,c,*], Akshay V. Daji, MD[a]

Abstract

Objectives: Fracture-related infections (FRI), infected nonunions, and osteomyelitis with bony instability require aggressive treatment involving systemic antibiotics and surgical debridement. Adjuvant local antibiotic therapy delivers higher and sustained concentrations directly to the site of infection while minimizing systemic toxicity. Antibiotic-loaded poly-methyl methacrylate remains a standard option but presents significant limitations, including nonbiodegradability, reduced antibiotic elution over time, and the need for subsequent removal. Cerament G is a bioabsorbable bone void filler composed of calcium sulfate, hydroxyapatite, and gentamicin sulfate. It provides sustained high-dose antibiotic release, promotes osteoconduction, and remodels into bone within 6 to 12 months, eliminating the need for removal. This makes Cerament G a compelling option for the treatment of FRI and osteomyelitis.

Methods: We describe a technique and case series using the Reamer-Irrigator-Aspirator (RIA) system, Cerament G injection via the 2Can device, and, when necessary, intramedullary nailing for the treatment of FRI and osteomyelitis. The technique was applied to 7 patients at a single Level-1 Trauma Center from 2022 to 2024 with FRI or osteomyelitis. Intramedullary nailing was performed in cases of nonunion or bony instability.

Results: The mean age of patients was 35 years, with a mean body mass index of 29.2. Three patients required adjuvant intramedullary nailing for stabilization. All patients were weight bearing as tolerated after surgery. At a mean follow-up of 14.4 months (6–21 months), there were no recurrence of infection, major complications, or amputations.

Conclusion: The combination of Cerament G and the RIA system represents a viable solution for FRI and osteomyelitis providing effective infection control and sustained antibiotic elution. This technique presents a promising alternative to traditional methods, although larger and longer-term studies are needed to confirm its efficacy.

Keywords: intramedullary nailing, absorbable antibiotic eluting bone graft substitute, bone graft substitute, osteomyelitis, fracture-related infections

1. Introduction

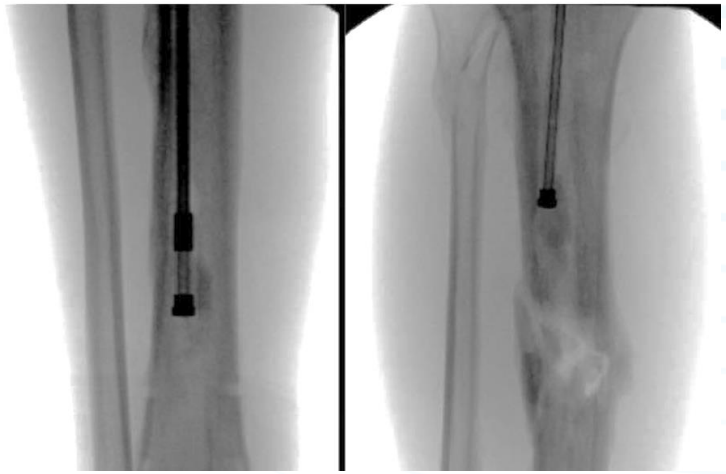
The initial treatment for fracture-related infections (FRI) and osteomyelitis (OM) is targeted systemic antibiotic therapy. When this is insufficient, debridement of necrotic bone to remove the infection nidus with local antibiotic therapy delivering high concentrations of antibiotics at the infection site is required. In cases where bony debridement compromises structural stability or in cases of infected nonunions, surgical intervention must address both the infection and bony instability simultaneously. First described in 2002 and now widely utilized, antibiotic coated nails (ACN) are an effective way to stabilize the bone while providing high concentrations of local antibiotics with low systemic toxicity.[1,2] Although prefabricated ACNs are available, most surgeons will create their own ACN using poly-methyl methacrylate (PMMA) mixed with antibiotics based on culture sensitivities coated around intramedullary nails, Ilizarov rods, guide rods, or threaded wires.

Although effective, using PMMA for ACN fabrication has several disadvantages. It is nonbiodegradable and necessitates reoperation for removal. In addition, PMMA and antibiotics can

Highlights:

- Case series on 7 pat with FRI using the Reamer-Irrigator-Aspirator (RIA) system, CERAMENT G injection via the 2Can device, and, when necessary, intramedullary nailing.
- At a mean follow-up of 14.4 months: No recurrence of infection, major complications, or amputations.

- Benchmark: Recurrance rate 13.3%[1]



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.

Trauma: Open fractures

BONESUPPORT

Trauma

Clinical/Basic Science Research Article

OTA ORTHOPAEDIC TRAUMA ASSOCIATION

OTA INTERNATIONAL

OPEN

Intramedullary nailing with absorbable antibiotic-eluting ceramic for fracture-related infection prophylaxis in high-risk open fractures: a case series and technique

Scott M. Sandilands, DO[a,b,c,*], Akshay V. Daji, MD[a]

Abstract

Objectives: Fracture-related infection (FRI) is a devastating complication of open fractures and remains common even with ideal open fracture care including prompt systemic antibiotics and thorough surgical debridement. There is growing interest in the use of adjuvant local antibiotics; however, traditional carriers like polymethylmethacrylate (PMMA) are limited by subtherapeutic elution, biofilm formation, and the need for secondary removal. We describe a technique of in vivo augmentation of intramedullary nailing with Cerament G, a resorbable gentamicin-eluting calcium sulfate/hydroxyapatite ceramic, delivered through the 2-CAN device for targeted antibiotic prophylaxis.

Methods: Nine patients (mean age 44 years; 22% female) with Gustilo–Anderson Type II (n = 3), IIIA (n = 4), IIIB (n = 1), and IIIC (n = 1) open fractures of the tibia, femur, or humerus underwent this technique at a Level 1 trauma center by a single fellowship-trained orthopaedic traumatologist. Postoperative outcomes included FRI incidence, fracture union, complications, and functional recovery.

Results: At a mean follow-up of 9.1 months (2.6–17.1 months), all fractures achieved union with no cases of FRI. Two GA IIIB/C cases required flap coverage, including one flap failure successfully revised. Self-limiting serous drainage (n = 3) resolved within 1 week. No secondary procedures for infection, implant removal, or amputations occurred.

Conclusion: Intramedullary nailing and intraoperative augmentation with Cerament G using the 2-CAN device offer a technically simple, time-efficient strategy for FRI prophylaxis in high-risk open fractures. The technique provides sustained local antibiotic delivery, avoids PMMA-related complications, and maximizes biomechanical stability by eliminating nail downsizing. Early results demonstrate promising infection prophylaxis, warranting further prospective trials to validate long-term efficacy and cost-effectiveness.

Keywords: intramedullary nailing, absorbable antibiotic-eluting bone graft substitute, absorbable antibiotic-eluting ceramic, open fracture

1. Introduction

Open fractures represent a significant challenge in orthopaedic trauma care, with fracture-related infections (FRIs) posing a major complication that adversely affects patient outcomes, prolongs length of stay, and significantly increases costs.[1] Despite adherence to established management practices—including prompt systemic intravenous (IV) antibiotic administration and surgical debridement—FRI rates remain unacceptably high.[2,3] These persistent infection risks underscore the limitations of systemic therapies, particularly in cases of compromised local vasculature, such as tibia fractures or mangled extremities, where inadequate tissue penetration or vascular compromise may diminish delivery of systemic IV antibiotics.

The limitations of systemic therapy have driven interest in local antibiotic delivery, with particular interest in antibiotic-loaded carriers for prolonged elution. Polymethylmethacrylate (PMMA) antibiotic beads and coated implants offer sustained antibiotic release; however, studies have found the elution to be characterized by a high initial burst, followed by prolonged subtherapeutic antibiotic levels below minimum inhibitory concentration

Trauma: Open fractures

BONESUPPORT

Trauma

Clinical/Basic Science Research Article

OPEN

Intramedullary nailing with absorbable antibiotic-eluting ceramic for fracture-related infection prophylaxis in high-risk open fractures: a case series and technique

Scott M. Sandilands, DO[a,b,c,*], Akshay V. Daji, MD[a]

Abstract

Objectives: Fracture-related infection (FRI) is a devastating complication of open fractures and remains common even with ideal open fracture care including prompt systemic antibiotics and thorough surgical debridement. There is growing interest in the use of adjuvant local antibiotics; however, traditional carriers like polymethylmethacrylate (PMMA) are limited by subtherapeutic elution, biofilm formation, and the need for secondary removal. We describe a technique of in vivo augmentation of intramedullary nailing with Cerament G, a resorbable gentamicin-eluting calcium sulfate/hydroxyapatite ceramic, delivered through the 2-CAN device for targeted antibiotic prophylaxis.

Methods: Nine patients (mean age 44 years; 22% female) with Gustilo–Anderson Type II (n = 3), IIIA (n = 4), IIIB (n = 1), and IIIC (n = 1) open fractures of the tibia, femur, or humerus underwent this technique at a Level 1 trauma center by a single fellowship-trained orthopaedic traumatologist. Postoperative outcomes included FRI incidence, fracture union, complications, and functional recovery.

Results: At a mean follow-up of 9.1 months (2.6–17.1 months), all fractures achieved union with no cases of FRI. Two GA IIIB/C cases required flap coverage, including one flap failure successfully revised. Self-limiting serous drainage (n = 3) resolved within 1 week. No secondary procedures for infection, implant removal, or amputations occurred.

Conclusion: Intramedullary nailing and intraoperative augmentation with Cerament G using the 2-CAN device offer a technically simple, time-efficient strategy for FRI prophylaxis in high-risk open fractures. The technique provides sustained local antibiotic delivery, avoids PMMA-related complications, and maximizes biomechanical stability by eliminating nail downsizing. Early results demonstrate promising infection prophylaxis, warranting further prospective trials to validate long-term efficacy and cost-effectiveness.

Keywords: intramedullary nailing, absorbable antibiotic-eluting bone graft substitute, absorbable antibiotic-eluting ceramic, open fracture

1. Introduction

Open fractures represent a significant challenge in orthopaedic trauma care, with fracture-related infections (FRIs) posing a major complication that adversely affects patient outcomes, prolongs length of stay, and significantly increases costs.[1] Despite adherence to established management practices—including prompt systemic intravenous (IV) antibiotic administration and surgical debridement—FRI rates remain unacceptably high.[2,3] These persistent infection risks underscore the limitations of systemic therapies, particularly in cases of compromised local vasculature, such as tibia fractures or mangled extremities, where inadequate tissue penetration or vascular compromise may diminish delivery of systemic IV antibiotics.

The limitations of systemic therapy have driven interest in local antibiotic delivery, with particular interest in antibiotic-loaded carriers for prolonged elution. Polymethylmethacrylate (PMMA) antibiotic beads and coated implants offer sustained antibiotic release; however, studies have found the elution to be character-ized by a high initial burst, followed by prolonged subtherapeutic antibiotic levels below minimum inhibitory concentration

Highlights:

- Case series on 9 pat with Gustilo–Anderson Type II-III open fractures using intramedullary nailing with CERAMENT G through the 2-CAN for targeted antibiotic prophylaxis.
- At a mean follow-up of 9.1 months: All fractures achieved union with no cases of FRI. No amputations.
- Benchmark: Standard of care: Infection rate average 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.

Trauma: Open fractures

BONESUPPORT

Trauma

Asano *et al.*
Journal of Orthopaedic Surgery and Research (2025) 20:610
https://doi.org/10.1186/s13018-025-05765-5

Journal of Orthopaedic Surgery and Research

RESEARCH Open Access

Adjuvant local antibiotic prophylaxis in Gustilo–Anderson IIIb open fractures: up to 10 years follow-up on clinical outcomes and complications

Eito Asano[1*], Hossai Hemat[1], Abdullah Bin Sahl[2,3*] and Anand Pillai[2]

Abstract

Background High-grade open fractures carry a significant risk of osteomyelitis, despite advancements in surgical techniques and treatment protocols. The use of prophylactic, adjuvant local antibiotics is controversially discussed in the literature. CERAMENT®G (BONESUPPORT™) is a novel synthetic bone substitute that effectively elutes gentamicin. This report presents the largest and longest follow-up data collected over the past decade, comparing these findings to our previous findings to identify long-term complications, as well as comparing the outcome against other forms of local antibiotic prophylaxis.

Methods A retrospective, descriptive analysis was conducted on patients with Gustilo–Anderson IIIb fractures treated with CERAMENT®G as an adjunct to the conventional fix-and-flap approach from June 2013 to August 2021. Patient demographics, orthoplastic interventions, microbiological findings, and the latest outcome data—including union rates, infection rates, mortality, and amputation outcomes—were extracted from electronic records up to April 2024.

Results Seventy-six patients with 78 fractures were included, with a mean follow-up period of 88.7 months. The primary union was achieved in 65 cases (83.3%), and secondary union following bone grafting was achieved in 5 of 13 non-union cases. Three mortalities were identified. Four cases required amputation due to osteomyelitis, flap failure leading to soft tissue infection, failure in bone reconstruction, and chronic pain. Superficial infections occurred in 33 cases (42.3%), and osteomyelitis in 4 cases (5.1%). No local or systemic adverse reactions, including ototoxicity, were reported.

Conclusion CERAMENT®G is a safe and effective option for local antibiotic delivery in high-grade open fractures as an adjunct to systemic antibiotic prophylaxis. Its adjunctive use significantly reduced the risk of osteomyelitis compared to systemic prophylaxis alone and was superior to PMMA beads alone.

Keywords Open fractures, Osteomyelitis, Local antibiotics, Gentamicin, Cerament GHealthcare access, Socio-economic disparities

Trauma: Open fractures

Trauma

Asano *et al.*
Journal of Orthopaedic Surgery and Research (2025) 20:610
https://doi.org/10.1186/s13018-025-05765-5

Journal of Orthopaedic Surgery and Research

RESEARCH Open Access

Adjuvant local antibiotic prophylaxis in Gustilo–Anderson IIIb open fractures: up to 10 years follow-up on clinical outcomes and complications

Eito Asano[1*], Hossai Hemat[1], Abdullah Bin Sahl[2,3*] and Anand Pillai[2]

Abstract

Background High-grade open fractures carry a significant risk of osteomyelitis, despite advancements in surgical techniques and treatment protocols. The use of prophylactic, adjuvant local antibiotics is controversially discussed in the literature. CERAMENT®G (BONESUPPORT™) is a novel synthetic bone substitute that effectively elutes gentamicin. This report presents the largest and longest follow-up data collected over the past decade, comparing these findings to our previous findings to identify long-term complications, as well as comparing the outcome against other forms of local antibiotic prophylaxis.

Methods A retrospective, descriptive analysis was conducted on patients with Gustilo–Anderson IIIb fractures treated with CERAMENT®G as an adjunct to the conventional fix-and-flap approach from June 2013 to August 2021. Patient demographics, orthoplastic interventions, microbiological findings, and the latest outcome data—including union rates, infection rates, mortality, and amputation outcomes—were extracted from electronic records up to April 2024.

Results Seventy-six patients with 78 fractures were included, with a mean follow-up period of 88.7 months. The primary union was achieved in 65 cases (83.3%), and secondary union following bone grafting was achieved in 5 of 13 non-union cases. Three mortalities were identified. Four cases required amputation due to osteomyelitis, flap failure leading to soft tissue infection, failure in bone reconstruction, and chronic pain. Superficial infections occurred in 33 cases (42.3%), and osteomyelitis in 4 cases (5.1%). No local or systemic adverse reactions, including ototoxicity, were reported.

Conclusion CERAMENT®G is a safe and effective option for local antibiotic delivery in high-grade open fractures as an adjunct to systemic antibiotic prophylaxis. Its adjunctive use significantly reduced the risk of osteomyelitis compared to systemic prophylaxis alone and was superior to PMMA beads alone.

Keywords Open fractures, Osteomyelitis, Local antibiotics, Gentamicin, Cerament GHealthcare access, Socio-economic disparities

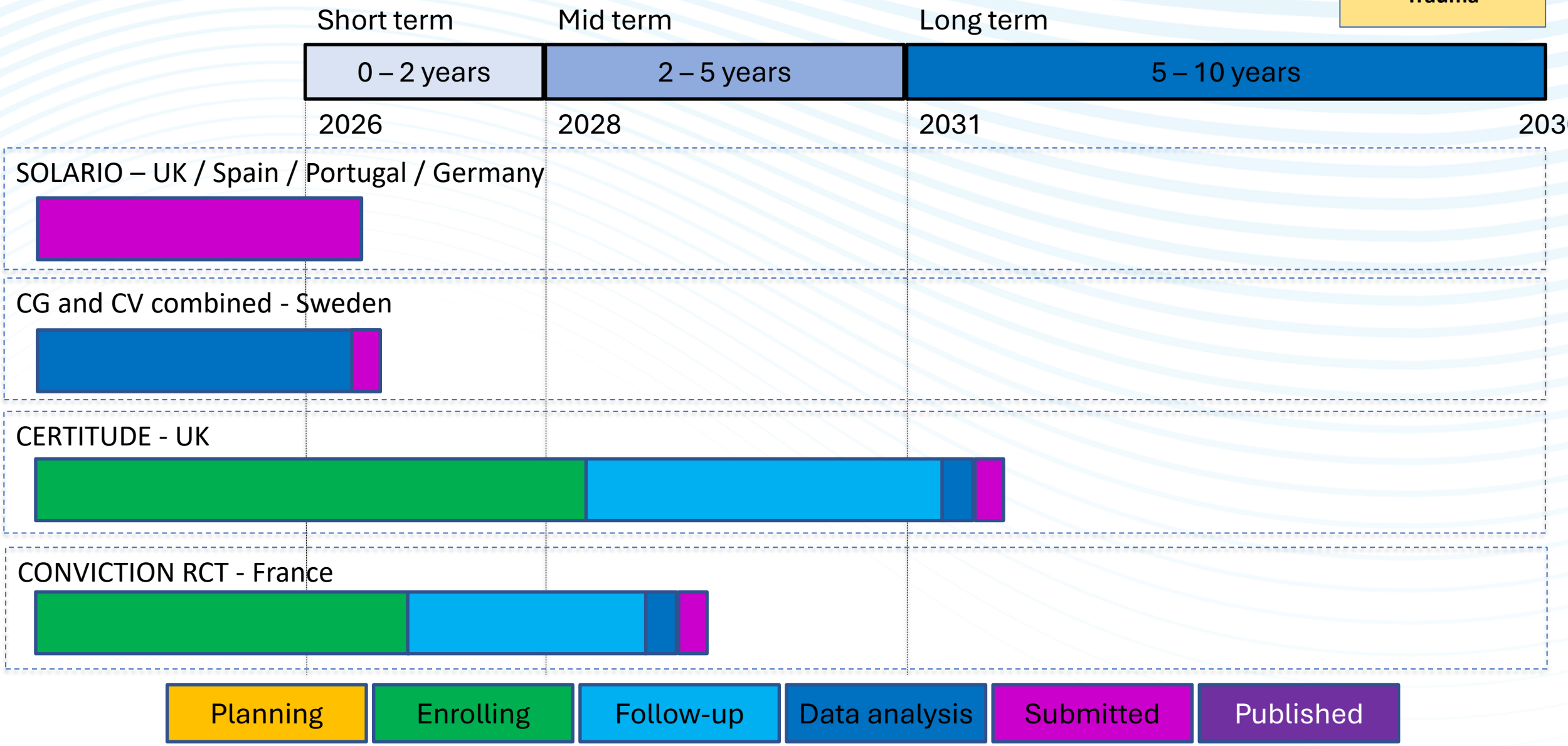
Highlights:

- A retrospective analysis on 76 patients with Gustilo–Anderson IIIb fractures with CERAMENT G
- Infection Rate: 5.1 % (4 cases of Osteomyelitis) at 88.7 months mean follow-up
- Benchmark: Standard of care: Infection rate average 15%[1]
- CERAMENT G is a safe and effective option for local antibiotic delivery in high-grade open fractures as an adjunct to systemic antibiotic prophylaxis.

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.

Trauma: Evidence pipeline

Trauma



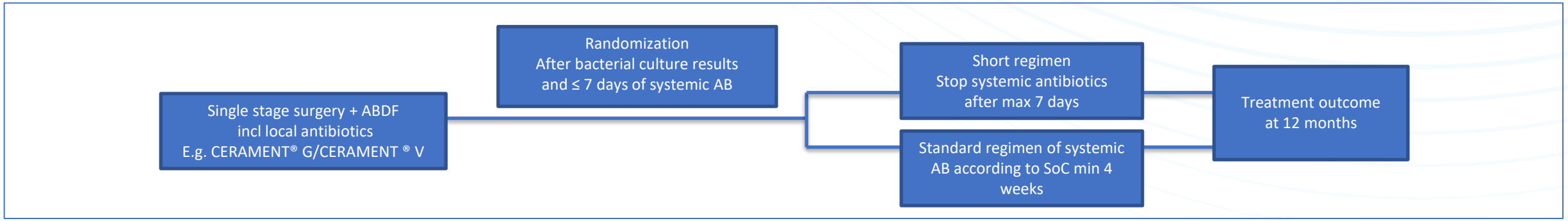

SOLARIO
Surgery with local antibiotic therapy and empiric systemic therapy
Organism fully resistant to local antibiotic identified EXCLUDE
Randomize at ≤ 7 Days
Stop systemic antibiotics (≤ 7 days)
Standard systemic antibiotics (≥ 4 weeks)
Baseline assessment
6 week F/U
3-6 month F/U
12 month F/U
EQ-5D-5L x2
Antibiotics
Side-effects
Prospective surveillance
12 months
Blinded Endpoint Committee assess criteria for recurrence
N=500
ITT
PP
10% margin
Clinicaltrials.gov
NCT03806166
Dudareva M et al. Trials 2019; 20: 693.
EBJIS2024
European Bone & Joint Infection Society
EB JIS
www.ebjis2024.org

SOLARIO - Short Or Long Antibiotic Regimes In Orthopaedics

BONESUPPORT

Trauma

Design	A multicenter, randomized, controlled, open-label, non-inferiority trial
Indications	Orthopedic infections: Osteomyelitis, Fracture-related infection, Diabetic Foot Osteomyelitis and Periprosthetic Joint Infection (excluding DAIR)
Patients	500 patients; 249 standard regimen (min. 4 weeks) and 251 short regimen (max. 7 days) of systemic antibiotic therapy
Treatment	Surgical debridement and licensed antibiotic-eluting bone defect filler (ABDF) and systemic antibiotic therapy immediately after surgery. After max. 7 days, the patients are randomized into two groups. 12 month follow up



[1] Dudareva M, Kumin M, Vach W, Kaier K, Ferguson J, McNally M, Scarborough M. Short or Long Antibiotic Regimes in Orthopaedics (SOLARIO): a randomized controlled open-label non-inferiority trial of duration of systemic antibiotics in adults with orthopaedic infection treated operatively with local antibiotic therapy. Trials 2019; 20: 693.

SOLARIO Top-line Results

Trauma

Primary endpoint met

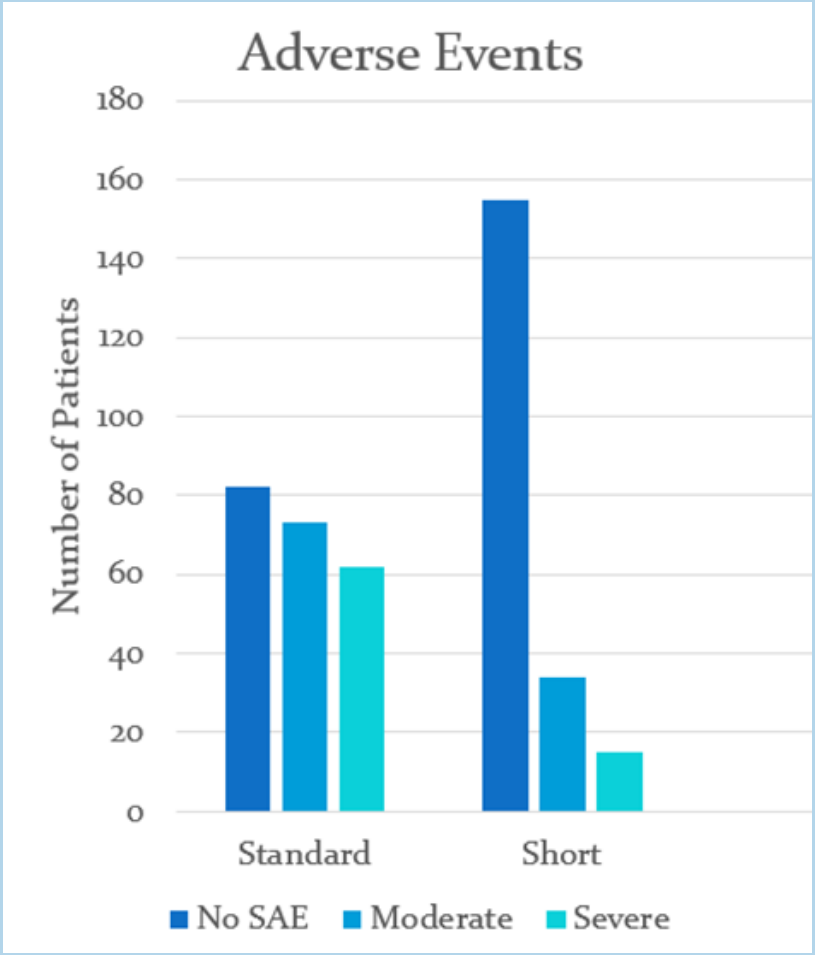
- The short regimen - with local antibiotics achieved equally good infection eradication as the standard of care long regimen

Shorter systemic antibiotic usage

- 5 calendar days compared to 37 calendar days (median)
- An average reduction of 47 antibiotic days[1]/patient, and a total **reduction of 11,275 antibiotic days**

Fewer adverse events (AE)

- The short regimen reduces adverse events



First 6 months after surgery

[1] Total antibiotic days: Each antibiotic on each day is reported separately. Many of the antibiotics are prescribed in combination dosages.

Licensed Antibiotic Eluting Bone Defect Filler

BONESUPPORT

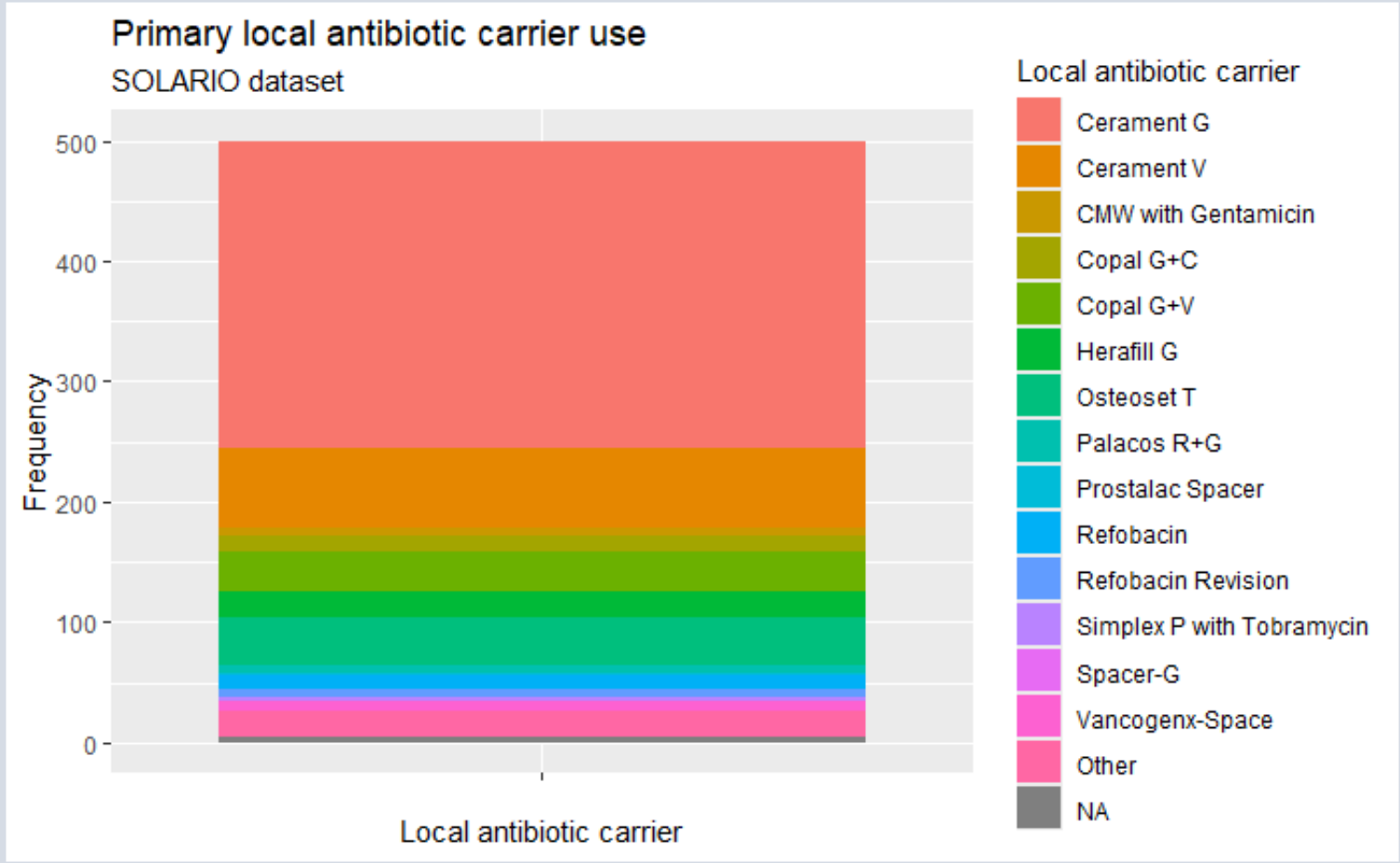
Trauma

All patients had:
- Local antibiotics
- Empiric systemic antibiotics

19 products used:
- Bioresorbable 79 %
- Bone cement (PMMA) 19 %

CERAMENT® G and CERAMENT® V:
- 81% of the bioresorbable products
- 64% of total procedures

Antibiotic used:
- Gentamicin 72%
- Vancomycin 19%



[1] EBJIS Annual Meeting 2024: Best Paper 6 Dudareva M et al., Poster 154 Tsang J et al

Advantages of Using Antibiotic-loaded CERAMENT with Short Antibiotic Regimen

BONESUPPORT

Trauma

- Promotes patient well-being
- Reduces antibiotic costs
- Reduces costs associated with adverse events
- Improves patient adherence
- Improves antibiotic use
- Decreases risk of AMR

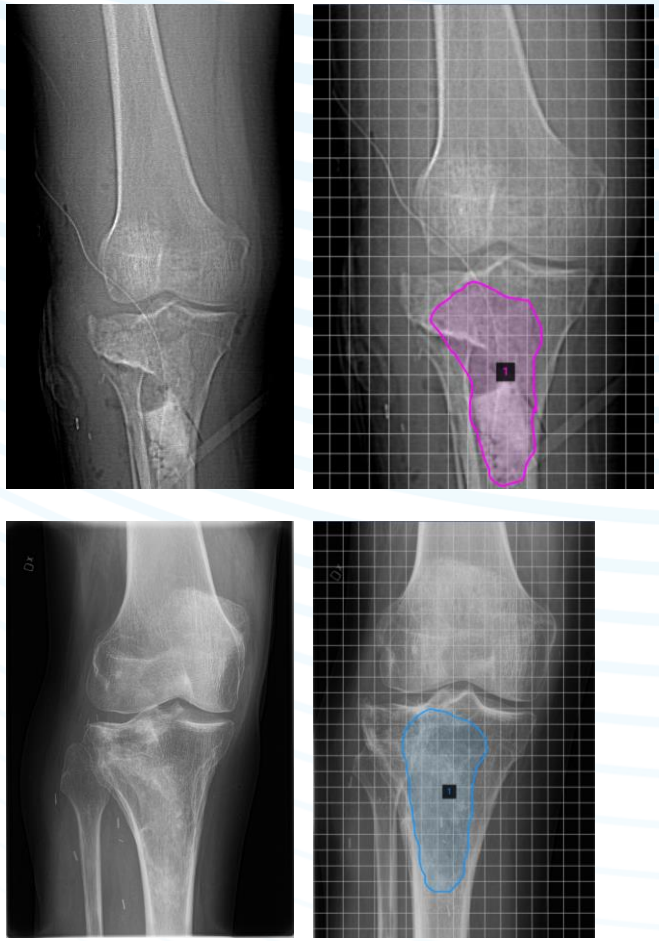
PARTNERS IN ANTIBIOTIC STEWARDSHIP

Trauma: Fracture Related Infection (FRI) CERAMENT G and CERAMENT V combined

BONESUPPORT

Trauma

Design: Retrospective Case Series
Indication: FRI
Patients: **28** Patients
Treatment: Debridement and dead space management with CERAMENT G combined with CERAMENT V
Hospital: Sahlgrenska, Gothenburg, Sweden
Progress: Manuscript submitted



Submitted

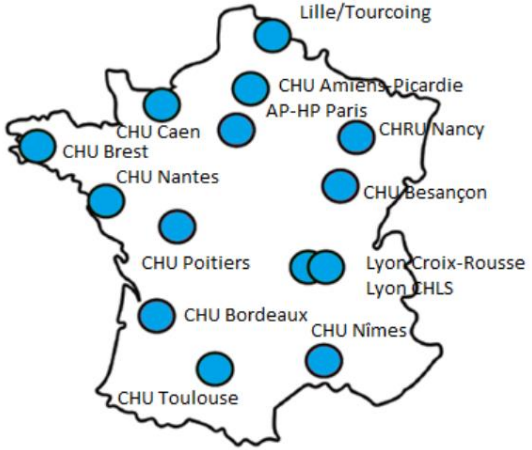
Trauma: Fracture Related Infection (FRI) CONVICTION study in France

BONESUPPORT

Trauma

Design: RCT, Superiority trial
Indication: Chronic osteomyelitis CM type III
Patients: 200 pat, **48** enrolled
Treatment: Debridement without dead-space management
vs. debridement with CERAMENT G
Progress: 8 sites are now enrolling, enrolment far below forecast

CONVICTION
RANDOMIZED CLINICAL TRIAL IN OSTEOMYELITIS



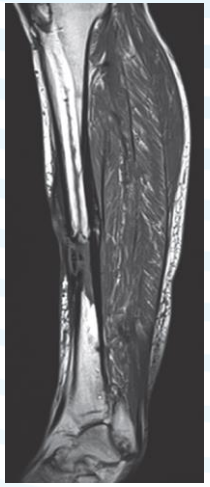
Enrolling

Trauma: Fracture Related Infection (FRI): CERTITUDE Post Market Surveillance (PMS) CG Clinical Study (demanded by FDA in the De Novo Approval)

BONESUPPORT

Trauma

Design: Consecutive case series
Indication: FRI and cOM
Patients: 121 subjects planned, **20** pat enrolled
Treatment: Oxford protocol with CERAMENT G
Hospital: Nuffield Orthopaedic Centre, Oxford University Hospitals
Follow-up: 3 years (LPI Aug 2027, LPO Aug 2030, CSR 2031)



CERTITUDE
CERAMENT® G in Osteomyelitis

Enrolling

BONESUPPORT

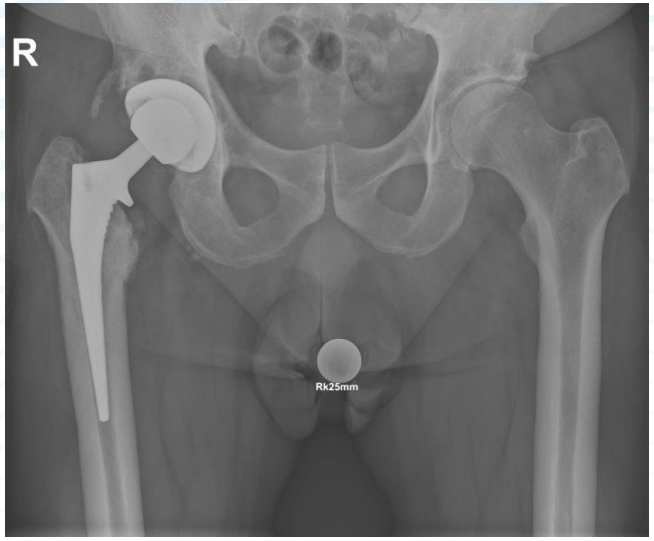
Foot & Ankle

Trauma

Arthroplasty

Spine

Arthroplasty: Periprosthetic Joint Infection (PJI)



Pre-op

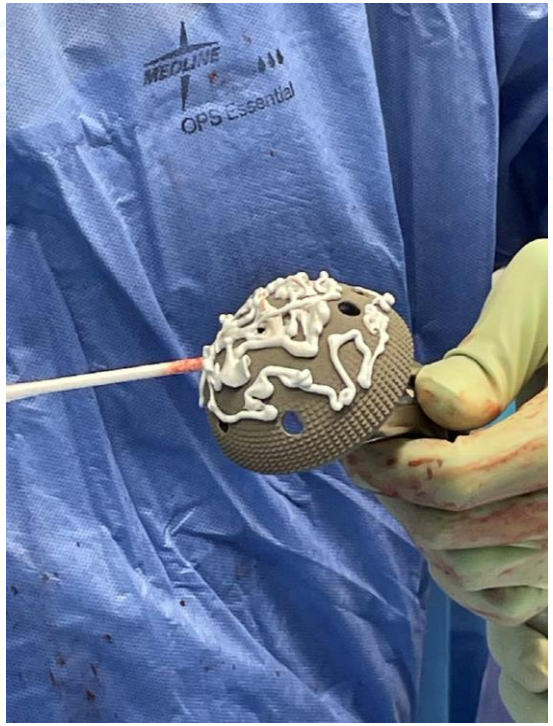
Illustrative example

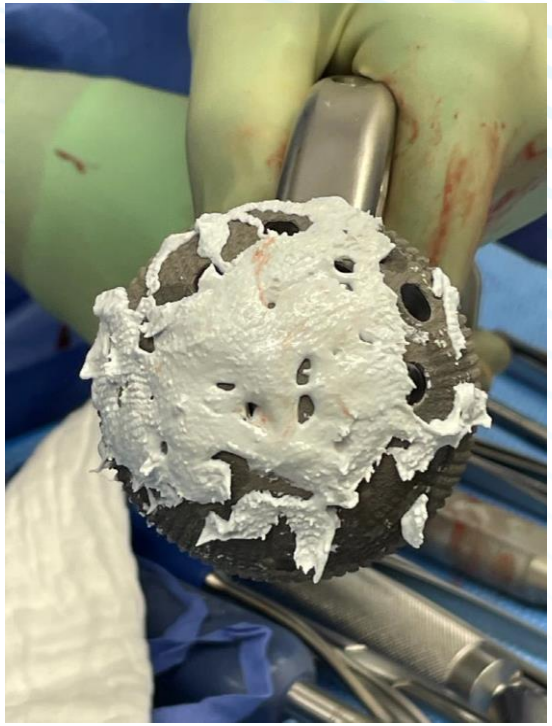
- Male 54-year-old patient with a periprosthetic joint infection (PJI) and osteolysis of the right hip .
- One stage exchange with CERAMENT G

Arthroplasty: Periprosthetic Joint Infection (PJI)

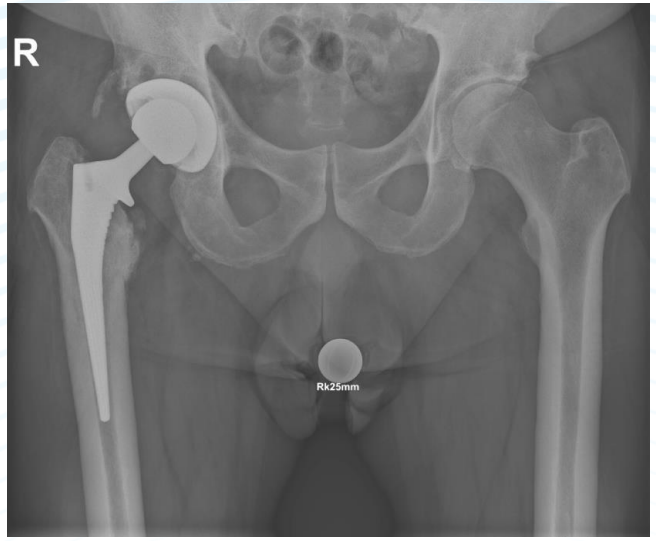
BONESUPPORT

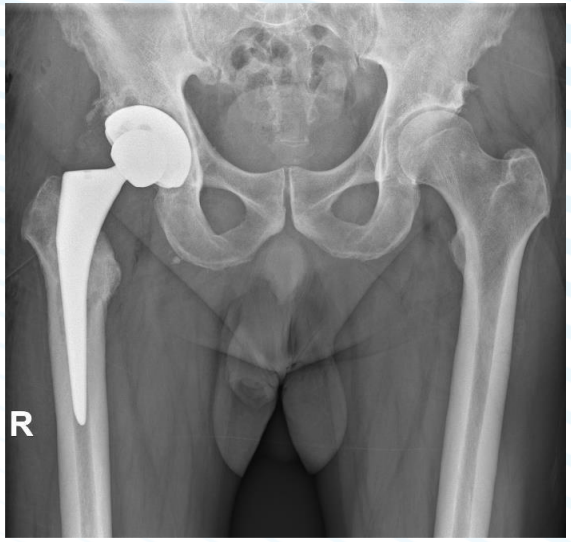
Arthroplasty





Arthroplasty: Periprosthetic Joint Infection (PJI)





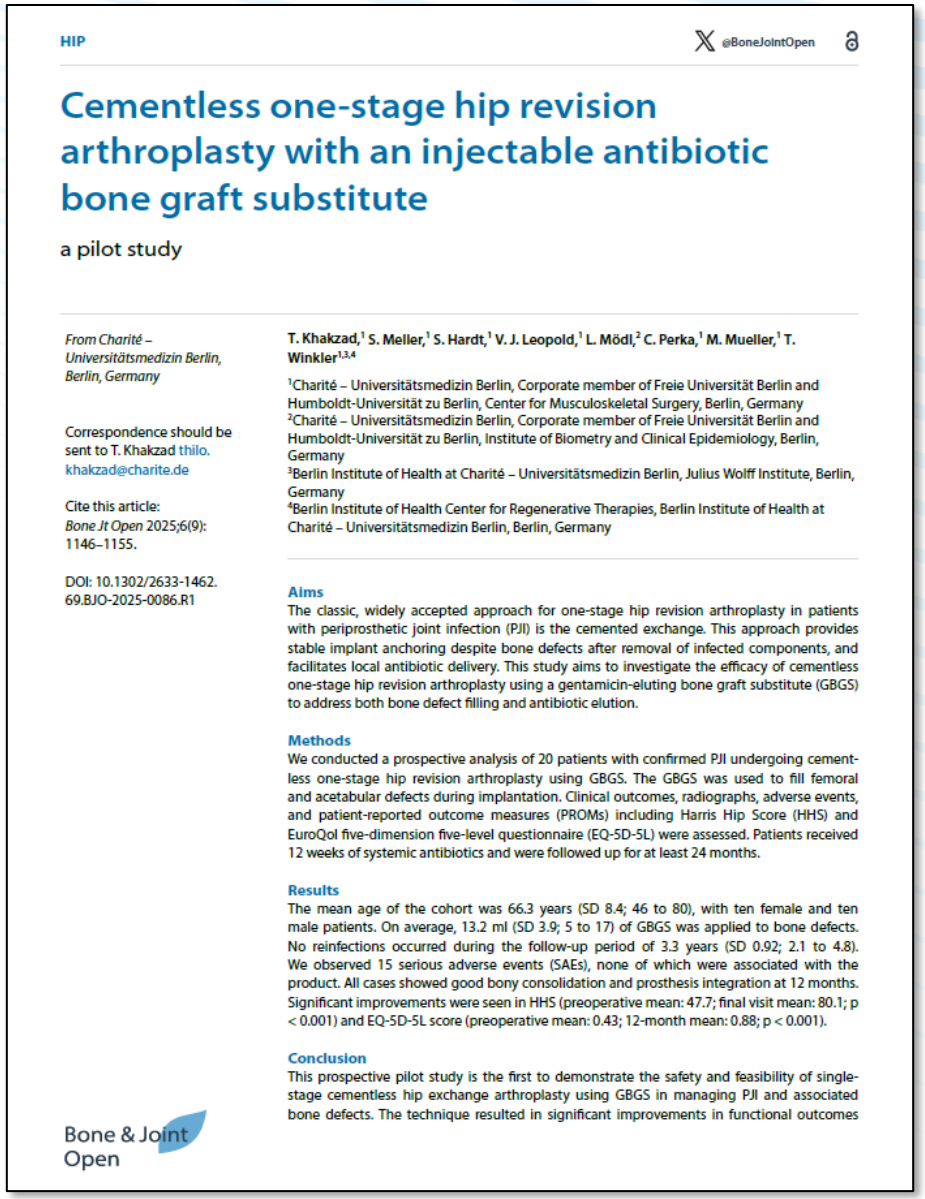
Pre-op

follow-up

Arthroplasty: Periprosthetic Joint Infection (PJI)

BONESUPPORT

Arthroplasty



HIP

@BoneJointOpen

Cementless one-stage hip revision arthroplasty with an injectable antibiotic bone graft substitute

a pilot study

From Charité – Universitätsmedizin Berlin, Berlin, Germany

Correspondence should be sent to T. Khakzad thilo.khakzad@charite.de

Cite this article: *Bone Jt Open* 2025;6(9): 1146–1155.

DOI: 10.1302/2633-1462.69.BJO-2025-0086.R1

T. Khakzad,[1] S. Meller,[1] S. Hardt,[1] V. J. Leopold,[1] L. Mödl,[2] C. Perka,[1] M. Mueller,[1] T. Winkler[1,3,4]

[1]Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Center for Musculoskeletal Surgery, Berlin, Germany
[2]Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Institute of Biometry and Clinical Epidemiology, Berlin, Germany
[3]Berlin Institute of Health at Charité – Universitätsmedizin Berlin, Julius Wolff Institute, Berlin, Germany
[4]Berlin Institute of Health Center for Regenerative Therapies, Berlin Institute of Health at Charité – Universitätsmedizin Berlin, Berlin, Germany

Aims

The classic, widely accepted approach for one-stage hip revision arthroplasty in patients with periprosthetic joint infection (PJI) is the cemented exchange. This approach provides stable implant anchoring despite bone defects after removal of infected components, and facilitates local antibiotic delivery. This study aims to investigate the efficacy of cementless one-stage hip revision arthroplasty using a gentamicin-eluting bone graft substitute (GBGS) to address both bone defect filling and antibiotic elution.

Methods

We conducted a prospective analysis of 20 patients with confirmed PJI undergoing cementless one-stage hip revision arthroplasty using GBGS. The GBGS was used to fill femoral and acetabular defects during implantation. Clinical outcomes, radiographs, adverse events, and patient-reported outcome measures (PROMs) including Harris Hip Score (HHS) and EuroQol five-dimension five-level questionnaire (EQ-5D-5L) were assessed. Patients received 12 weeks of systemic antibiotics and were followed up for at least 24 months.

Results

The mean age of the cohort was 66.3 years (SD 8.4; 46 to 80), with ten female and ten male patients. On average, 13.2 ml (SD 3.9; 5 to 17) of GBGS was applied to bone defects. No reinfections occurred during the follow-up period of 3.3 years (SD 0.92; 2.1 to 4.8). We observed 15 serious adverse events (SAEs), none of which were associated with the product. All cases showed good bony consolidation and prosthesis integration at 12 months. Significant improvements were seen in HHS (preoperative mean: 47.7; final visit mean: 80.1; $p < 0.001$) and EQ-5D-5L score (preoperative mean: 0.43; 12-month mean: 0.88; $p < 0.001$).

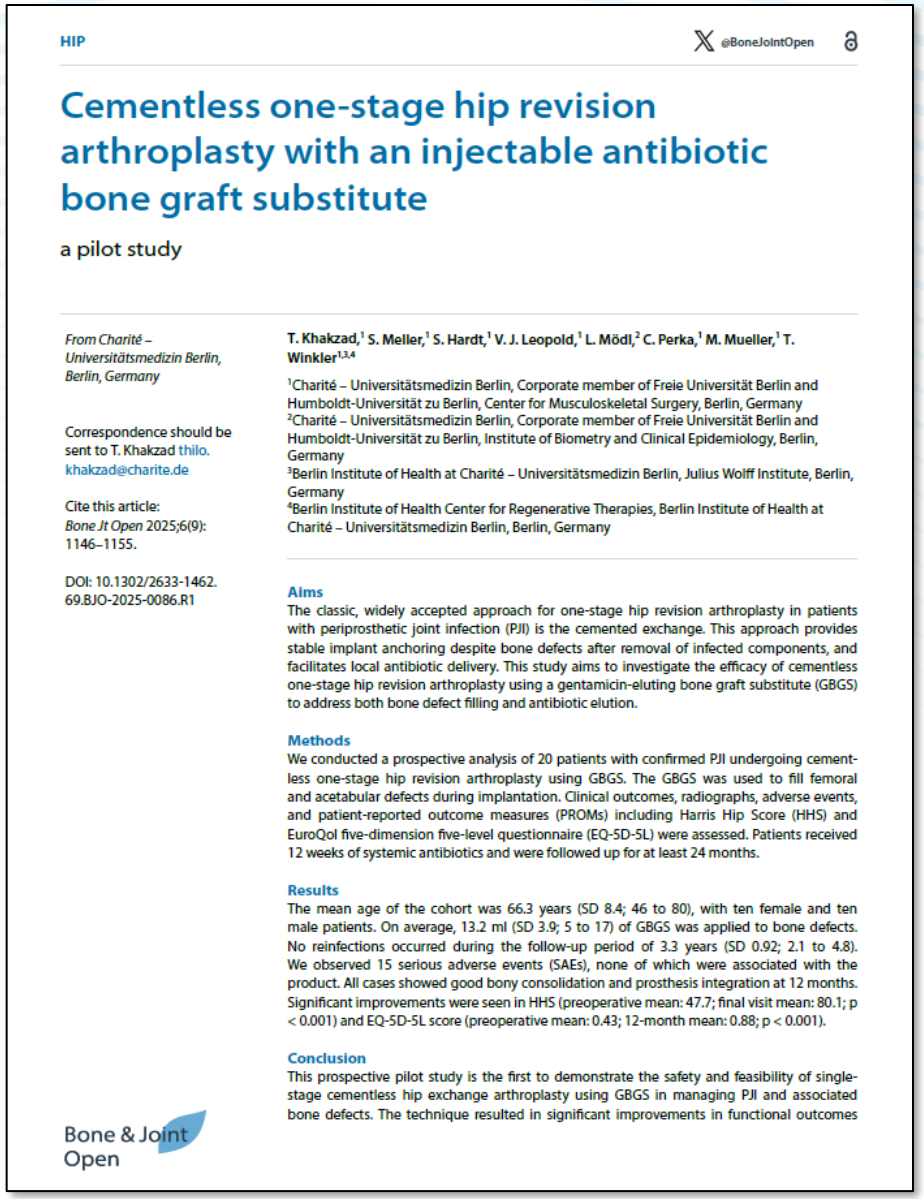
Conclusion

This prospective pilot study is the first to demonstrate the safety and feasibility of single-stage cementless hip exchange arthroplasty using GBGS in managing PJI and associated bone defects. The technique resulted in significant improvements in functional outcomes

Bone & Joint Open

Arthroplasty: Periprosthetic Joint Infection (PJI)

Arthroplasty



HIP

@BoneJointOpen

Cementless one-stage hip revision arthroplasty with an injectable antibiotic bone graft substitute

a pilot study

From Charité – Universitätsmedizin Berlin, Berlin, Germany

T. Khakzad,[1] S. Meller,[1] S. Hardt,[1] V. J. Leopold,[1] L. Mödl,[2] C. Perka,[1] M. Mueller,[1] T. Winkler[1,3,4]

[1]Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Center for Musculoskeletal Surgery, Berlin, Germany
[2]Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Institute of Biometry and Clinical Epidemiology, Berlin, Germany
[3]Berlin Institute of Health at Charité – Universitätsmedizin Berlin, Julius Wolff Institute, Berlin, Germany
[4]Berlin Institute of Health Center for Regenerative Therapies, Berlin Institute of Health at Charité – Universitätsmedizin Berlin, Berlin, Germany

Correspondence should be sent to T. Khakzad thilo.khakzad@charite.de

Cite this article: *Bone Jt Open* 2025;6(9): 1146–1155.

DOI: 10.1302/2633-1462.69.BJO-2025-0086.R1

Aims

The classic, widely accepted approach for one-stage hip revision arthroplasty in patients with periprosthetic joint infection (PJI) is the cemented exchange. This approach provides stable implant anchoring despite bone defects after removal of infected components, and facilitates local antibiotic delivery. This study aims to investigate the efficacy of cementless one-stage hip revision arthroplasty using a gentamicin-eluting bone graft substitute (GBGS) to address both bone defect filling and antibiotic elution.

Methods

We conducted a prospective analysis of 20 patients with confirmed PJI undergoing cementless one-stage hip revision arthroplasty using GBGS. The GBGS was used to fill femoral and acetabular defects during implantation. Clinical outcomes, radiographs, adverse events, and patient-reported outcome measures (PROMs) including Harris Hip Score (HHS) and EuroQol five-dimension five-level questionnaire (EQ-5D-5L) were assessed. Patients received 12 weeks of systemic antibiotics and were followed up for at least 24 months.

Results

The mean age of the cohort was 66.3 years (SD 8.4; 46 to 80), with ten female and ten male patients. On average, 13.2 ml (SD 3.9; 5 to 17) of GBGS was applied to bone defects. No reinfections occurred during the follow-up period of 3.3 years (SD 0.92; 2.1 to 4.8). We observed 15 serious adverse events (SAEs), none of which were associated with the product. All cases showed good bony consolidation and prosthesis integration at 12 months. Significant improvements were seen in HHS (preoperative mean: 47.7; final visit mean: 80.1; $p < 0.001$) and EQ-5D-5L score (preoperative mean: 0.43; 12-month mean: 0.88; $p < 0.001$).

Conclusion

This prospective pilot study is the first to demonstrate the safety and feasibility of single-stage cementless hip exchange arthroplasty using GBGS in managing PJI and associated bone defects. The technique resulted in significant improvements in functional outcomes

Bone & Joint Open

Highlights:

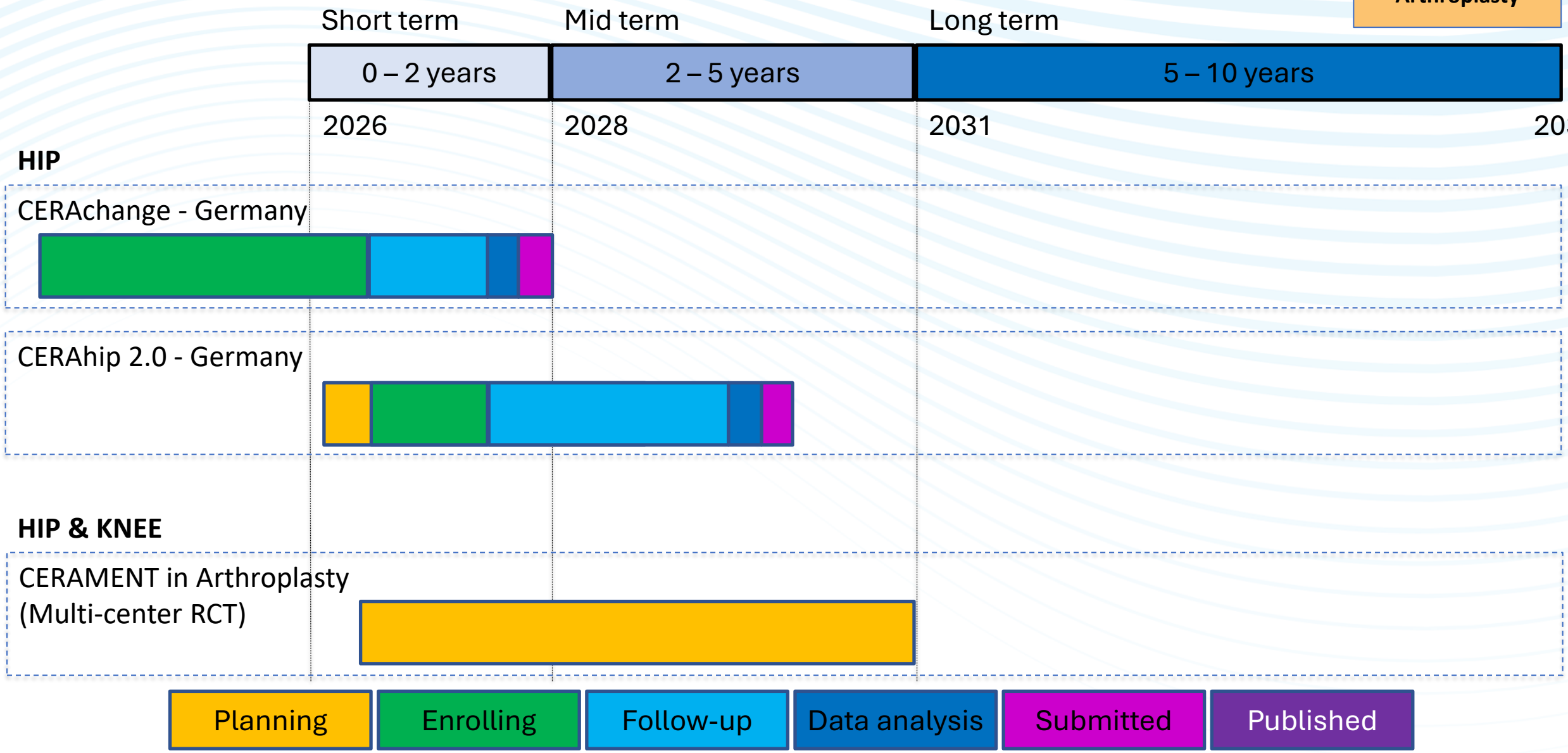
- A prospective analysis on 20 patients with confirmed PJI of the hip (EBJIS criteria)
- Recurrance rate: 0 % during the follow-up period of 3.3 years

- Benchmark: Recurrance rate: Around 15%[1] at 4 years

van den Kieboom J, Tirumala V, et al. One-stage revision is as effective as two-stage revision for chronic culture-negative PJI after total hip and knee arthroplasty. Bone Joint J. 2021 Mar;103-B(3):515-521.

Arthroplasty: Evidence pipeline

Arthroplasty



CERAchange: Two stage hip exchange in PJI: CERAMENT G/V vs. Spacer

BONESUPPORT

Arthroplasty

Design: Pilot-RCT
Indication: PJI of the hip
Patients: 18 of 20 pat. enrolled
Treatment: Two stage hip exchange,
First stage spacer vs. CERAMENT G and V
Hospital: University Hospital Munich LMU

Enrolling

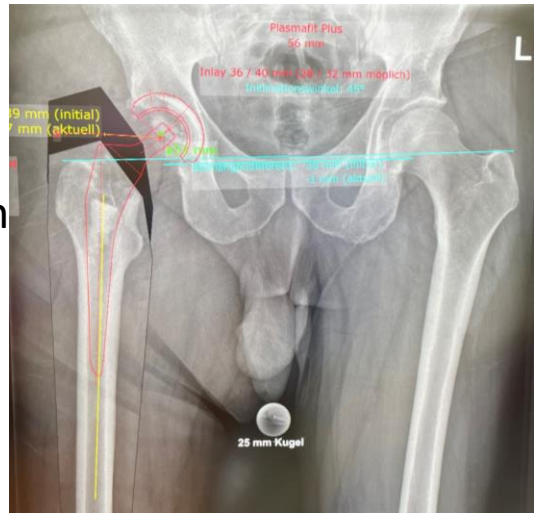
CERAchange: Two stage hip exchange in PJI: CERAMENT G/V vs. Spacer

BONESUPPORT

Arthroplasty

1st stage
Removal of
THA

2nd stage
Implantation
Of new THA



Enrolling

CERAhip 2.0: Single-Stage-Revision in PJI of the hip with CERAMENT G

BONESUPPORT

Arthroplasty

Design: Prospective treatment group with retrospective control
Indication: PJI of the hip
Patients: 30 patients
Treatment: Single-Stage-Exchange in PJI of the hip with CERAMENT G
Hospital: Charitè University Hospital Berlin

Planning

CERAMENT in Arthroplasty

BONESUPPORT

Arthroplasty

Design: International multi-center RCT
Indication: PJI of the hip / knee
Patients: around 300 pat.
Treatment: Single-Stage-Exchange in PJI of the hip / knee with CERAMENT G and short duration of systemic antibiotics vs. no local antibiotic and long duration of systemic antibiotics
Hospital: around 20 hospitals

Planning

BONESUPPORT

Foot & Ankle

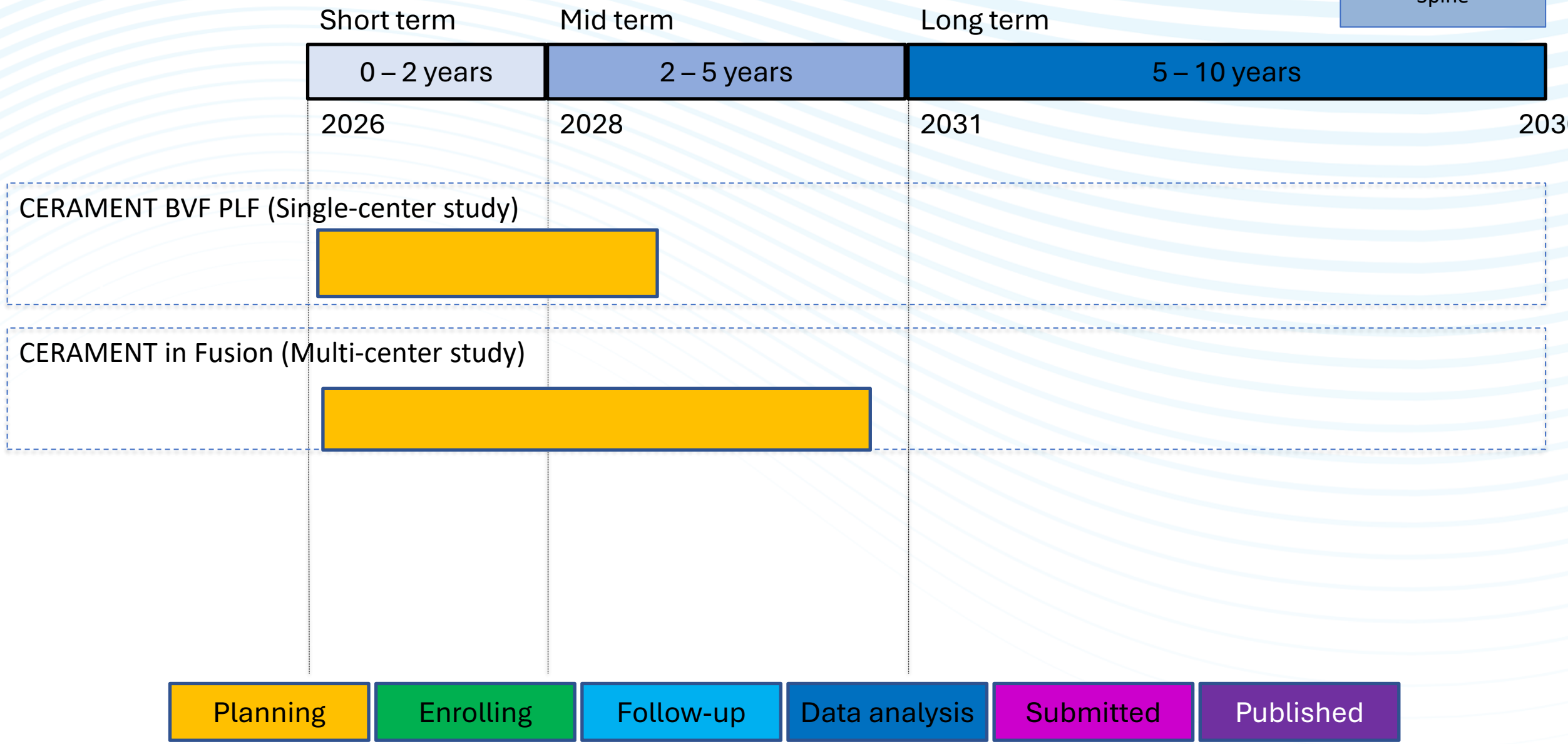
Trauma

Arthroplasty

Spine

Spine: Evidence pipeline

Spine

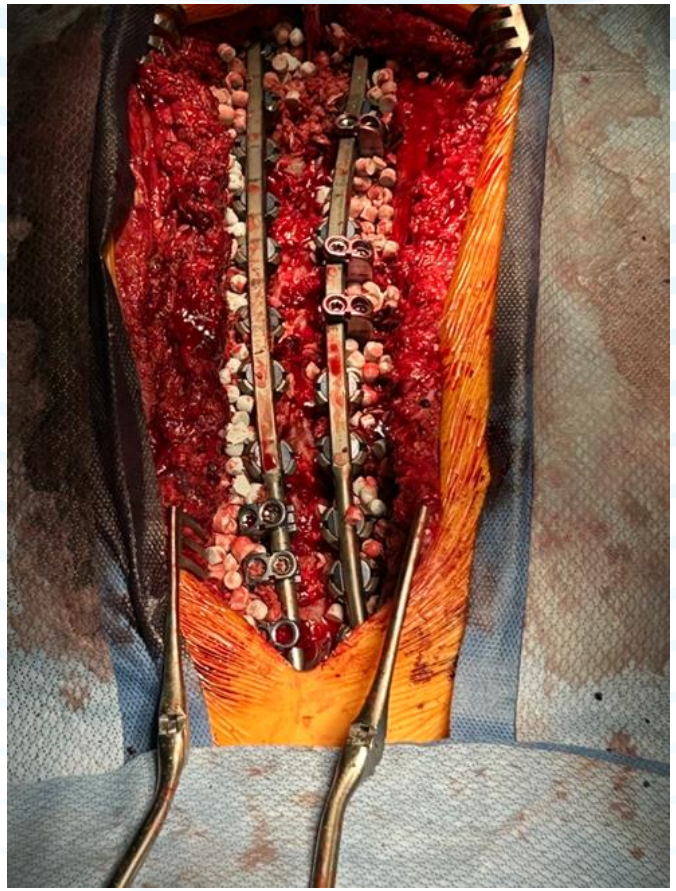


Spine: Evidence pipeline: CERAMENT BVF PLF

BONESUPPORT

Spine

Design: Single center case series
Indication: Posterolateral Fusion (PLF)
Patients: 20 patients planned
Treatment: CERAMENT BVF plus autograft in instrumented PLF
Hospital: Single center in Canada



Planning

Spine: Evidence pipeline: CERAMENT in Fusion

BONESUPPORT

Spine

Design: Multi-center study
Indication: PLF in high-risk patients for infection
Patients: ~300-400 pat
Treatment: Antibiotic eluting CERAMENT plus autograft in instrumented PLF
Hospital: Multi-center study in Canada

Planning

BONESUPPORT

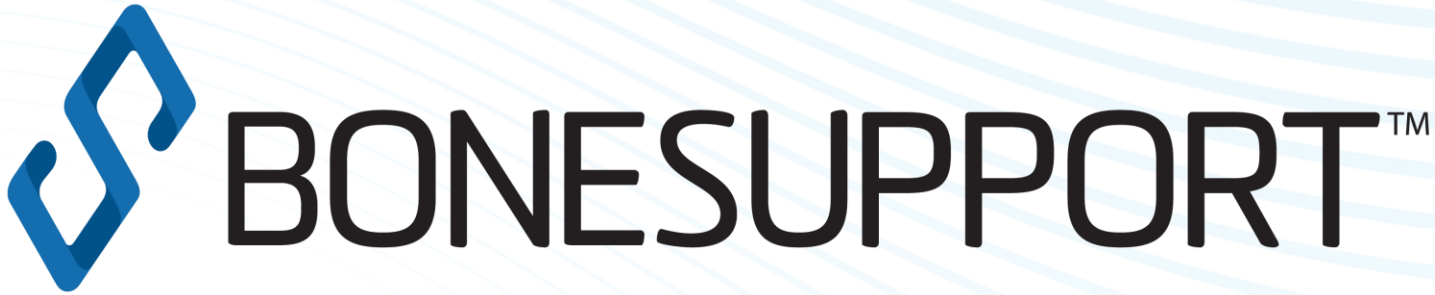
Foot & Ankle

Trauma

Arthroplasty

Spine

BONESUPPORT



Q&A

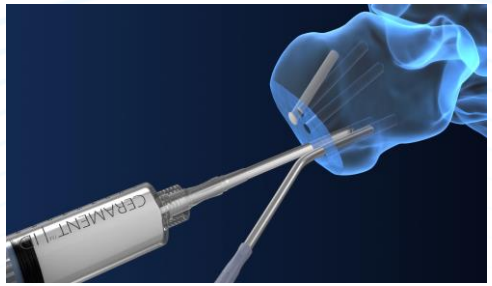
Capital Markets Day 2026

Product Demonstrations

Fika and product demonstrations

Please grab a coffee and visit one of the mixing stands to see CERAMENT being mixed and find out about how it is used in our different indications

A. FOOT & ANKLE



Diabetic foot osteomyelitis and the Silo Technique

Karin Kings
Director Medical Education EUROW

B. TRAUMA

Open trauma and fracture-related infection, with the 2-CAN delivery device

Candice Maxwell
Director Medical Education US

C. ARTHROPLASTY

Hip revisions

Pia Walby
Director Product Management

[1] INSERT FOOTNOTE

Capital Markets Day 2026

Clinical Experiences

Michael Diefenbeck, Chief Medical Officer

Introducing the presenters

Sebastian Meller, MD

Consultant for Orthopaedic surgery

Head of the Department of Hip Arthroplasty and Infection Surgery
Charité, Universitätsmedizin Berlin

Paul E. Matuszewski, MD

Associate Professor of Orthopaedic Surgery

Chief, Orthopaedic Trauma Service
Director, Orthopaedic Trauma Research
Department of Orthopedic Surgery and Sports Medicine
College of Medicine, University of Kentucky

Single stage approach in PJI treatment of the Hip

Investor Meeting 2026

Sebastian Meller

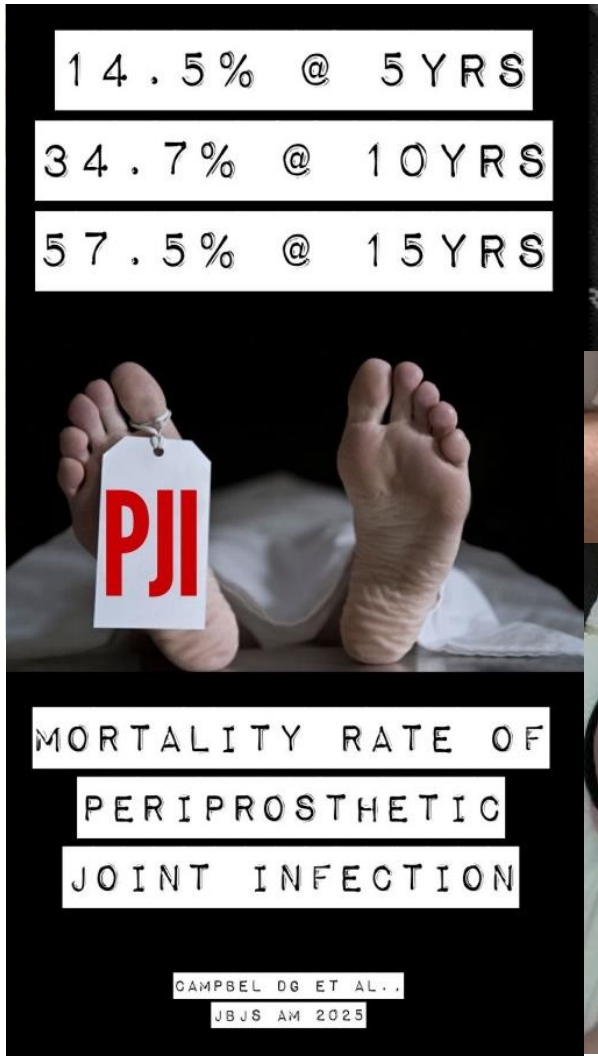
CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN

CENTRUM FÜR
MUSKULOSKELETALE
CHIRURGIE

JULIUS WOLFF INSTITUT

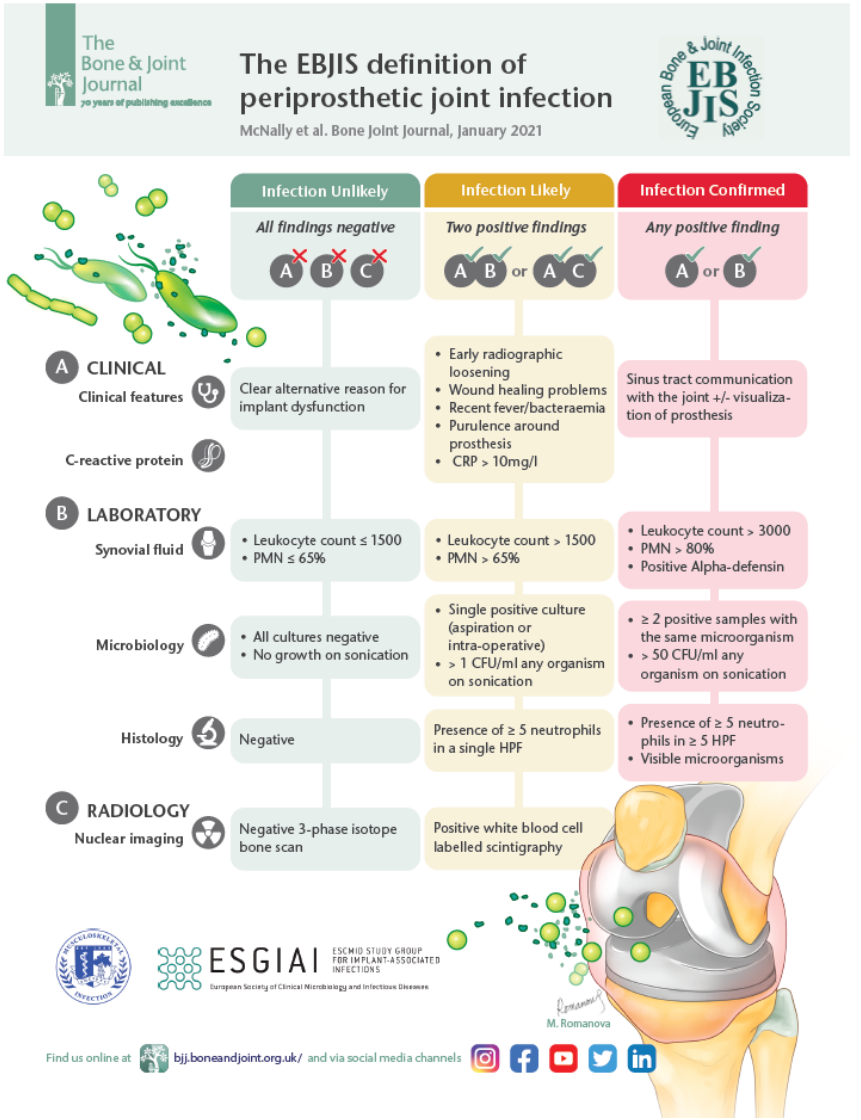
Periprosthetic Joint infections - Challenges

- Major problem
- Time-consuming
- High costs
- Worse function
- Worse outcomes
- High morbidity and mortality



PJI Definition

- Infection of a joint replacement and surrounding tissues
- **Biofilm-driven** predominantly caused by **bacterial** pathogens
- Difficult to **diagnose → EBJIS / Charité Definition**
- Often requires **revision surgery**, implant exchange and prolonged antimicrobial therapy



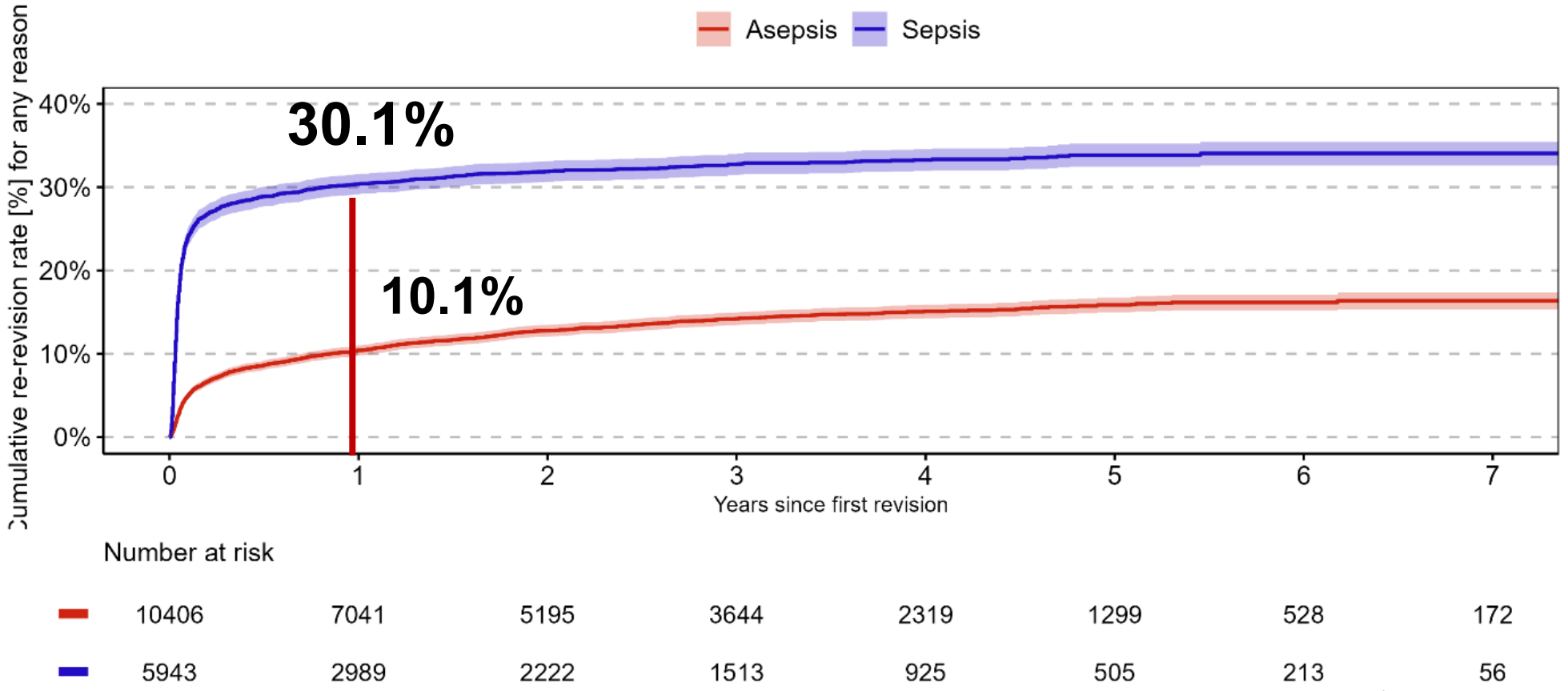
Reasons for Hip Reoperations in Germany

	Proportion [%]		m/f [%]	BMI	ASA
Infection	16.4	73	50 / 50	28.1	2.6
Loosening	22.7	75	42 / 58	26.9	2.5
Cup	12.0	75	35 / 65	26.7	2.4
Stem	8.7	75	51 / 49	27.4	2.4
Cup and stem	2.0	77	46 / 54	26.5	2.6
Osteolysis with fixed component	0.6	73	58 / 42	26.4	2.3
Cup	0.3	74.5	65 / 35	27.2	2.2
Stem	0.2	68.5	67 / 33	25.7	2.4
Cup and stem	0.1	75	35 / 65	26.4	2.3
Periprosthetic fracture	15.9	81	34 / 66	25.8	2.7
Dislocation	13.6	79	35 / 65	26.1	2.6
Wear	5.8	74	42 / 58	27.0	2.4
Component failure	2.1	75	38 / 62	26.4	2.5
Malalignment	1.9	73	31 / 69	26.4	2.4
Progression of arthrosis	0.5		33 / 67	25.7	2.3
Condition after removal	11.1	72	49 / 51	27.8	2.6
Other reasons	9.3	74	39 / 61	27.0	2.4

The German Arthroplasty Registry (EPRD)

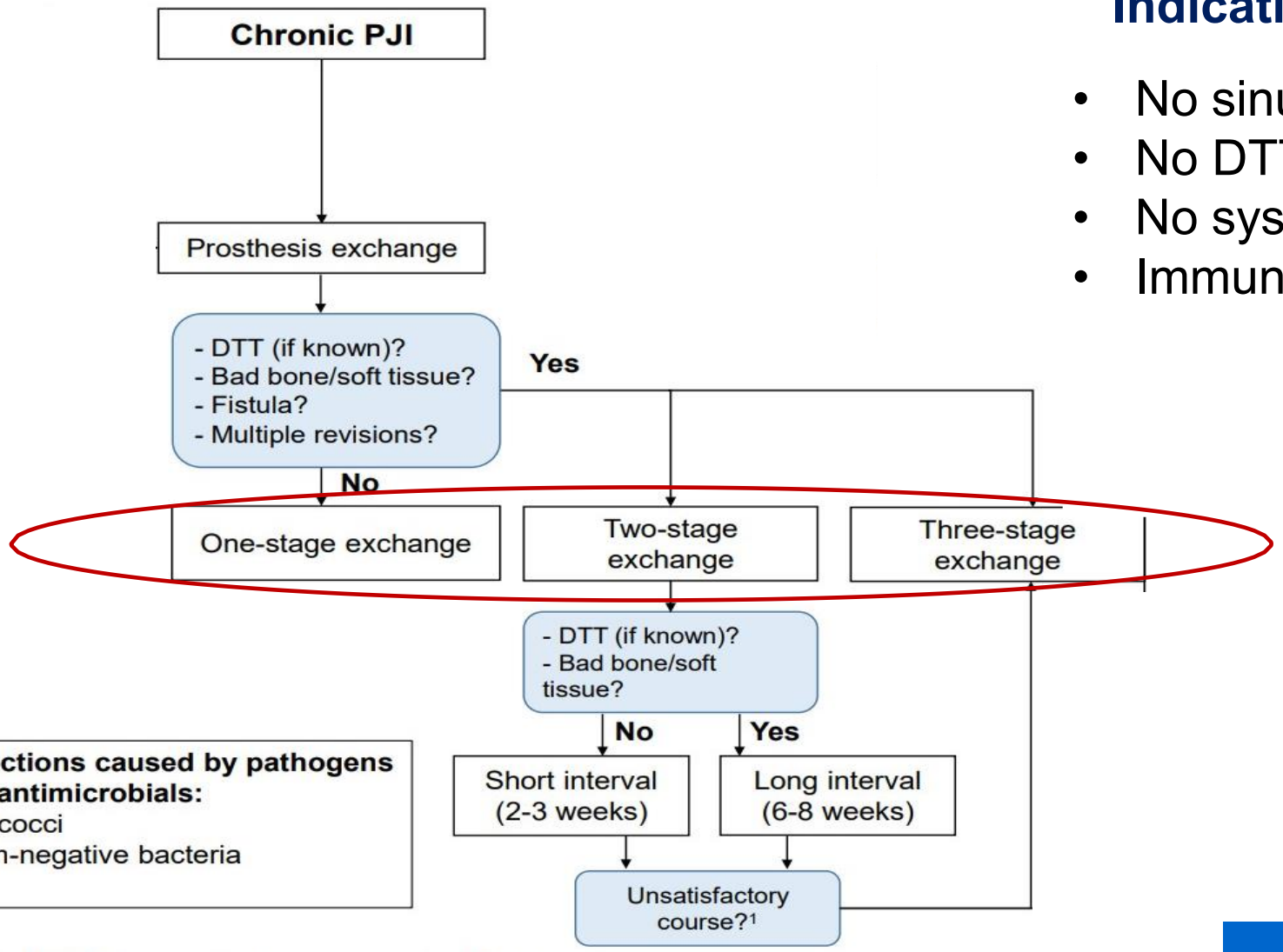
Almost 30 % of all hip revisions are beeing caused by infections!

Re-revision rate after hip revision arthroplasty



The best surgical treatment strategy

Treatment algorithm for chronic PJI



DTT = difficult-to-treat infections caused by pathogens resistant to biofilm-active antimicrobials:
- Rifampin-resistant staphylococci
- Ciprofloxacin-resistant gram-negative bacteria
- Fungi (Candida)

[1] clinical signs of infection, elevated CRP, intraoperative pus, compromised tissue

Indication 1-stage exchange

- No sinus tract /good soft tissue
- No DTT (if known)
- No systemic infections
- Immunocompetent host

PRO-IMPLANT FOUNDATION

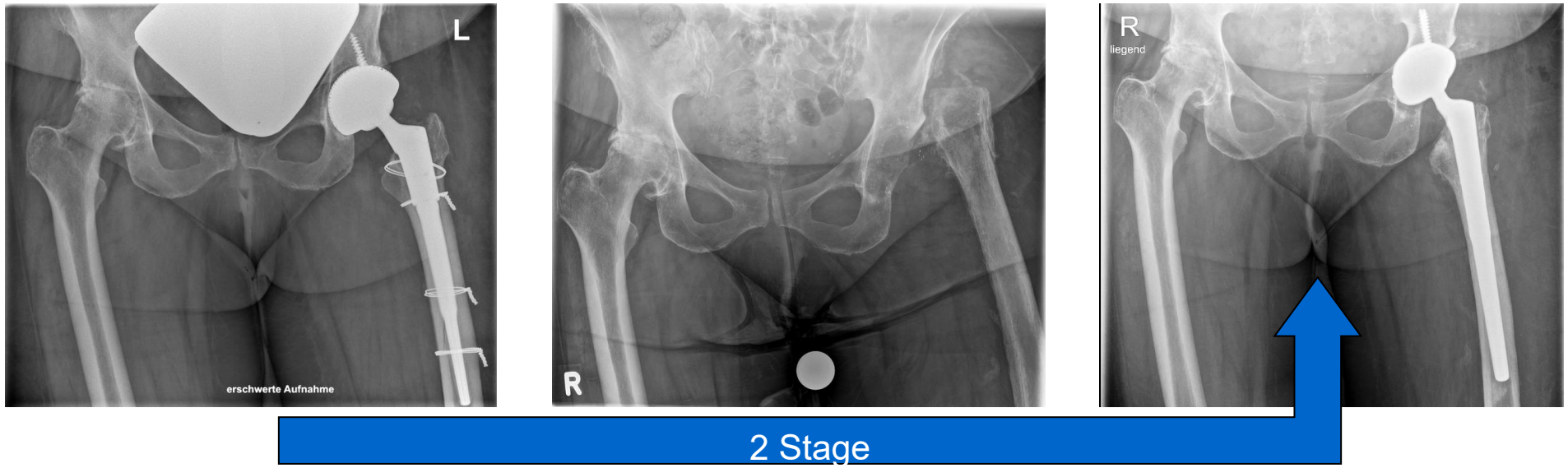
JULIUS WOLFF INSTITUT

Treatment algorithm – 2 Stage Exchange

Current Gold Standard and most frequently used technique:

Two Stage Exchange (with antibiotic loaded spacer) is currently the most common procedure in complex PJI cases for hip and knee revision

Tsukayama et al. JBJS 1996, Masri et al. JOA 2007, Ibrahim et al. BJJ 2014, Whitehouse et al. BJJ 2017, Petis et al. JBJS 2019, Goumenos, Meller et al. JOA 2024



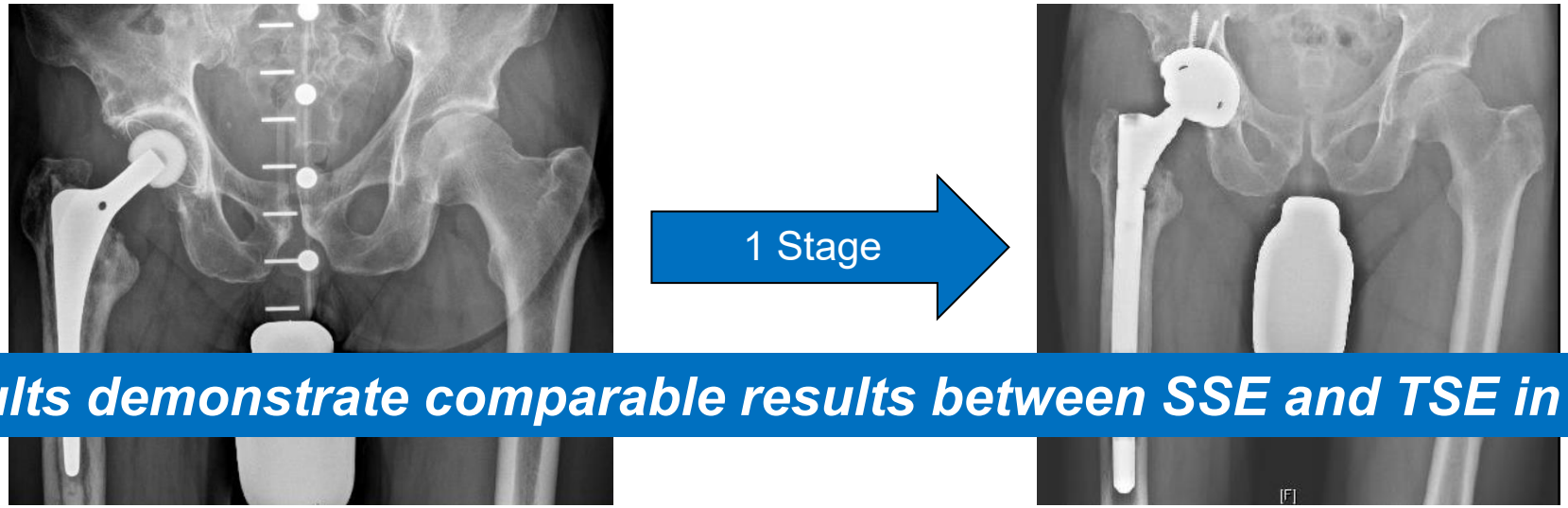
Treatment algorithm – 1 stage exchange

Reliable Option with increasing application (in centers):

Single Stage Exchange successful in “good **Hosts**” and **sensitive Pathogens**

Thakrar et al. BJJ 2019, van den Kieboom et al. BJJ 2021, Lamo-Espinosa et al. J Am Acad Orthop Surg 2024;

,



„(…) the results demonstrate comparable results between SSE and TSE in PJI of the hip…“

Treatment algorithm – We need to improve our results

→ However, treatment failure rates in complex PJI remains **high**.

→ **Failure rates / reinfection rates with „strict criteria“ > 20%**

→ **Identifying and modifying the risk factors involved can be crucial for better outcomes.**

Host Factors Local Antibiotics Defect / Dead Space Management

Gomez et al. JBJS 2015
Cancienne et al. JOA 2017
Tan et al. JOA 2018
Kandel CE et al O F Infect Dis. 2019
Goumenos, Meller et al, J Arthoplasty 2024

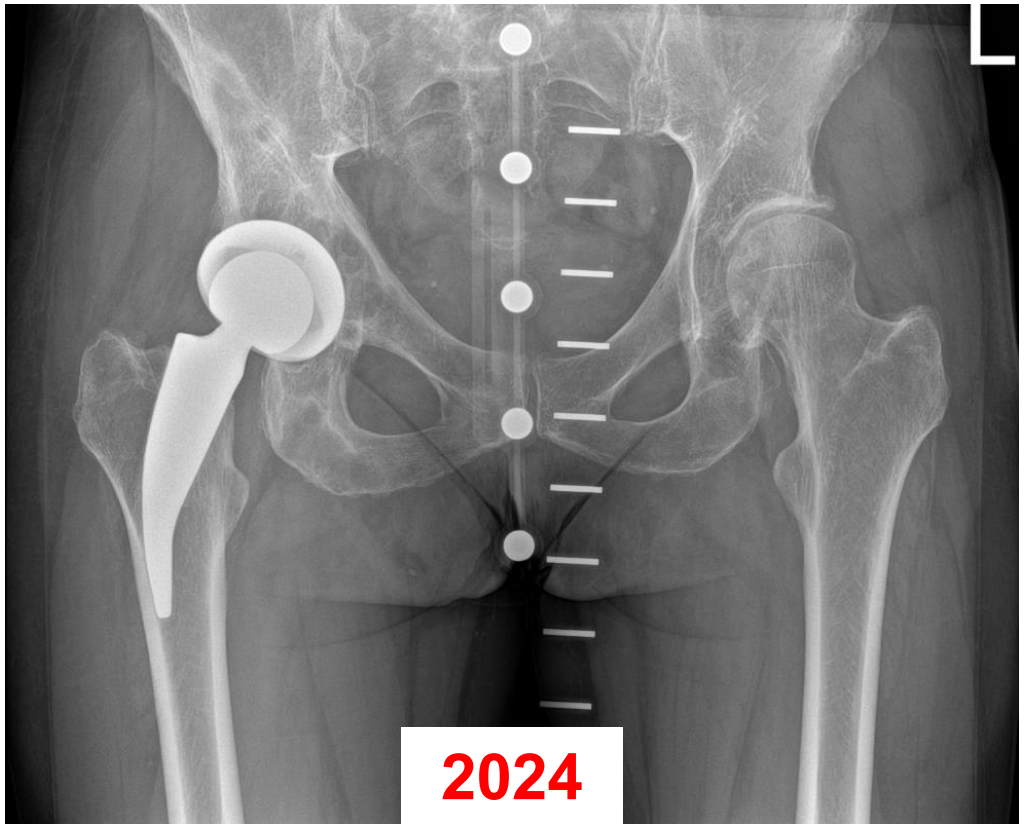
Our Surgical Approach for a single-stage exchange

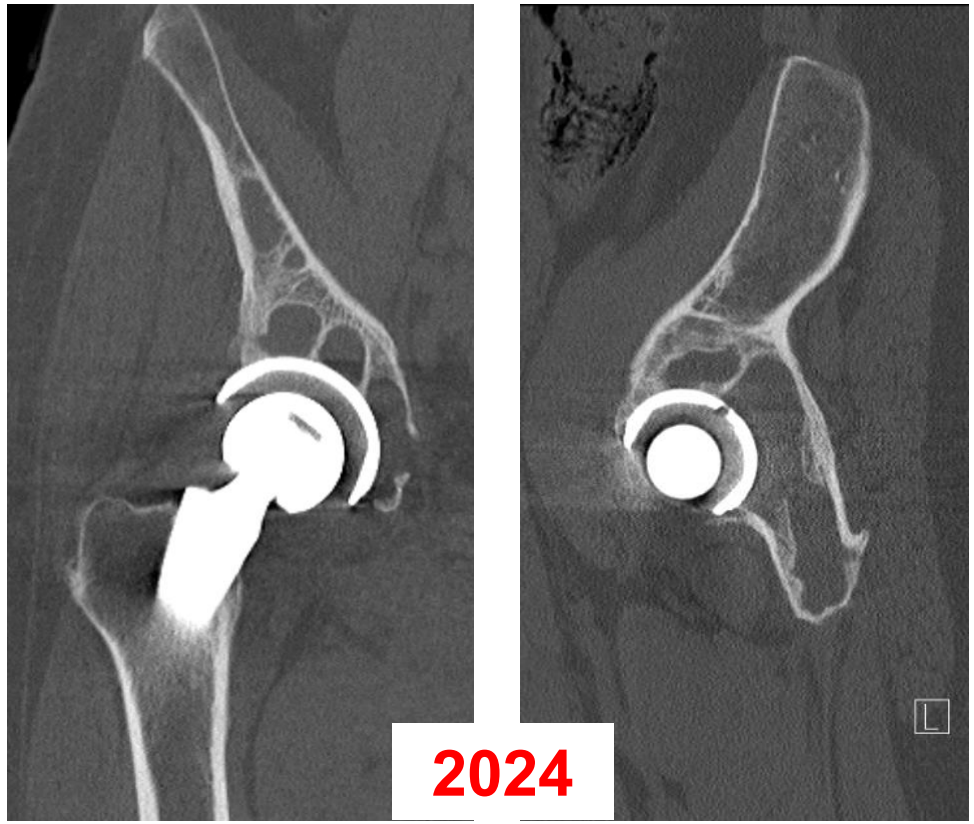
Case

Ulrike 59 years PJI right hip

Total Hip Arthroplasty (THA) 09/2021

Steatosis hepatis





Case

Ulrike 59 years PJI right hip

THA 09/2021

Steatosis hepatis

Aspiration:

MIKROBIOLOGISCHER BEFUND

Entnahmedatum/-zeit: 25.03.24 / 09:29

Untersuchungsmaterial :
Abstrich (intra-OP) tief
rechte Hüfte
Anforderung:
Untersuchung auf Pilze
Erreger und Resistenz
Ergebnis der Kultur :
1.n.Anr. Staphylococcus capitis
- Wachstum nach 14 Tagen Bebrütung.

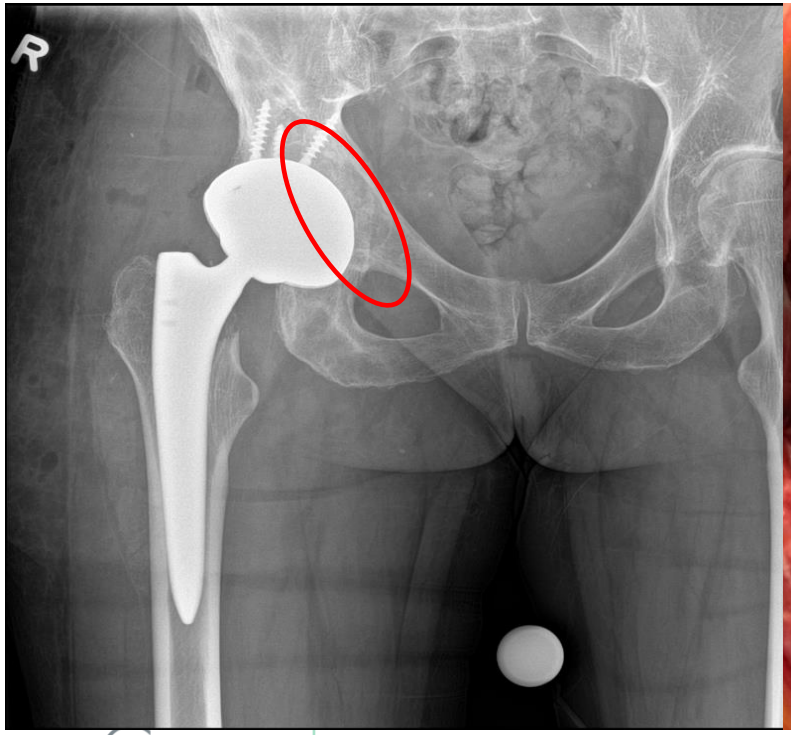
ANTIBIOGRAMM:	1. MHK
Ampicillin/Sulb. i.v.	S
Piperacillin/Tazob.	S
Oxacillin	S <=0,25
Flucloxacillin	S
Cefazolin	S
Cefuroxim i.v.	S
Imipenem	S

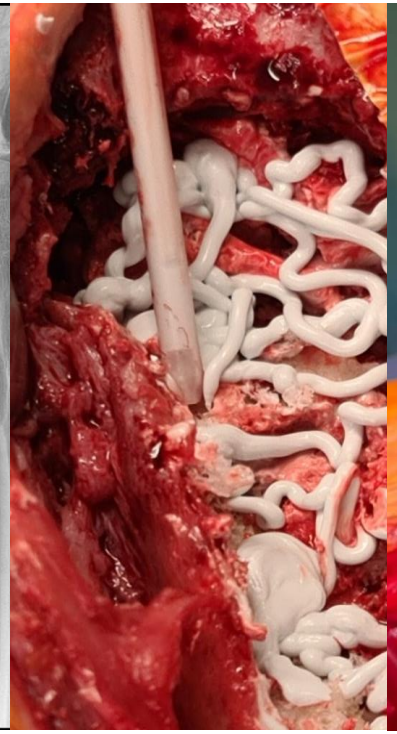
Case

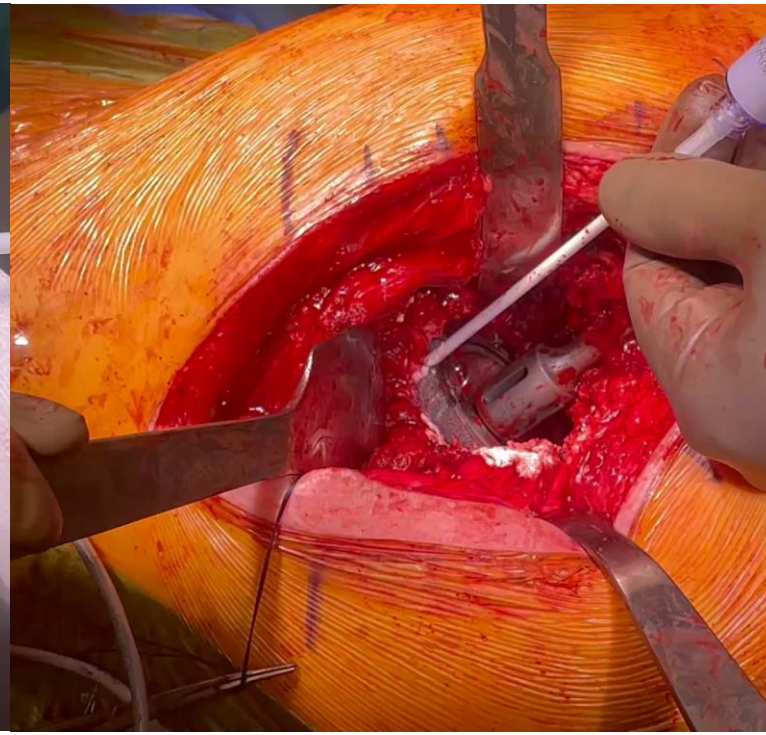
Ulrike 59 years PJI right hip

→ **Single Stage Exchange** with allograft and CERAMENT G

→ Multi disciplinary team approach: Levofloxacin 2x500mg p.o. plus Rifampicin 2x450mg p.o. for 12 weeks





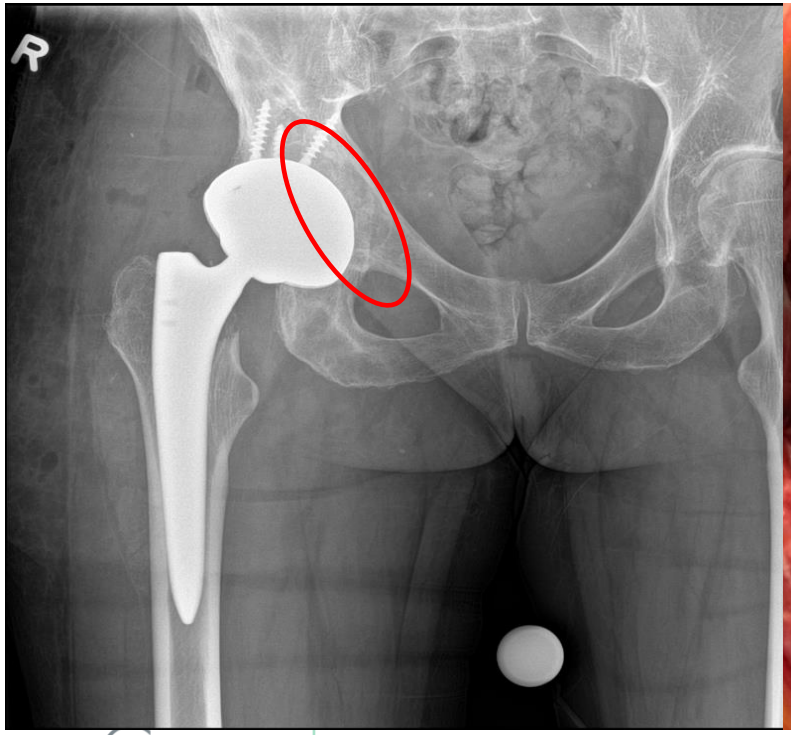
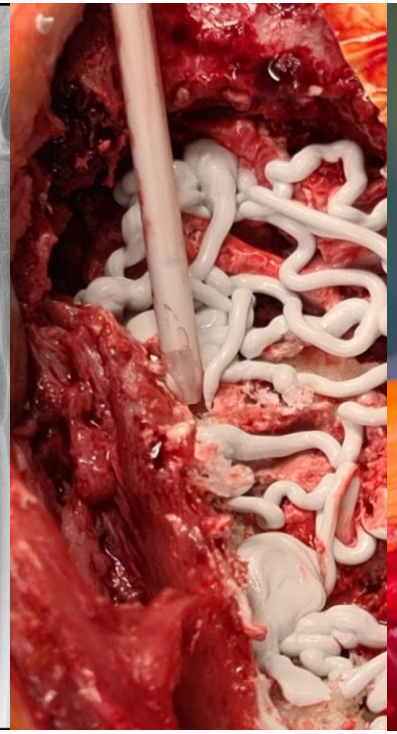


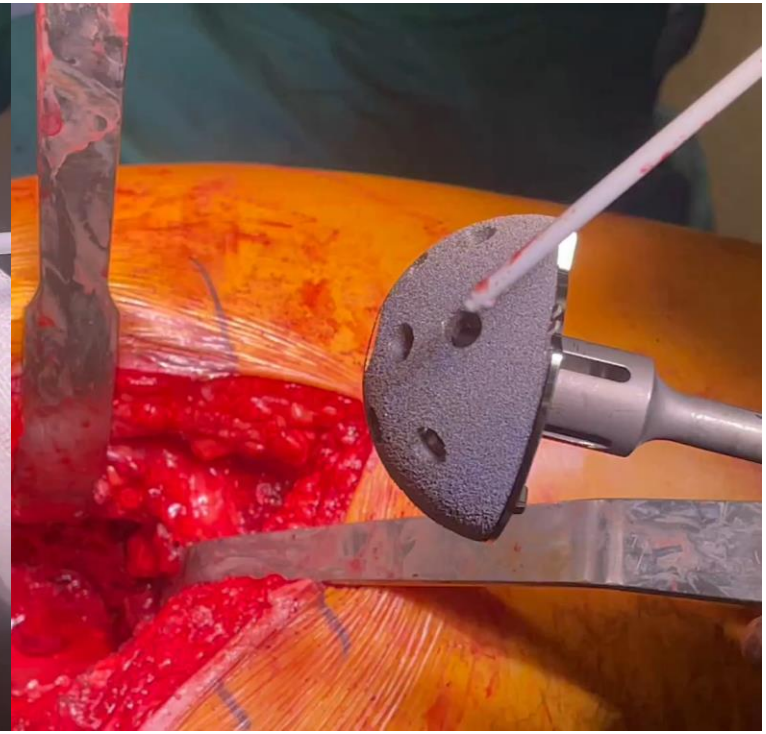
Case

Ulrike 59 years PJI right hip

→ **Single Stage Exchange** with allograft and CERAMENT G

→ Multi disciplinary team approach: Levofloxacin 2x500mg p.o. plus Rifampicin 2x450mg p.o. for 12 weeks



Our Surgical Approach

CERAMENT Augmentation Technique

CERAMENT in Stem Revision

Step 1: Drying the Bone / Femur

Absorb blood and fluids using compresses and suction device to keep the area dry for optimal visibility and application.

Step 2: Application of CERAMENT

Filling the femur retrogradely without pressure. Insert CERAMENT deep into the femur under the stem.

My CERAMENT Technical Augmentation II

Step 3: Augment the Implant with CERAMENT

Apply CERAMENT on the surface of the implant. Use notches, grooves and holes on the implant to fill them.

Step 4: Prosthesis Implantation

Complete the surgical procedure by implanting the prosthesis as per standard protocol.

My CERAMENT Technical Augmentation III

Step 5: Filling and Augmenting Dead Space and Defects with CERAMENT

Fill any remaining dead space, cavities, or defects between the bone and the implant.

My CERAMENT Technical Augmentation IV

Step 5: Filling and Augmenting Dead Space and Defects with CERAMENT

Fill any remaining dead space, cavities, or defects between the bone and the implant.

Step 6: Compression and Drying of CERAMENT

Allow CERAMENT to fully harden and stabilize before proceeding.

Wait 8-10 minutes to fully set and harden.

My CERAMENT Technical Augmentation IV

Step 5: Filling and Augmenting Dead Space and Defects with CERAMENT

Fill any remaining dead space, cavities, or defects between the bone and the implant.

Step 6: Compression and Drying of CERAMENT

Allow CERAMENT to fully harden and stabilize before proceeding.

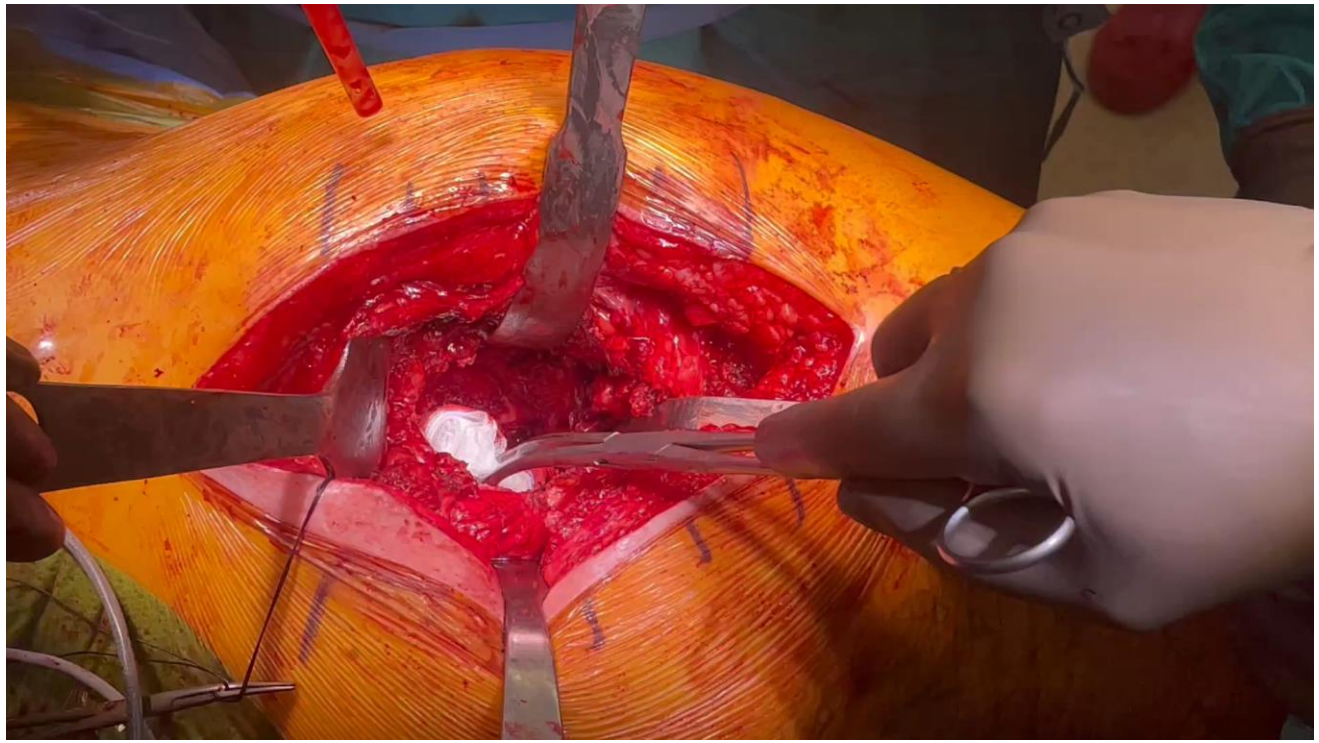
Wait 8-10 minutes to fully set and harden.

➔ Make a X-Ray

CERAMENT in CUP Revision

Step 1: Drying the Bone / Acetabulum

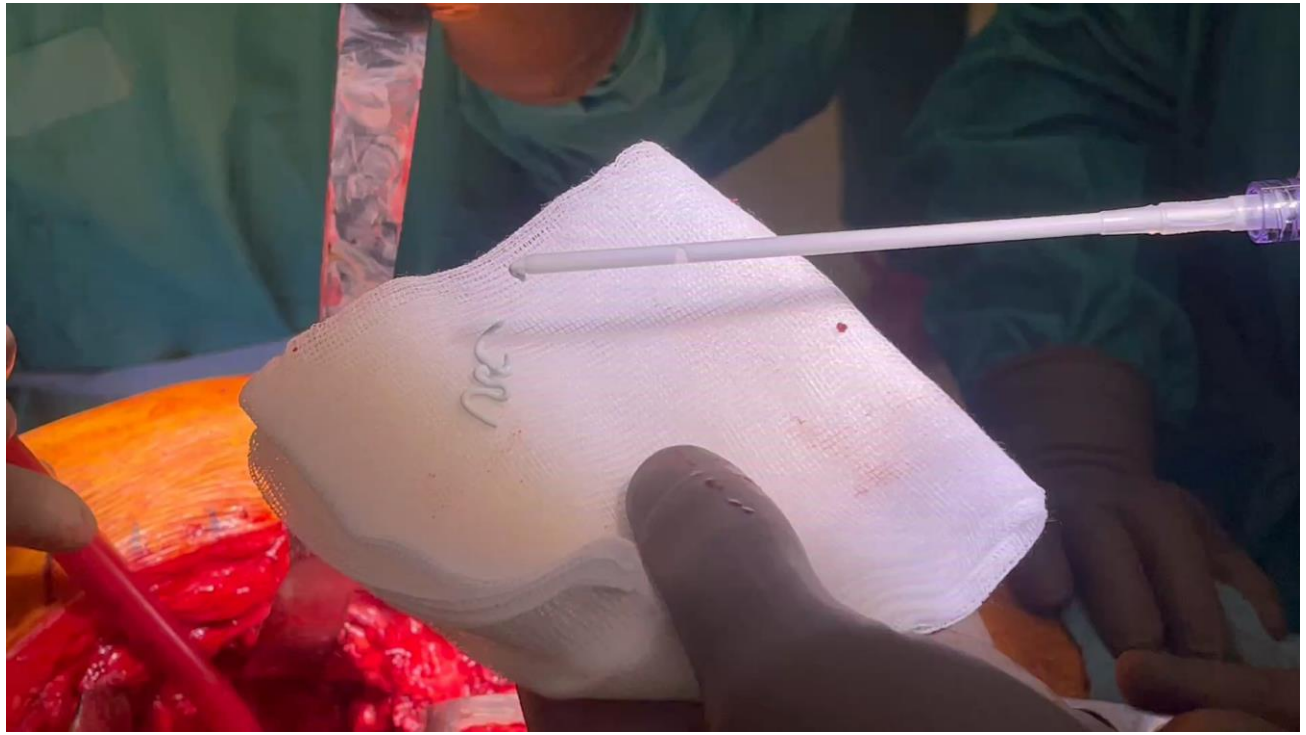
Absorb blood and fluids using compresses and suction device to keep the area dry for optimal visibility and application.



CERAMENT in CUP Revision

Step 2: Application of CERAMENT

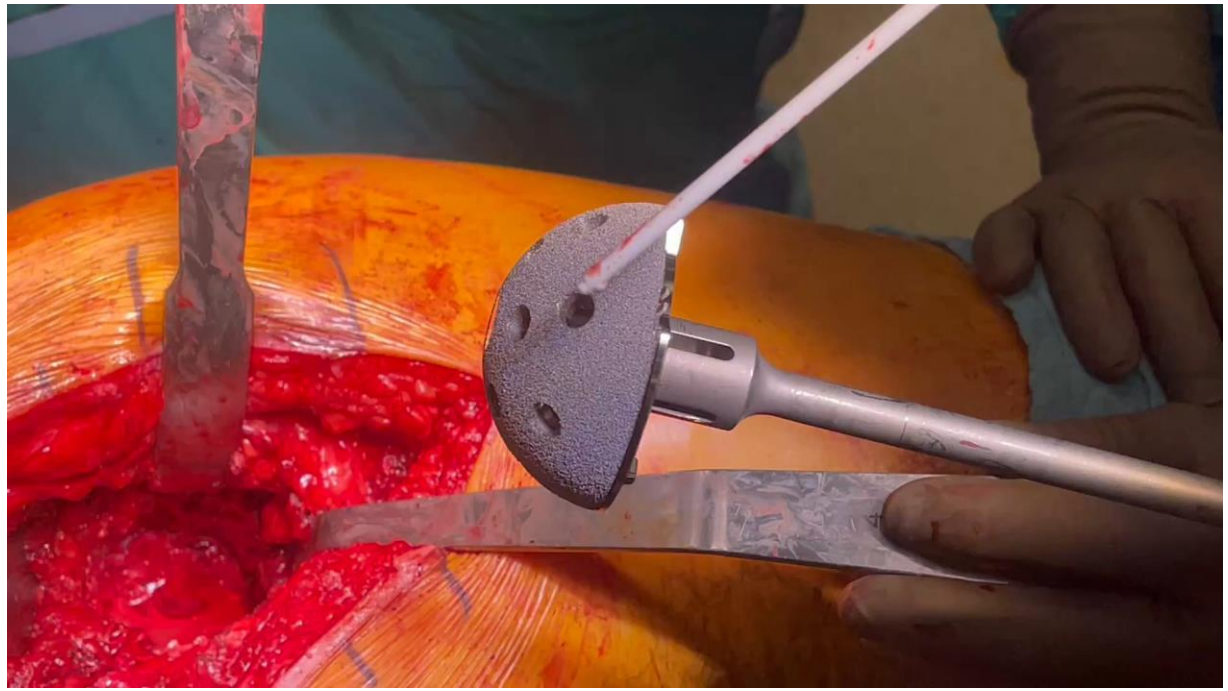
CERAMENT is applied into bony defects (osteolytic areas, cysts, cavitary lesions), followed by a **sandwich technique** using structural allografts and **impaction bone grafting again with CERAMENT** for enhanced defect filling and mechanical stability.



CERAMENT in CUP Revision

Step 3: Augment the Implant with CERAMENT

Apply CERAMENT on the surface of the implant. Use notches, grooves and holes on the implant to fill them.



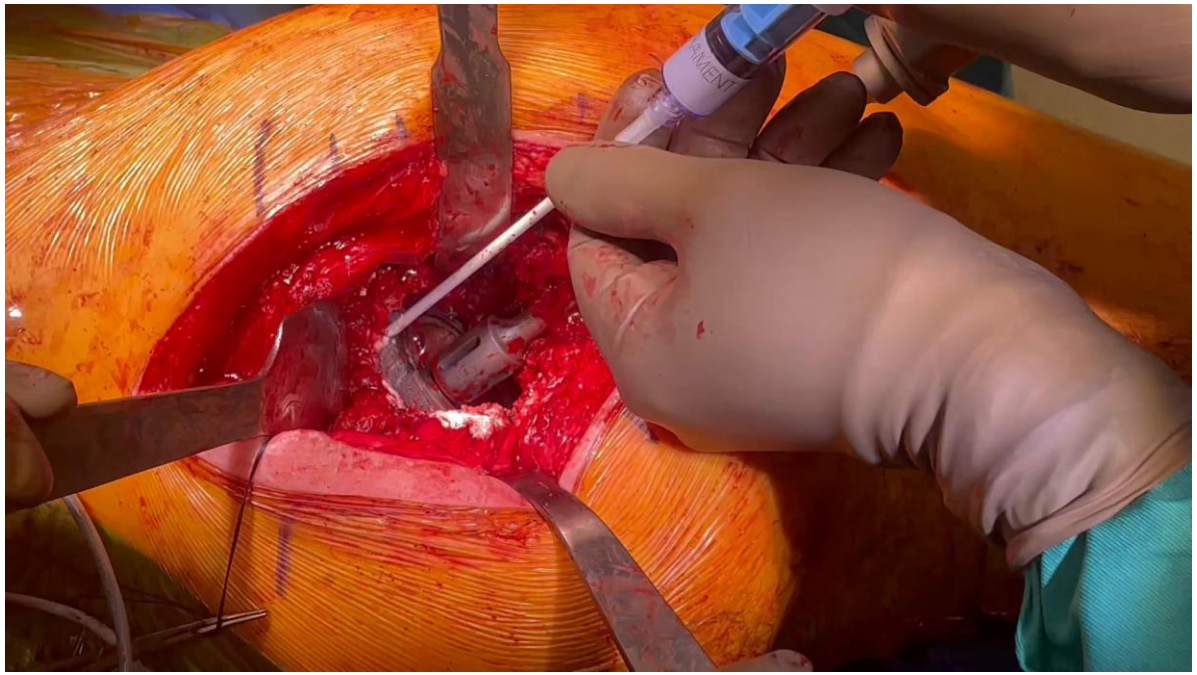
Step 4: Prosthesis Implantation

Complete the surgical procedure by implanting the prosthesis as per standard protocol.

CERAMENT in CUP Revision

Step 5: Filling and Augmenting Dead Space and Defects with CERAMENT

Fill any remaining dead space, cavities, or defects between the bone and the implant.



Step 6: Compression and Drying of CERAMENT

Allow CERAMENT to fully harden and stabilize before proceeding.

Wait 8-10 minutes to fully set and harden.

CERAMENT in CUP Revision

Step 5: Filling and Augmenting Dead Space and Defects with CERAMENT

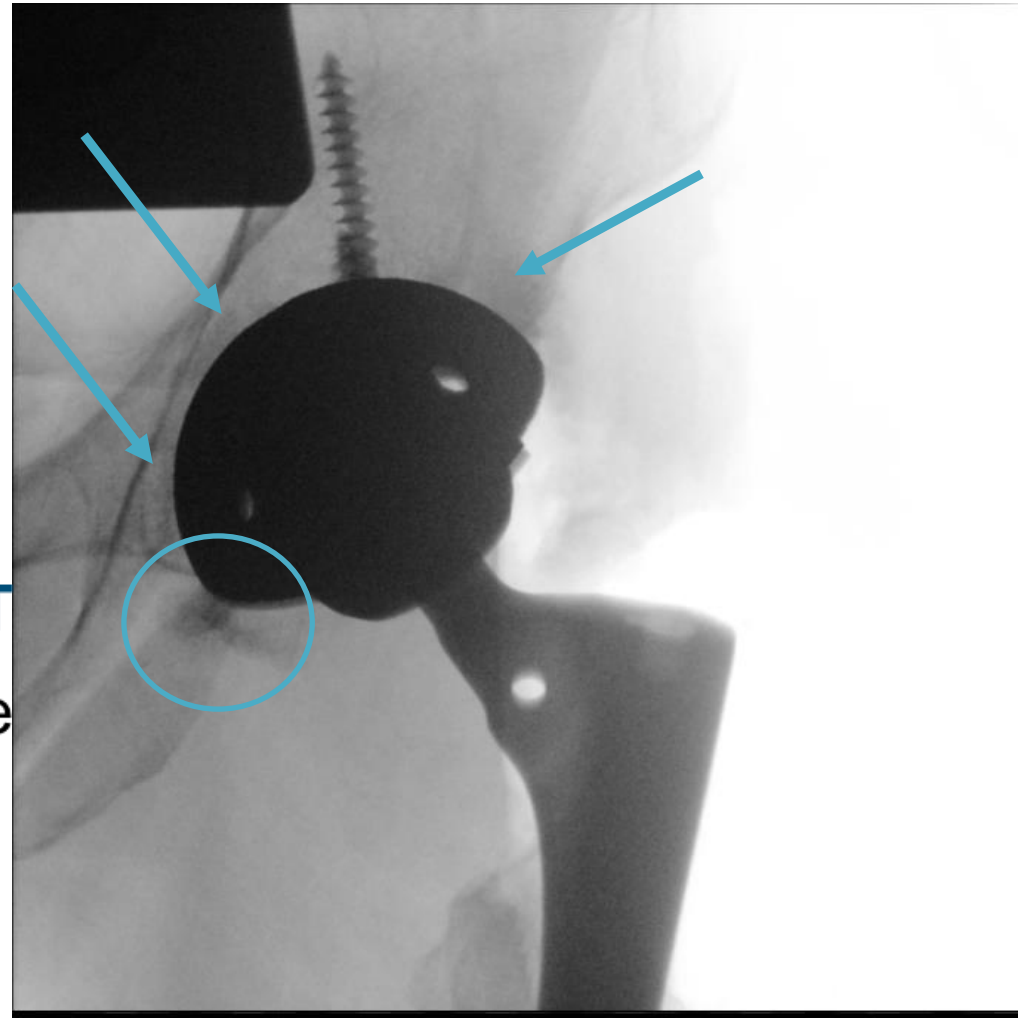
Fill any remaining dead space, cavities, or defects between the bone and the implant.

Step 6: Compression and Drying of CERAMENT

Allow CERAMENT to fully harden and stabilize before proceeding.

Wait 8-10 minutes to fully set and harden.

→ **Finally: Take X-ray**



5 Pitfalls CERAMENT-Augmentation I

1. Incorrect patient selection

- Use despite contraindications

Sepsis / systemic infection

Poor soft tissue conditions

Bone defects that are too large → Metallic augments are required

Resistant pathogens (e.g. DTT)

👉 **Strict selection criteria for 1-stage necessary**

5 Pitfalls CERAMENT-Augmentation II

2. Insufficient drying of the bone → poor adhesion

3. High pressure application → misdistribution

4. Incomplete filling of defects/dead space → Residual spaces between implant and bone remain

5. Wound closure too early (no hardening awaited ~8–10 min)

A PILOT STUDY

HIP

@BoneJointOpen

Cementless one-stage hip revision arthroplasty with an injectable antibiotic bone graft substitute

a pilot study

CeraHIP Study

From Charité – Universitätsmedizin Berlin, Berlin, Germany

T. Khakzad,[1] S. Meller,[1] S. Hardt,[1] V. J. Leopold,[1] L. Mödl,[2] C. Perka,[1] M. Mueller,[1] T. Winkler[1,3,4]

[1]Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Center for Musculoskeletal Surgery, Berlin, Germany
[2]Charité – Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Institute of Biometry and Clinical Epidemiology, Berlin, Germany
[3]Berlin Institute of Health at Charité – Universitätsmedizin Berlin, Julius Wolff Institute, Berlin, Germany
[4]Berlin Institute of Health Center for Regenerative Therapies, Berlin Institute of Health at Charité – Universitätsmedizin Berlin, Berlin, Germany

Correspondence should be sent to T. Khakzad thilo.khakzad@charite.de

Cite this article:
Bone Jt Open 2025;6(9):
1146–1155.

Khakzad, Meller et al. Bone Jt Open 2025

CeraHip Design

- **Prospective** Study
- Confirmed PJI according to **EBJIS** criteria
- **20** study patients included
- Follow-up **2 years**

- **CERAMENT G** in defects and dead space around stem and cup
- 12 weeks postop. antibiotic therapy
- HHS, EQ-5D-5L
- pain visual analogue scale (VAS), medication,
- extensive blood laboratory, adverse events
- radiographs

Khakzad, Meller et al. Bone Jt Open 2025

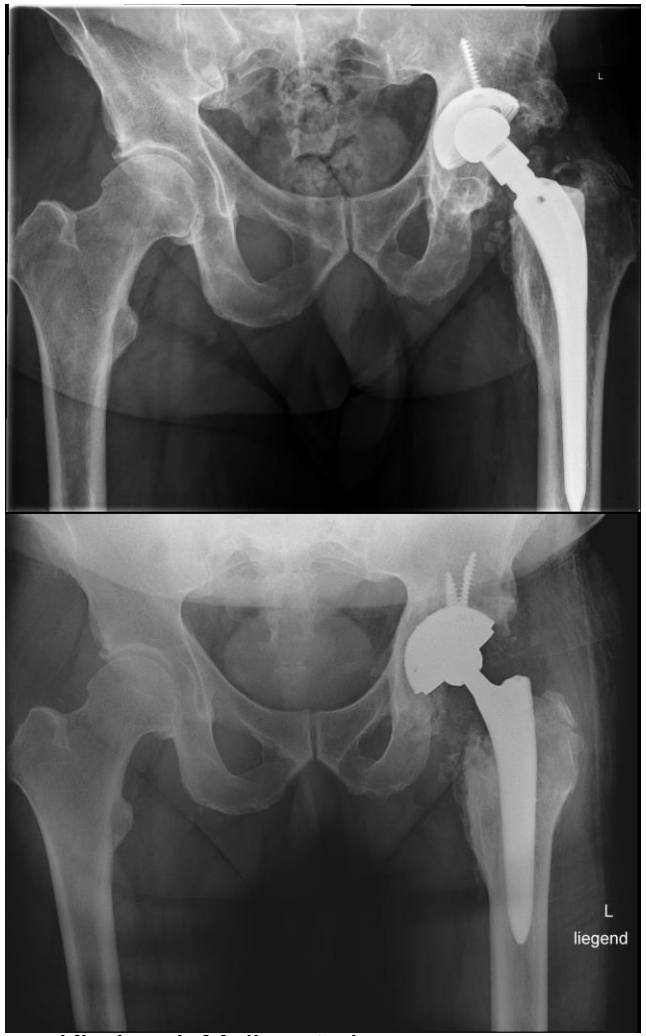
CeraHip Results I

Patients characteristics

- 20 patients (10m : 10f) with PJI of the hip
- Mean age 66,3 years (46-80 years)

- 16 Patients cementless THA
- 04 Patients cemented THA (stem cemented)

- 06 Patients with 1 previous revision (aseptic)



Khakzad, Meller et al. Bone Jt Open 2025

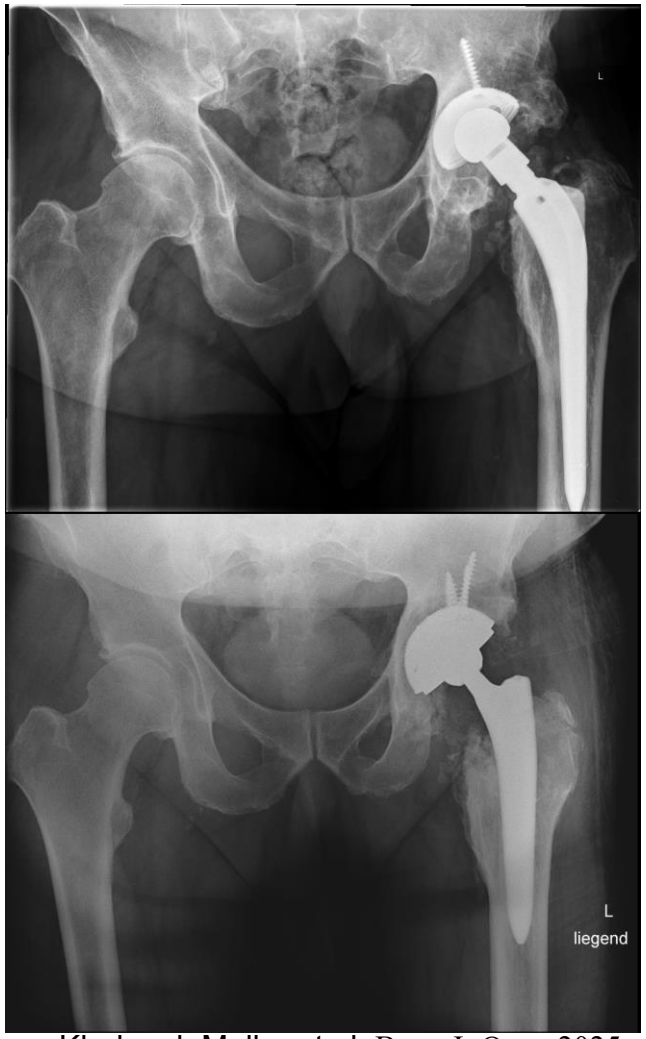
CeraHip Results II

Intra-operative Characteristics

- Confirmation of PJI in all patients intraoperatively
- Positive microbiological and histopathological results
- Mean usage of **13.2 ml CERAMENT G per patient**

Post-operative Characteristics

- 19/20 reached follow up (one patient lymphoma)
- One aseptic dislocation of the cup
- No wound complication, no drainage



Khakzad, Meller et al. Bone Jt Open 2025

CeraHip Results - Pathogens

Bacteria

- 60% Coagulase Negative Stafphylococci
- *Staphylococcus epidermidis* → main pathogen (≈ 30 %)
- Polymicrobial Infections: ca. 15–20 %
- Culture-negative Infections: ca. 20–25 %

Table II. Detected microorganisms and antibiotic therapy.

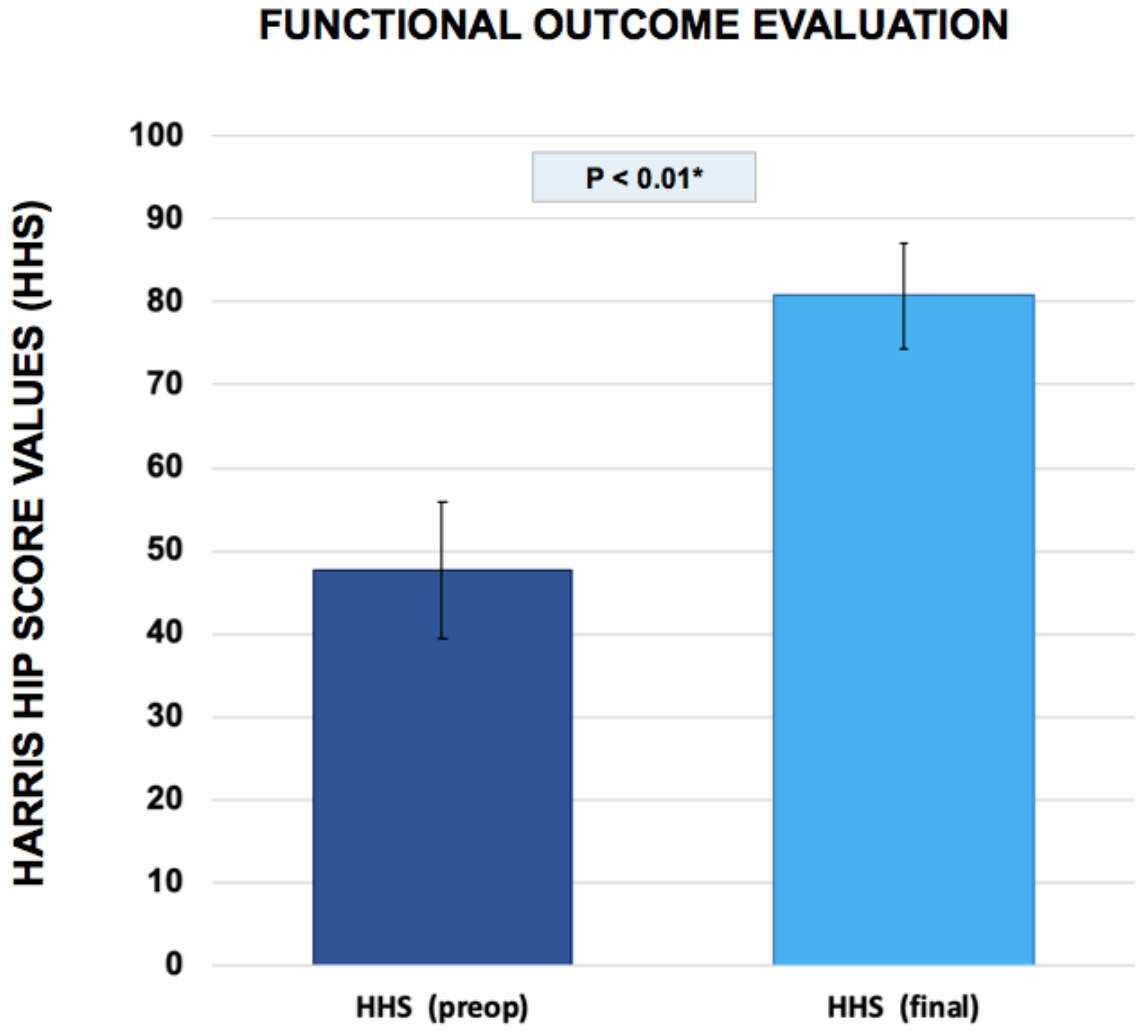
ID	Intravenous antibiotics	Oral antibiotics	Detected microorganisms
1	Ampicillin/Sulbactam Fosfomycin	Levofloxacin Rifampicin	*Staphylococcus epidermidis*
2	Ampicillin/Sulbactam Vancomycin	Amoxicillin	*Cutibacterium acnes/ Staph. epidermidis*
3	Ampicillin/Sulbactam Vancomycin	Amoxicillin Levofloxacin Rifampicin	*Staphylococcus hominis* ssp *Cutibacterium acnes*
4	Ampicillin/Sulbactam Fosfomycin	Levofloxacin Rifampicin	Without pathogen detection
5	Ampicillin/Sulbactam Vancomycin	Levofloxacin Rifampicin	Without pathogen detection
6	Ampicillin/Sulbactam Vancomycin	Levofloxacin Rifampicin	*Staphylococcus haemolyticus/Cutibacterium acnes*
7	Ampicillin/Sulbactam Fosfomycin	Levofloxacin Rifampicin	*Staphylococcus capitis*
8	Piperacillin/Tazobactam Fosfomycin	Ciprofloxacin Rifampicin	*Staph. epidermis*
9	Ceftriaxon Fosfomycin	Ciprofloxacin Rifampicin	*Cutibacterium acnes*
10	Ampicillin/Sulbactam Fosfomycin	Levofloxacin Rifampicin	*Staph. epidermidis/Klebsiella pneumoniae*
11	Piperacillin/Tazobactam Fosfomycin	Levofloxacin Rifampicin	*Cutibacterium acnes*
12	Ampicillin/Sulbactam Fosfomycin	Levofloxacin Rifampicin	*Cutibacterium acnes*
13	Ampicillin/Sulbactam Vancomycin	Cotrimoxacol Rifampicin Doxycliclin	*Staph. epidermidis/Cutibacterium acnes*
14	Ampicillin/Sulbactam Vancomycin	Levofloxacin Rifampicin	Without pathogen detection
15	Vancomycin Fosfomycin	Levofloxacin Rifampicin	Without pathogen detection
16	Ampicillin/Sulbactam Fosfomycin	Levofloxacin Rifampicin	*Staph. epidermidis*
17	Cefuroxim Fosfomycin	Levofloxacin Rifampicin	Without pathogen detection
18	Ampicillin/Sulbactam Vancomycin	Levofloxacin Rifampicin	*Staph. lugdunensis/Staph. hominis*
19	Cefuroxim Vancomycin	Levofloxacin Rifampicin	*Staphylococcus epidermidis*
20	Ampicillin/Sulbactam Vancomycin	Levofloxacin Rifampicin	*Staphylococcus capitis*

Khakzad, Meller et al. Bone Jt Open 2025

CeraHip Results

Post-operative Characteristics

- HHS improved (p<0.01)

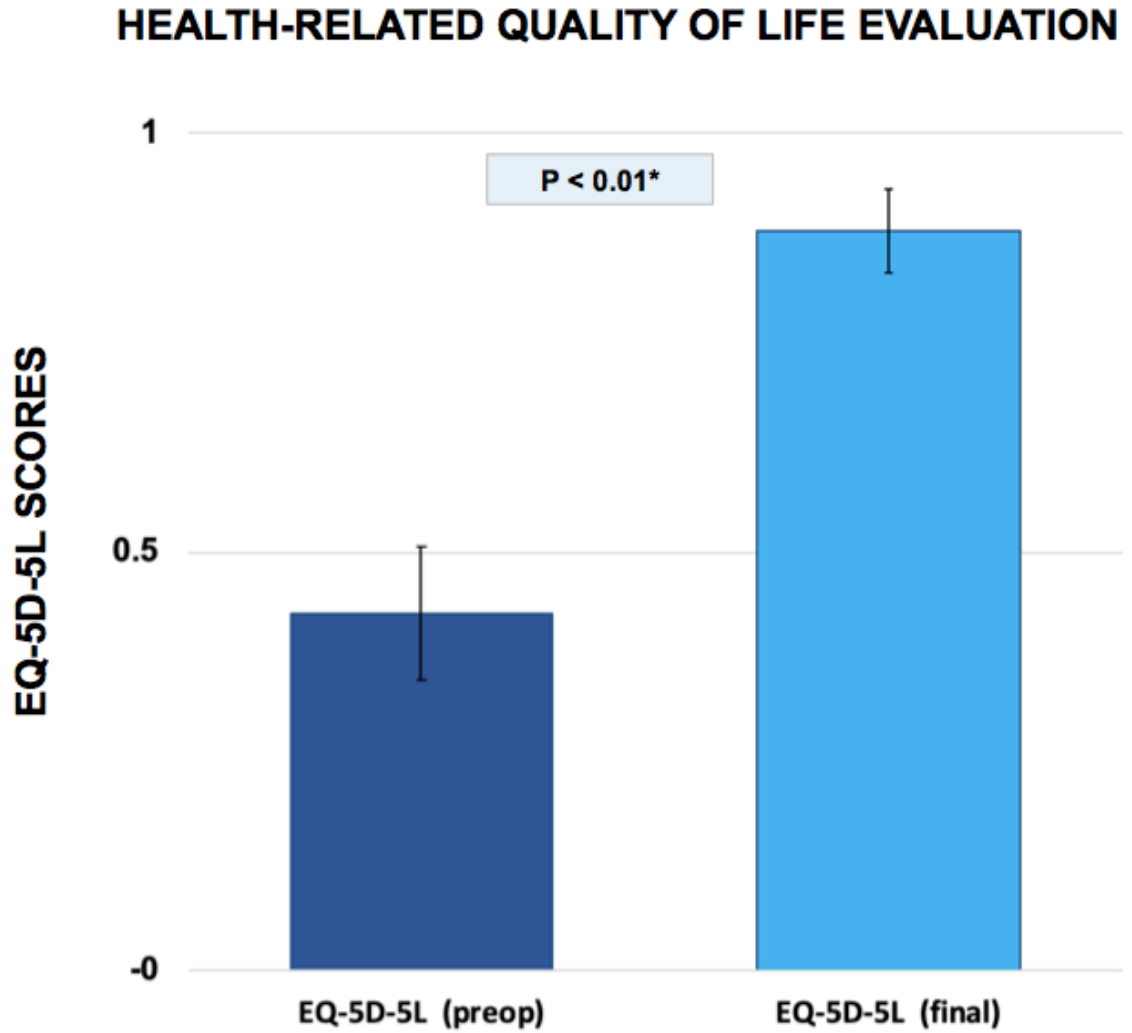


Khakzad, Meller et al. Bone Jt Open 2025

CeraHip Results

Post-operative Characteristics

- HHS improved (p<0.01)
- EQ-5D-5L improved (p<0.01)

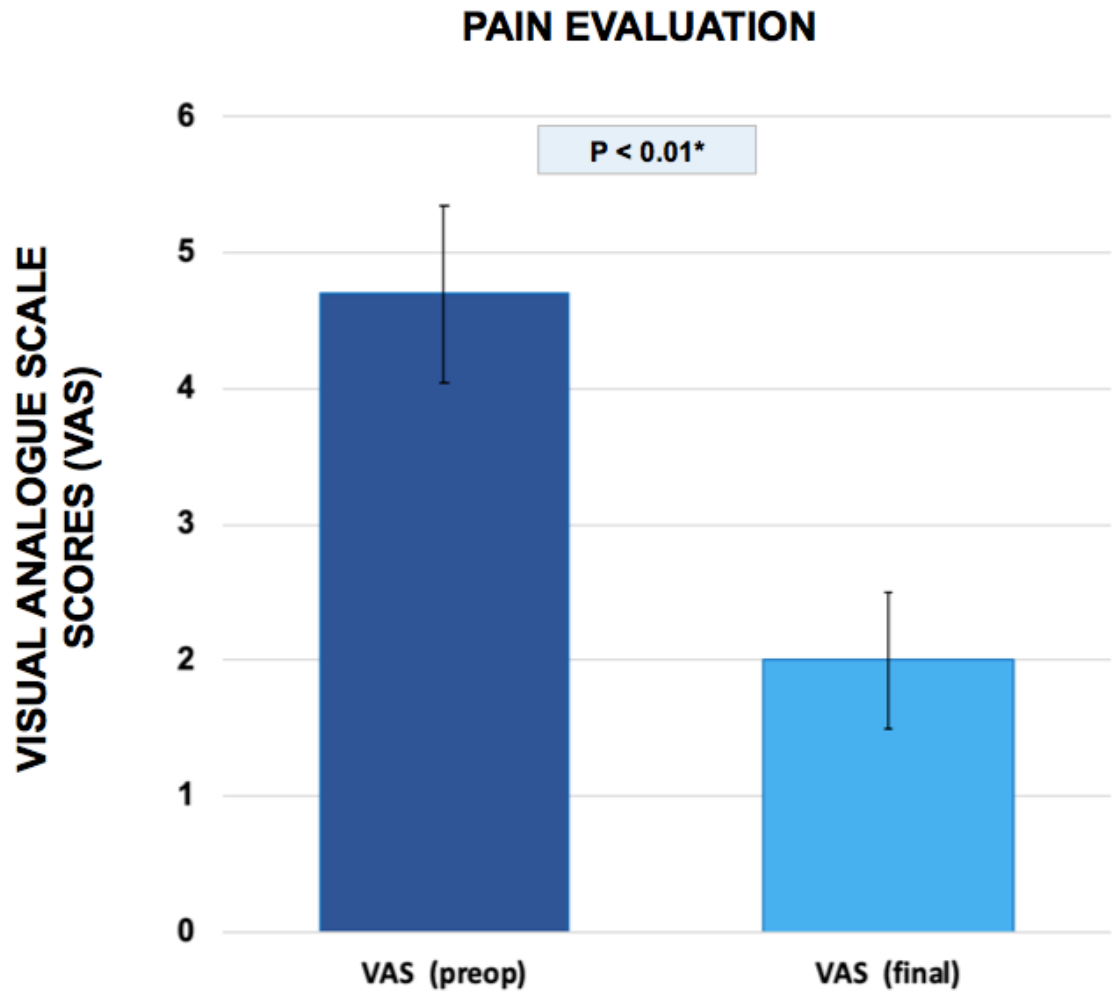


Khakzad, Meller et al. Bone Jt Open 2025

CeraHip Results

Post-operative Characteristics

- HHS improved (p<0.01)
- EQ-5D-5L improved (p<0.01)
- Pain Evaluation improved (p<0.01)



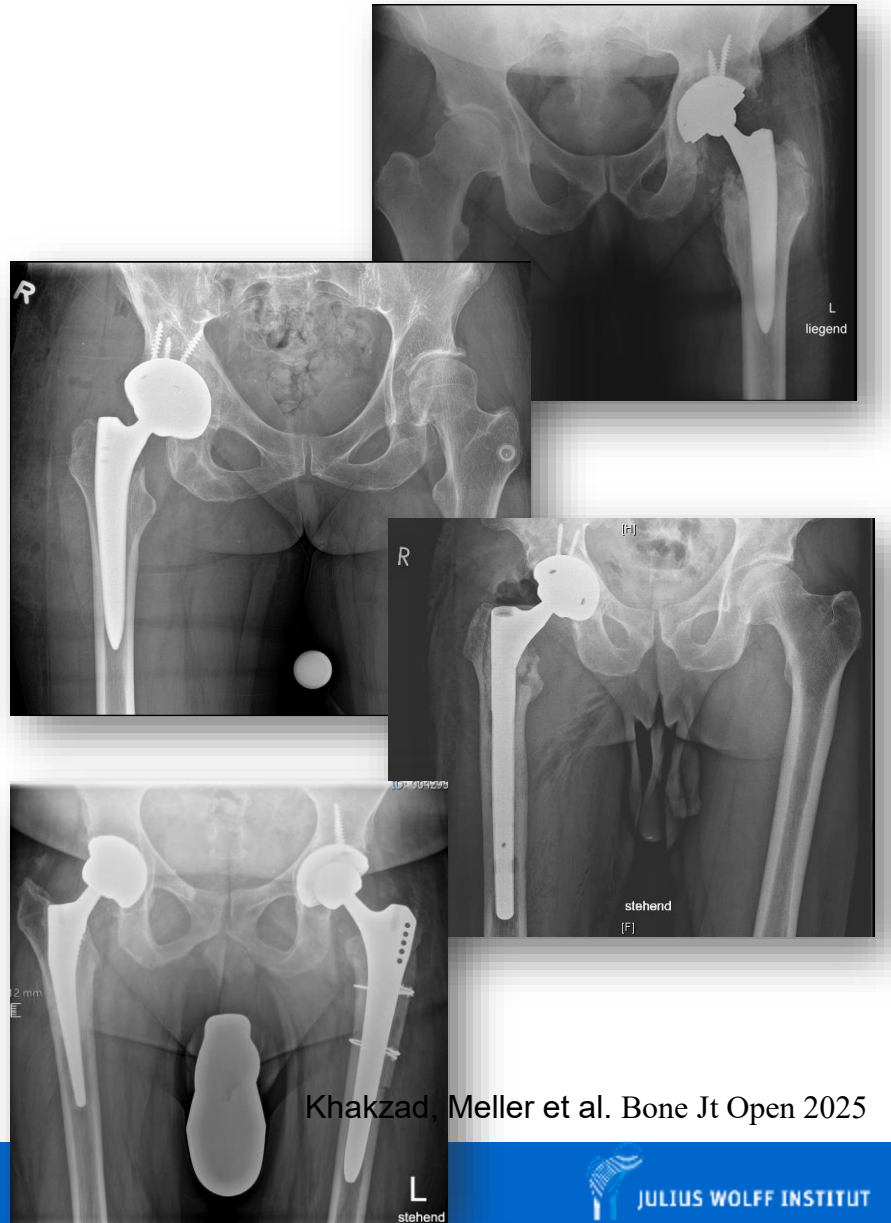
Khakzad, Meller et al. Bone Jt Open 2025

CeraHip Results

Mean Follow up 3,5 years

- ✓ No Reinfection
- ✓ Excellent functional results
- ✓ Good radiographic results

- Longer FU and more patients necessary for future investigations



Khakzad, Meller et al. Bone Jt Open 2025

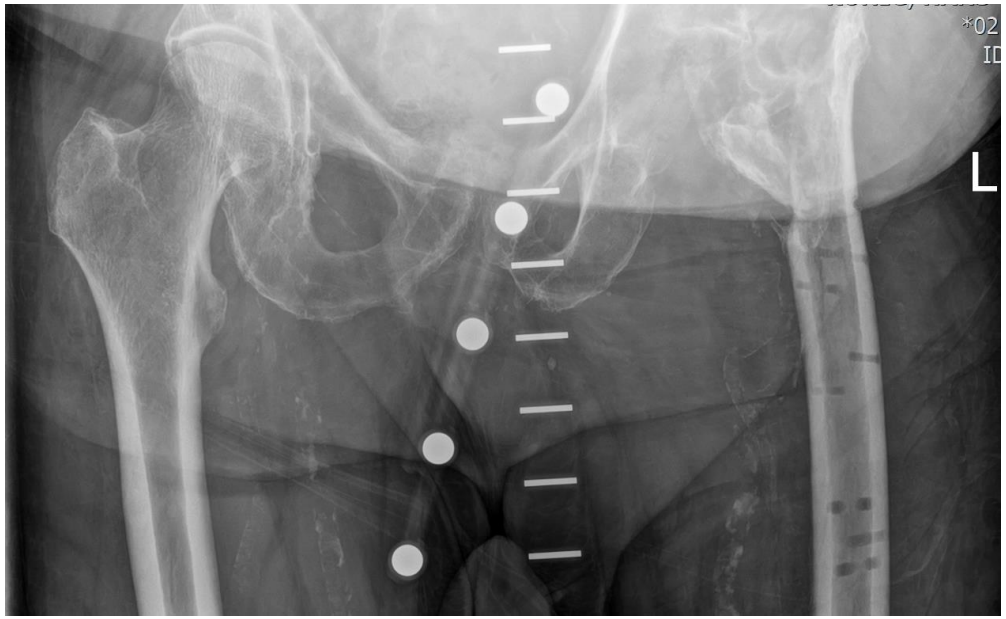
Our Surgical Approach for a two-stage exchange

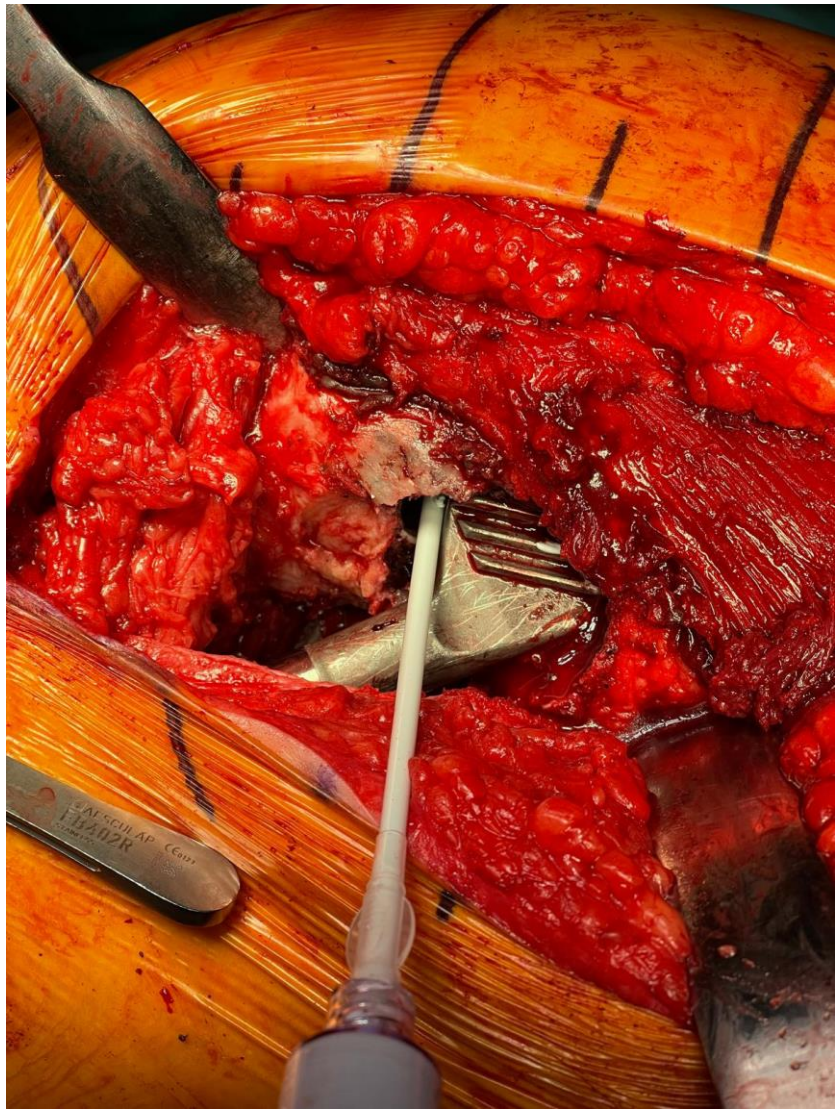
CERAMENT in Two-Stage Surgery

- Hip replacement left hip 2006
- Explantation and Girdlestone procedure 12/2023 (Staphylococcus epidermidis)
- 07/2024 Re-Implantation and fracture
- 08/2024 Again Explantation and Girdlestone procedure (Staph. epidermidis + haemolyticus)
- 11/2025 Debridement and biopsy Girdlestone revision at Charité (Staph. epidermidis)

- 01/2026 Re-Implantation at Charité with CERAMENT G (no pathogen found)

CERAMENT in Two-Stage Surgery





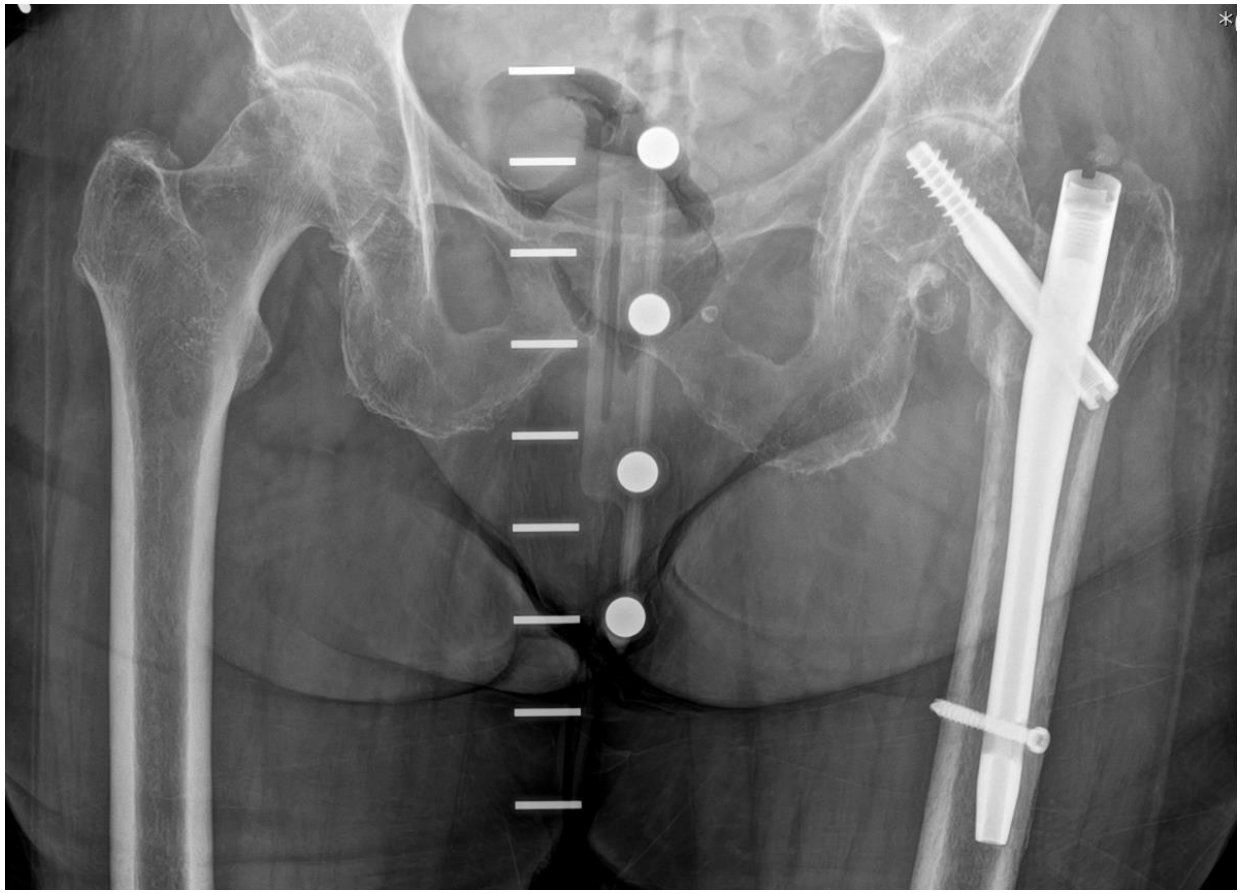
Our Surgical Approach for prophylactic use

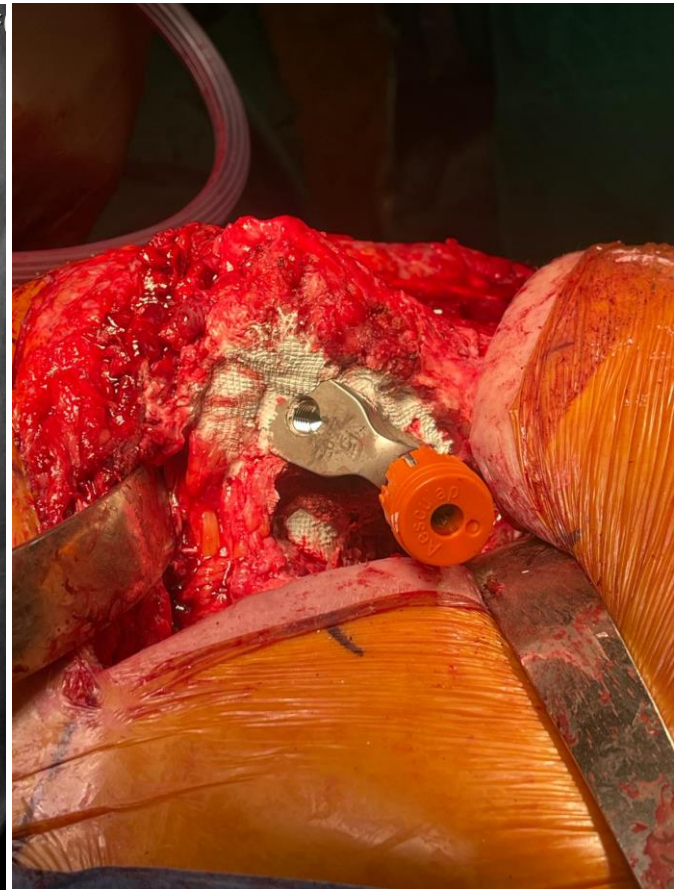
CERAMENT IN HIGH RISK REVISION

Indication: Progressive pain due to secondary left hip osteoarthritis after nail fixation

Diagnosis: Left hip osteoarthritis

Treatment: Implant removal and left total hip arthroplasty with CERAMENT G





Take home message

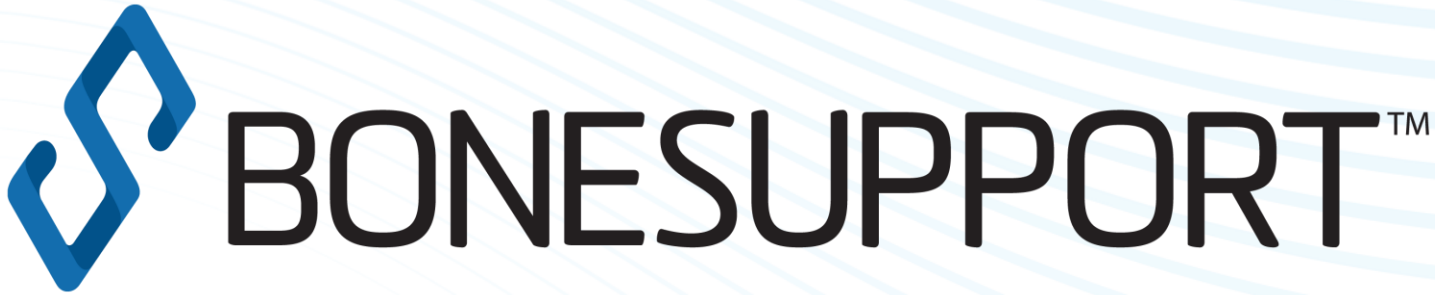
- ✓ TSE is currently the gold standard, but SSE getting more popular
- ✓ For single-stage revision procedures a critical patient election is mandatory
- ✓ CERAMENT G is firmly established in our treatment algorithm as a local antibiotic eluting bone graft substitute for defect augmentation in PJI treatment
- ✓ CERAMENT G is utilized according to a standardized protocol: debridement, bone preparation, and application in defects and around „hardware“ (acetabulum, femur, tibia)
- ✓CERAHIP study showed good functional and radiographic results
- ✓Could be used prophylactically in high-risk revision cases.

sebastian.meller@charite.de

Thank you!

sebastian.meller@charite.de

BONESUPPORT



Q&A

The Burden of Infection on Society and The Patient: The Case for Single Stage, Outpatient Surgery

College of Medicine
Orthopedic Surgery and Sports Medicine

Paul E. Matuszewski, MD
Chief, Orthopaedic Trauma Service
Director, Orthopaedic Trauma Research
Vice Chair, Research
Associate Professor of Orthopaedic Traumatology
Department of Orthopedic Surgery and Sports Medicine
College of Medicine, University of Kentucky

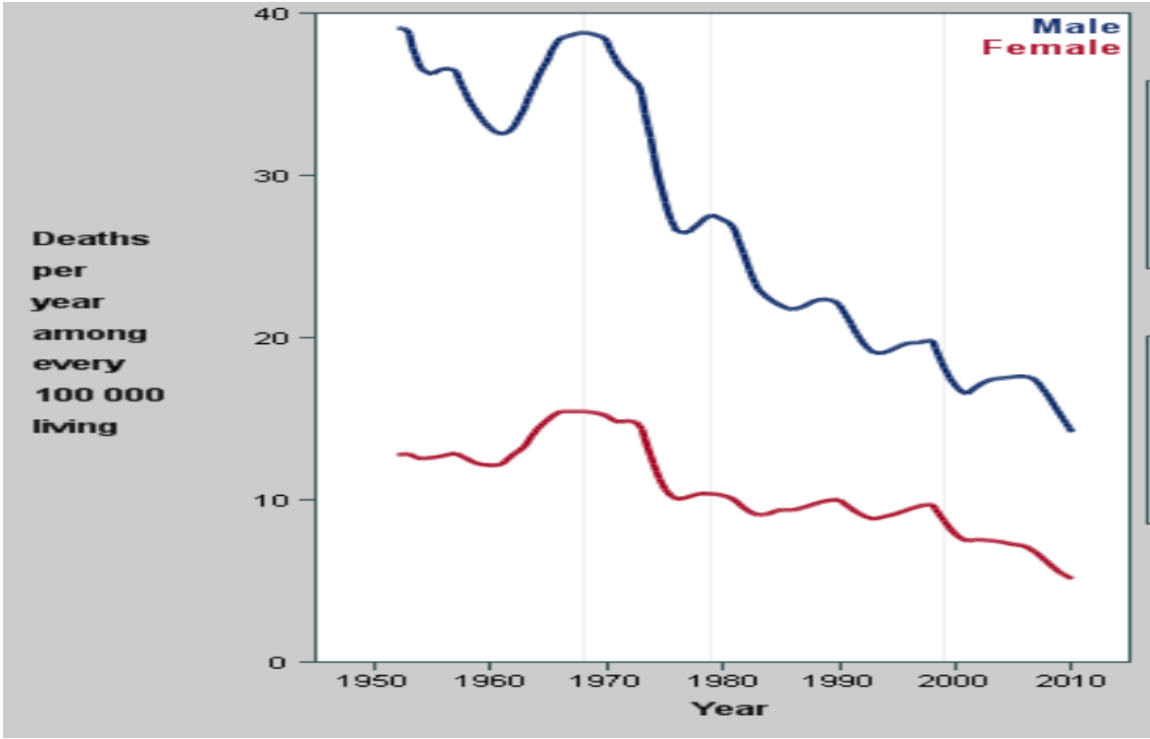
University of Kentucky

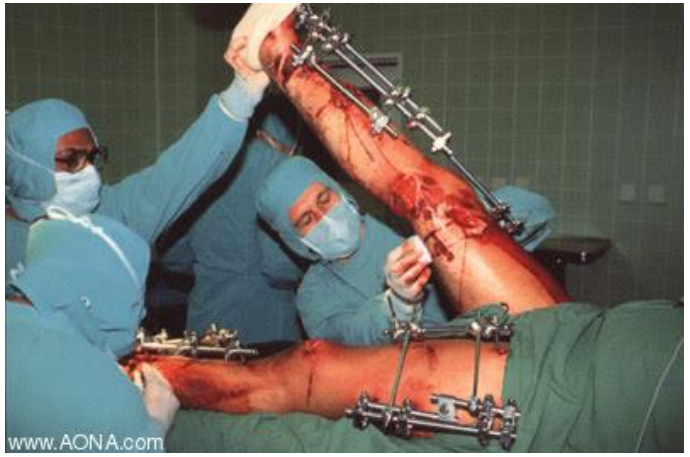
The Burden is High

- The socioeconomic in the treatment of fracture related infection is high
- Context: The rate of infection depending on the injury is from 1%-30%, depending on the injury type
- The rate of infection does not seem to be decreasing over the years
- Why?

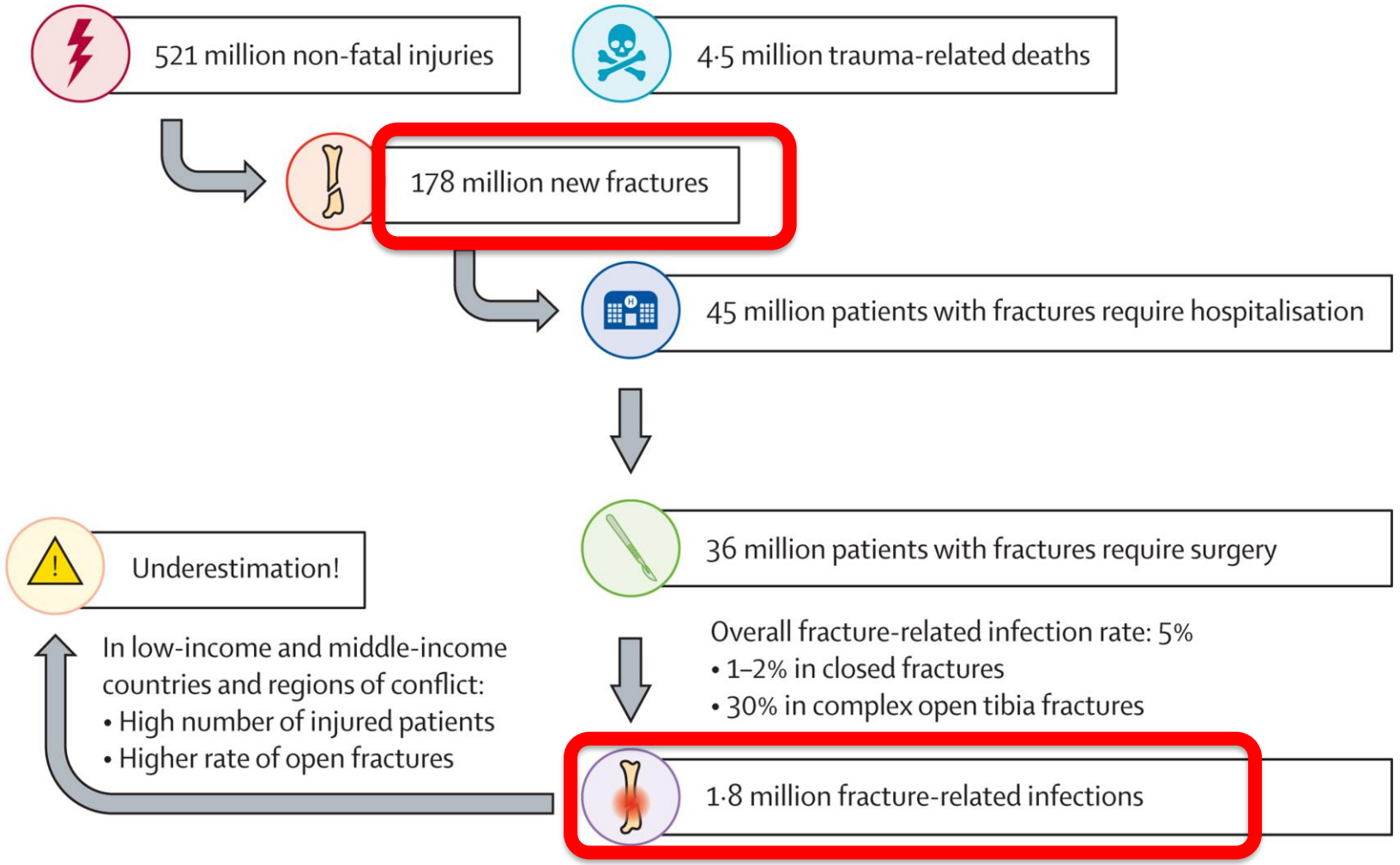
Burden continued

- Advances in treatment/safety have allowed patients with severe traumatic injury to survive
- Result: Orthopaedists left to treat more complex injuries
- More complex => higher rate of infection





Yearly Worldwide Perspective



Societal Economic Costs

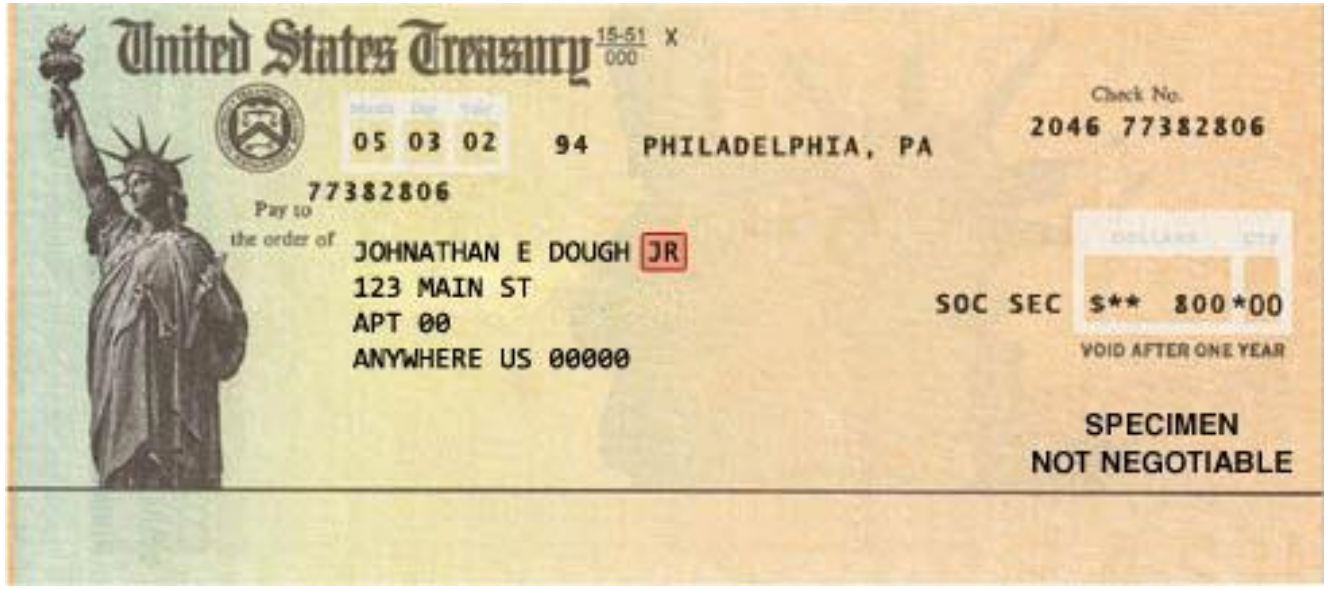
- Treatment is costly for infection, up to 6.5x more than original cost of fracture care
- Upwards of $108,000 USD, likely more (older data)
- Largest costs associated with **increased hospital length of stay (62%)**
  - 54 hospital days over 3 admissions (vs 1 admission/7 day LOS)
- Followed by surgical cost and pharmaceuticals (~30% cost)
- As age/comorbidities increase, expense appears to increase

Societal Costs

- > $100,000 USD / infection
- Consider 1.8m fracture-related infections globally
- Approaching 180B USD yearly???

Societal Costs cont.

- 45% increased risk of requiring supplemental governmental financial support, following FRI (O'Hara et al, JAMA network, 2021)



What about the Individual?

- The individual cost is tremendous
- Why?
- Consider how we treat infection and how “good” are we…

Historical Treatment - Timeline

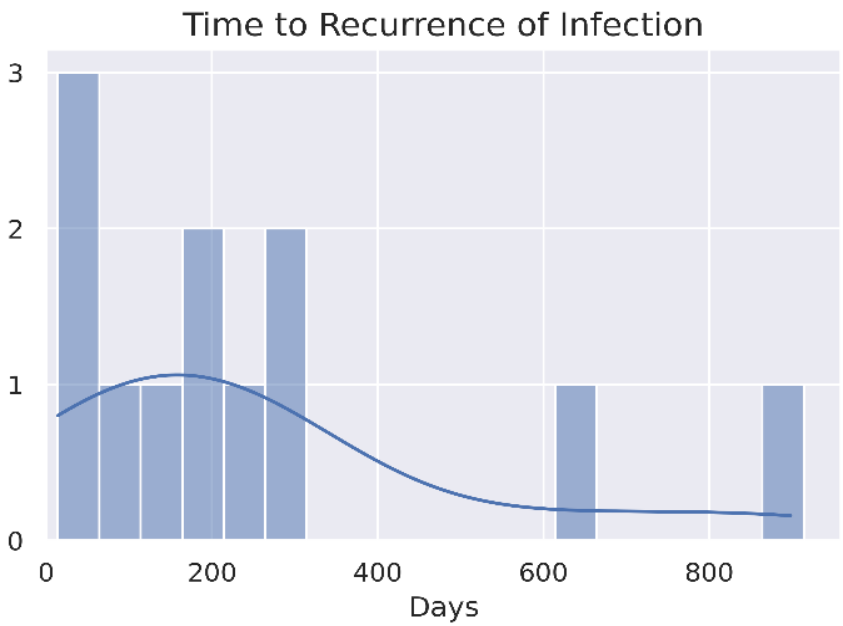
- Early infection: Treatment with debridement, irrigation, retention of implants, antibiotic suppression => 60-70% success
  - Timeline – 6 weeks+
- Later infection: Removal of implants, resection, debridement, treatment with IV antibiotics, return to the operating room for staged treatment => Similar Success rate
  - Timeline 3 months +
- These timelines: Only if successful on the first try

The UK (not Great Britain) Experience

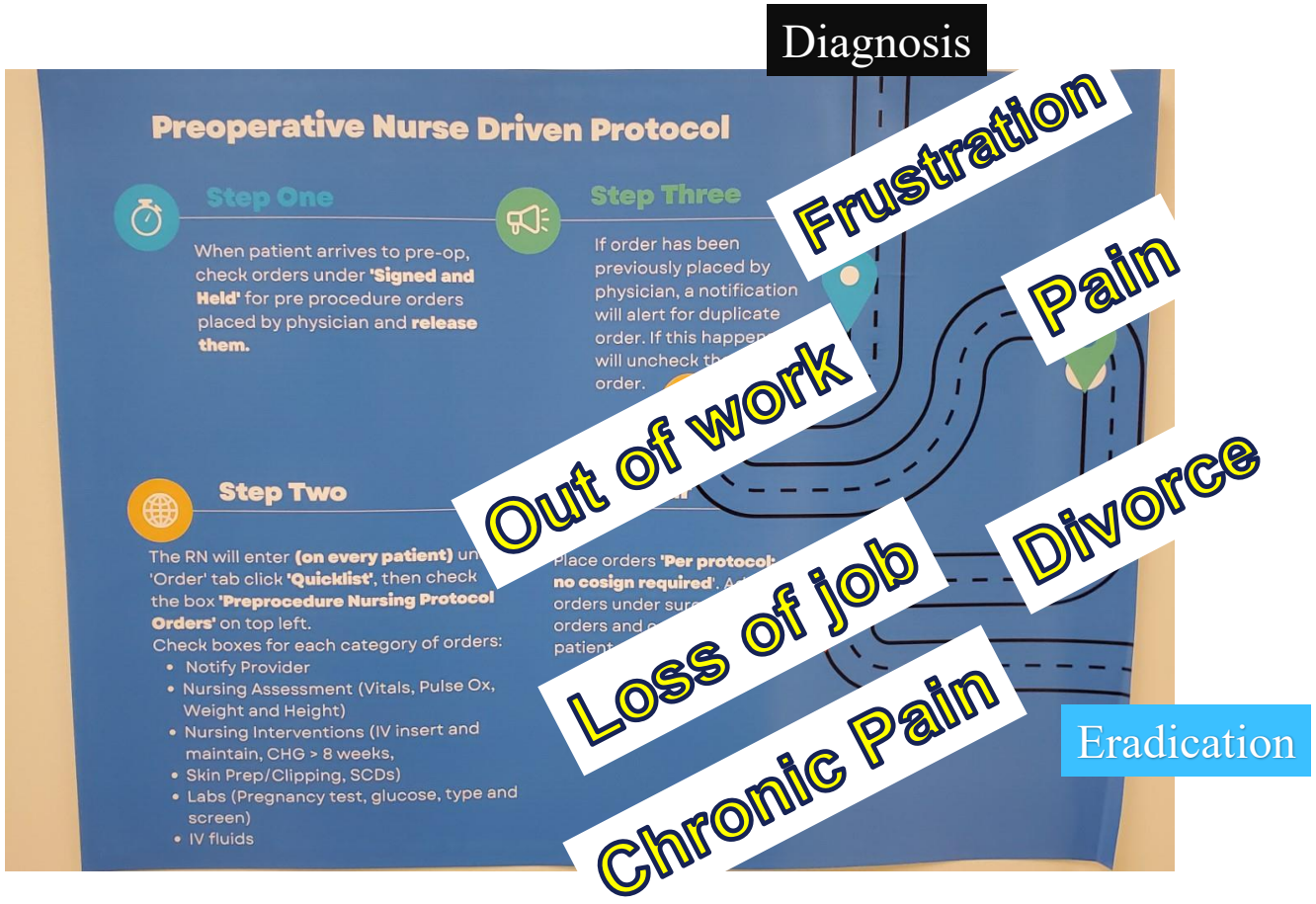
- Looking at our history of osteomyelitis/bone infection treatment (prior to my tenure)
- **ONLY 43% two stages (two surgeries) fit that criteria**
- 29% three stages
- 27% four or more stages

Primary Endpoint

- 58.5% success rate, no recurrence of infection or infection related procedure
- 32% had infection recurrence
- **Mean time to recurrence was 8-9 months**
- 3 patients had amputations related to infection
- Lots of other complications: delayed wound healing, fracture, etc.



So Let's Get Back to the Patient



Timeline:
3 months
6 months
9 months++

The Effect on the Patient (Beyond Cost)

- Tangible Limitations following FRI can be devastating:
- Immobility
- Amputation 3-17%
- Complications from Antibiotics
- Loss of function
- Substance Abuse Disorder

Emotional and Mental Impact – Intangible

- Anxiety
- Sleep disturbance
- Pain
- Concentration issues
- Restriction on daily activities
- Reliance on others
- Depression and suicidal thoughts
- Substance dependance

Long Term Impact

- Years after successful treatment FRI, the impact still resides
  - Reported **decreased quality of life**
  - Severe psychological burden in up to 20% of patients after 4 years (Walter et al, Bone Joint Res 2021)

The Effect of Treatment and Time: Psychological

- Prolonged treatment => Worsened themes
- Longer treatment = more time for complications
- Longer the treatment =>
  - Psychological burden++

State of the Union – Where does that leave us?

- Fractures are increasing
- Patients / injuries are becoming more complex
- Complications and infections are increasing in prevalence, but not necessarily incidence
- How do we do better and what have we learned?

Is there a precedent for improved outcome?

- Yes!
- Extrapolate experience from Joint Replacement:
- More outpatient procedures
  - Recover from home
  - Decreased hospital LOS
  - Improved outcomes
- Infection/Revisions:
- Single Stage Versus Two Stage:
  - Positive perception of wellness
  - Minimal pain
  - Reduced dependance on aids
  - Greater mobility
  - Greater Independence

Osteomyelitis/FRI
The Extrapolation

- If we:
  - Decrease # of procedures
  - Decrease hospitalization occurrences
  - Decrease length of stay
- What happens?
  - Decrease anxiety and uncertainty
  - Quicker return to life/work
  - Decreased pain/burden
  - Decrease cost: Hospital, patient, society
- So, can we do it? – I think we are working our way there….
- How? – Incremental improvements

Recent Improvement #1:

- **Use of local antibiotics to improve eradication**
- Historical, Systemic Antibiotics (via IV):
  - Can be effective, mainstay of treatment
  - Limited by concentration/dose
  - Do not specifically target area of interest
  - Can’t give high doses – toxic
  - Have systemic complications
- Modern, Local Antibiotics:
  - Deliver at high concentration (orders of magnitude)
  - Help breakdown biofilm
  - Direct to source
  - Improved rates of success with local therapy
  - Require appropriate carrier to have sustained delivery

Recent Improvement #1 Cont.

- **Clinical evidence supports local antibiotics**
- In BOTH prevention AND Treatment
- VANCO/TOBRA trial – Decreased rate of infection: 6.4% vs 9.8% (50% reduction in some types of infections)
- Treatment: Many studies show improved success when local antibiotics are used (with a carrier)

Recent Improvement #2

- **Decreased reliance on IV antibiotics**
- Difficulty with IV antibiotics:
  - Inconvenient
  - High cost of delivery
  - Increased length of stay to place more permanent (PICC) line
  - PICC Line infections
  - Systemic issues
  - Guidelines unclear: 6 weeks? 12 weeks?
- Oral antibiotics
  - Easy to administer
  - Lower cost
  - No PICC line related issues
- Clinical evidence supports use:
  - POvIV: Oral Non inferior
  - OVIVA Trial: 13.2 vs 14.6%, oral non-inferior

Recent Improvement #3

- **Single Stage Treatment**
- Historical: Dual or multi-stage treatment
- **More modern**:
- Use of antibiotic eluting bone graft substitute to provide local delivery and treatment of defects
- Good clinical evidence:
  - 6 year f/u, 94% infection free

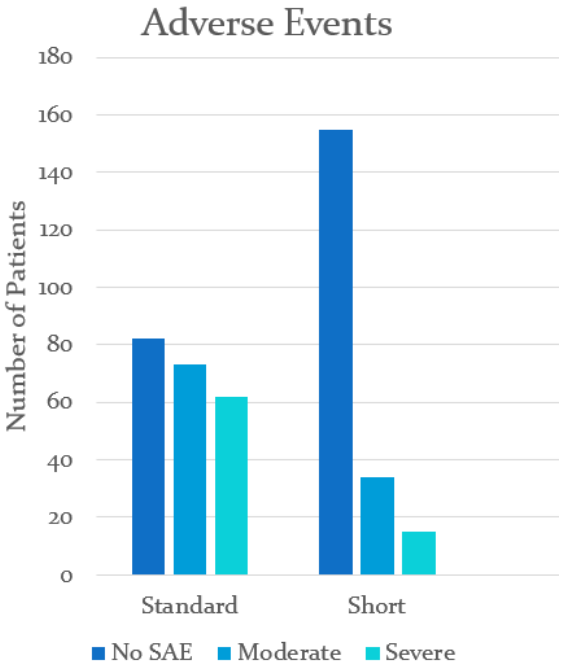
› Bone Joint J. 2022 Sep;104-B(9):1095-1100. doi: 10.1302/0301-620X.104B9.BJJ-2022-0396.R1.

Mid- to long-term results of single-stage surgery for patients with chronic osteomyelitis using a bioabsorbable gentamicin-loaded ceramic carrier

Martin A McNally [1], Jamie Y Ferguson [1], Matthew Scarborough [1], Alex Ramsden [1], David A Stubbs [1], Bridget L Atkins [1]

Recent Improvement #4

- **Combination of techniques**
- SoLario trial:
  - –Local antibiotic therapy PLUS
  - –Short course antibiotics <7 days
  - –Long course (standard)
- Short: Non-inferior (11.1% vs 14.1% failure)
- Decreased rate of adverse events



Conclusions on Improvements

- Combinations of these improvements are dramatically changing the clinical landscape
- **CERAMENT G plays an important role as the only FDA approved BVF to be combined with antibiotics**
- **Which means you get:**
- #1: Local antibiotic delivery to improve eradication
- #2: Bone graft substitute => Single stage

Case Example: MF

- 41F, 2 years s/p ORIF of ankle fracture (outside surgeon)
- New onset pain about the tibia, worse at night
- No obvious physical exam findings other than tenderness to palpation
- Healthy, active mom

Xrays

Treatment Choices:

Choice 1 - Traditional

- Address infection w/ OR procedure to remove hardware/bone
- Admit to hospital
- Initiate IV ABX 6 weeks+
- Discharge
- Return OR for bone grafting/spacer removal
- Possible second admission

Choice 2 – Modern Strategy

- Address infection w/ OR procedure to remove hardware/bone or exchange
- Treat with local antibiotics and bone void filler
- Discharge on oral antibiotics
- Possible IV antibiotics, arranged as outpatient
- Clinical Surveillance as outpatient

We Chose #2

- Outpatient surgery – Day 1
- Removed foreign body, placed biphasic calcium sulfate/hydroxyapatite with gentamycin (CERAMENT G), discharged home (same day)
- Two weeks oral antibiotics
- Positive cultures – (POD #3)
- Referral to ID (outpatient)
- No systemic antibiotics, complete resolution

Evaluation

- Definitely a success
- Minimal disruption to patient life
- Back to work quickly
- No additional visits/procedures
- What about hospital bill/cost, any evidence for improvement?

Single Stage vs Two Stage: Economic Analysis

- We looked at earlier return to work and decreased interactions with healthcare system
- Economic modeling of single versus two stage:
- Savings: $27,943-$31,457, with large component from surgery (~$9,000), but others including antibiotics (Carter MJ, 2023)
- Small QALY improvement (Carter MJ, 2023)
- Bottom line: Good for patient AND payer/healthcare system

What about hospitals?

- A little more complicated, actually
- Currently in US, complications/secondary procedures are still reimbursed currently
- Reimbursement not directly tied to performance, for these diagnoses
- More interactions => More revenue

The Numbers

- Hospitals look at total cost by case and their margin (in US)
- My experience: Total cost of care, tremendous – **usually a loss for hospital**
- All CERAMENT G cases (inpatient and outpatient)
  - Negative margin of about $4,000 USD
- Isolating outpatients, flipped margin positive >$1000 USD
- Conclusion from hospital:
  - Benefit to patients, outweighs cost.
  - BUT, our recommendation: Outpatient preferred.

It’s not just the money

- New techniques allow creative ways to care for patients
- Beneficial to patients/physicians (and hospitals)
- Some patients avoid traditional care
- We can now treat them

Consider the Case: 48F

- Hx bicondylar tibial plateau (knee) fracture, open wound with tissue loss
- Hx of implant infection, treatment, removal of implants
- Symptom Free period (6mo), shortly after abx
- Now with drainage about the proximal tibia

Hx cont

- Patient has multiple medical comorbidities
- Last outpatient treatment of antibiotics
  - Poorly tolerated
  - Severe nausea, diarrhea, kidney damage, etc
- Not interested in “long term antibiotics”
- Does not want prolonged hospitalization
- Not interested in infectious disease follow-up

Options?

- Refuse surgery?
- Authoritarian strategy? – Force the issue, but will the patient comply?
- New Strategies? I can offer the patient something different
- Outpatient surgery, debridement, local antibiotics (CERAMENT G), oral antibiotics

Intraop

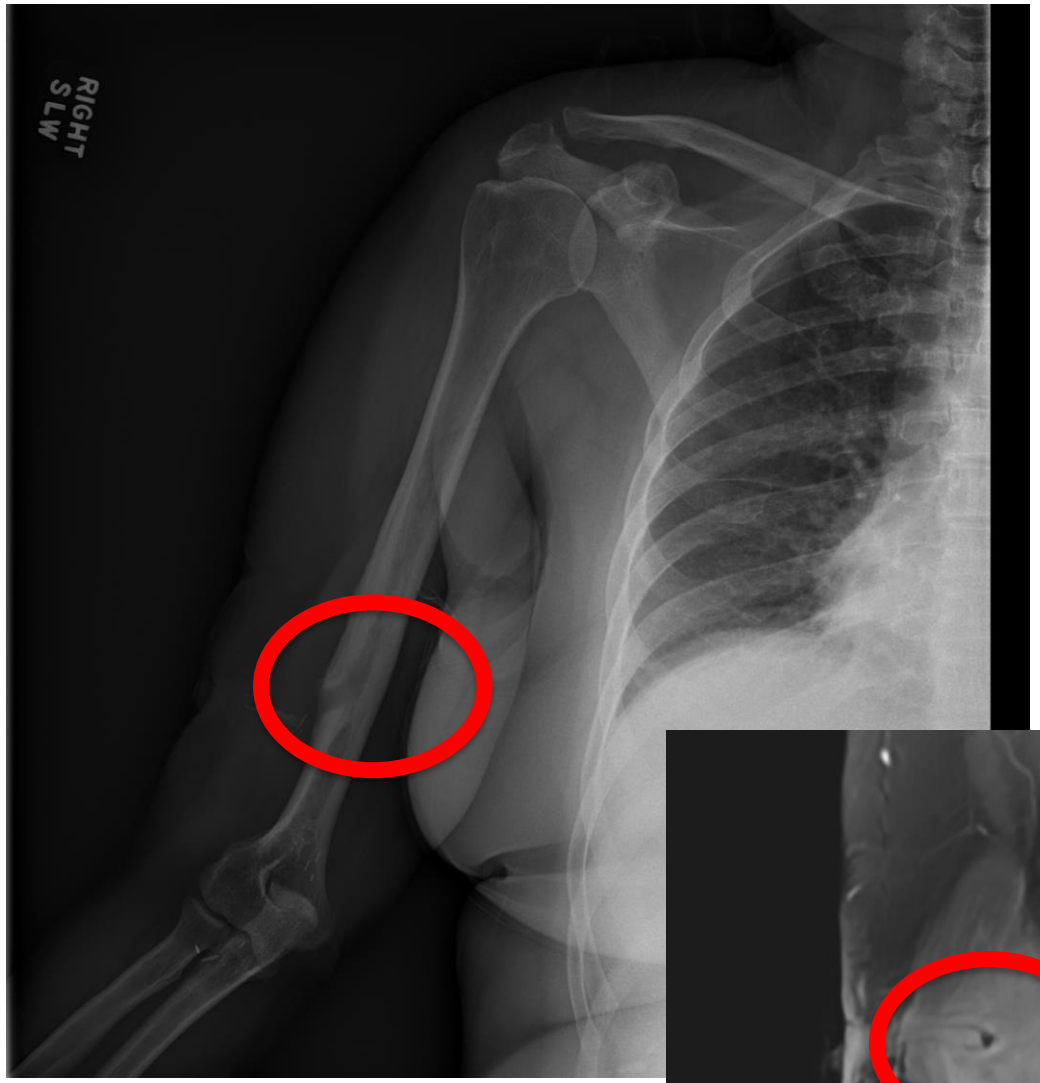
Complete resolution

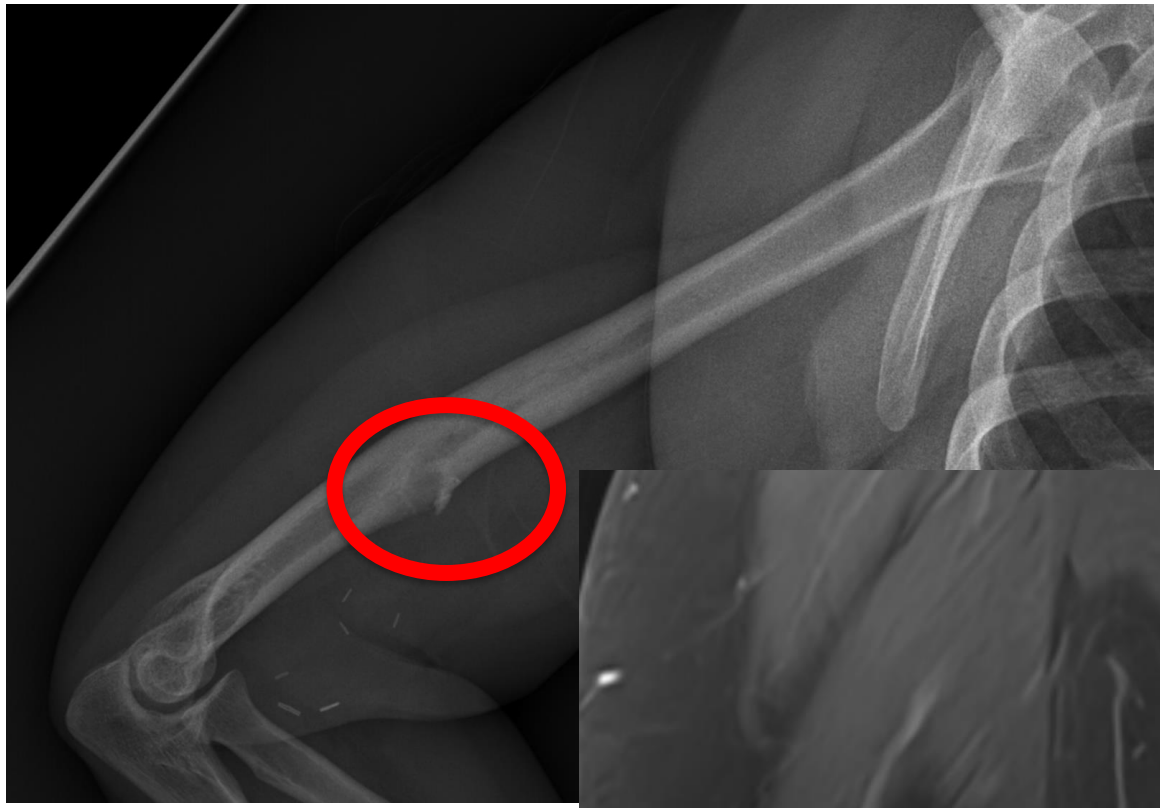
2mo Postop

5 mo Postop

Another complicated case

- 49F, EtOH, hx Schizophrenia, tobacco use
- Prior trauma, elbow injury, previous ex fix, draining wound x 4 years

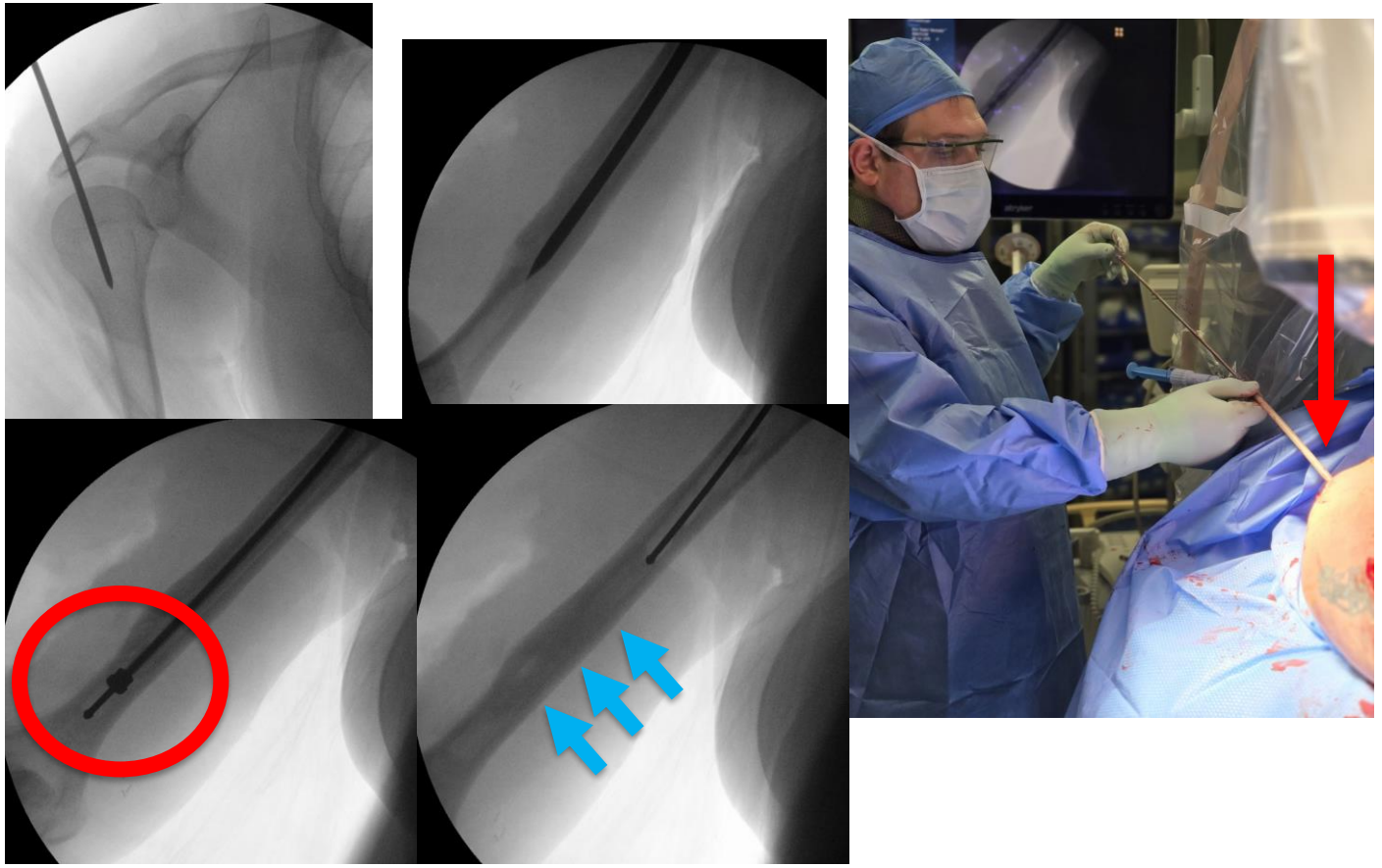

RIGHT
SLW



Diagnosis

- Chronic localized/ bone infection
- Difficult social situation
- Plan: Local treatment, minimally invasive, oral antibiotic (2 weeks), and referral for OPAT
- Pathway: Outpatient surgery, outpatient antibiotics

2 incisions: Cannula + Local control/washout



How it Went

- Patient grew MRSA
- Discharged from outpatient surgery
- Followed up 1-2 weeks with ID
- Prescribed linezolid
- “Never received”
- Not ideal (common), but local Abx decreases concern – patient still being treated – compliance 100%

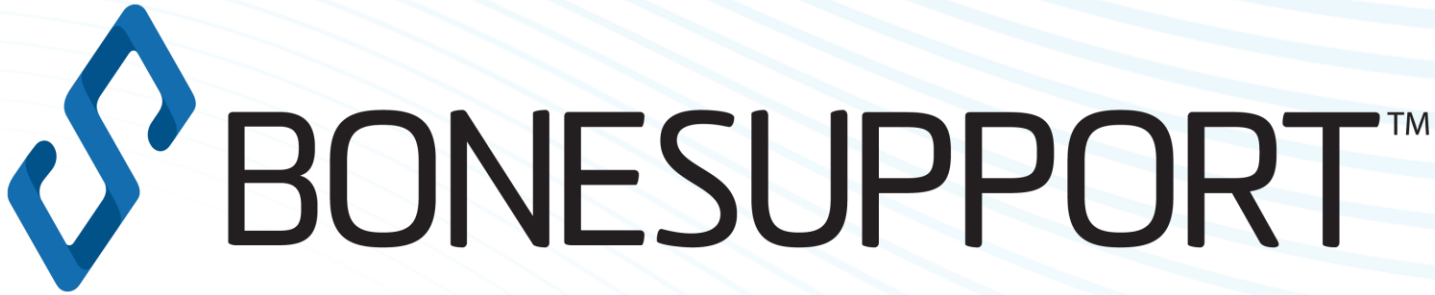
6 mo – no symptoms

Conclusions

- # of infections / need for complicated scenario treatment continues to increase
- Patient's deserve more streamlined, tailored treatment
- Outpatient pathways and single stage procedures improve the quality of care and cost of care

Thank you

BONESUPPORT



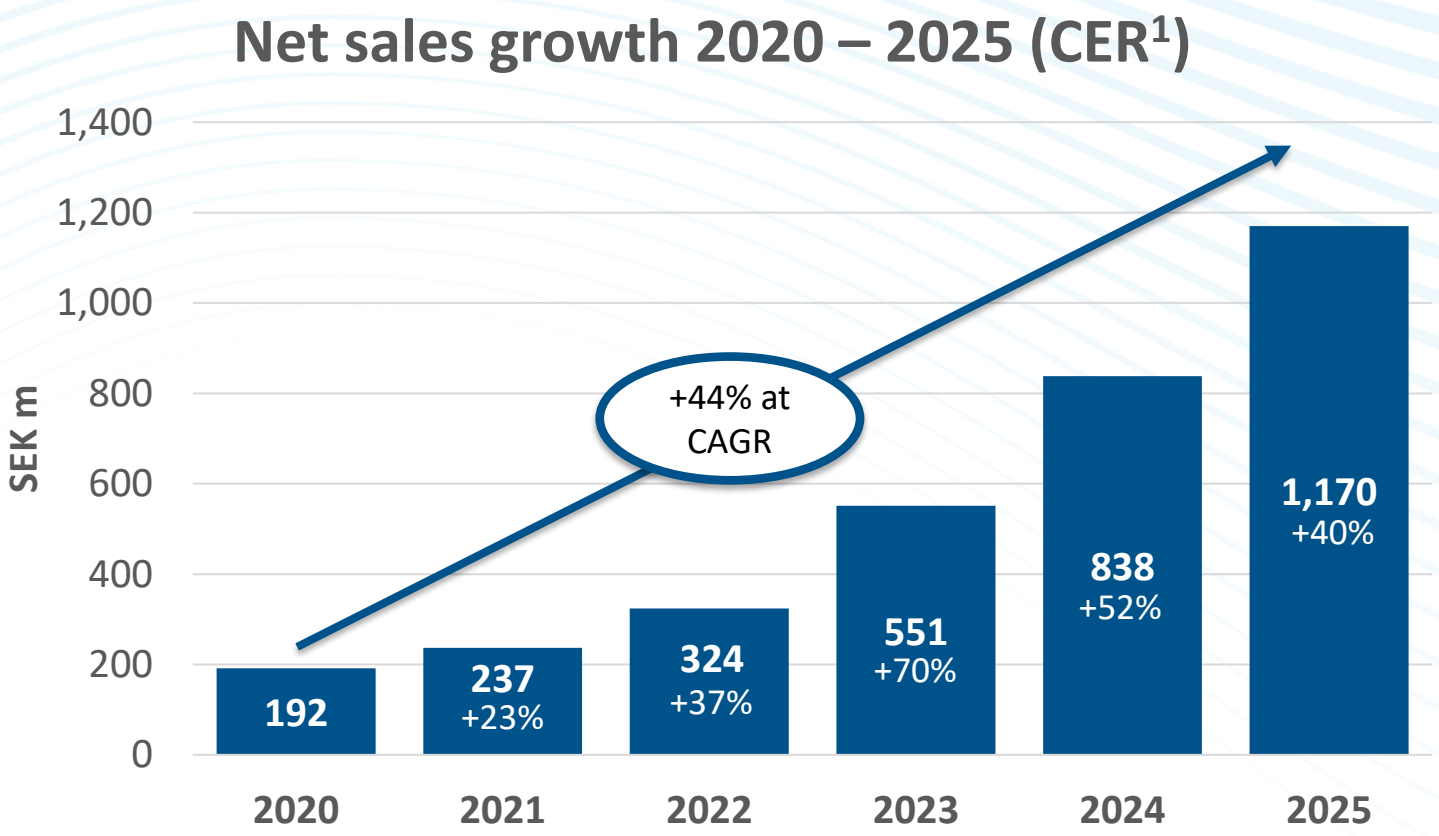
Q&A

Capital Markets Day 2026

Value Creating Technology & Operating Model

Håkan Johansson, CFO

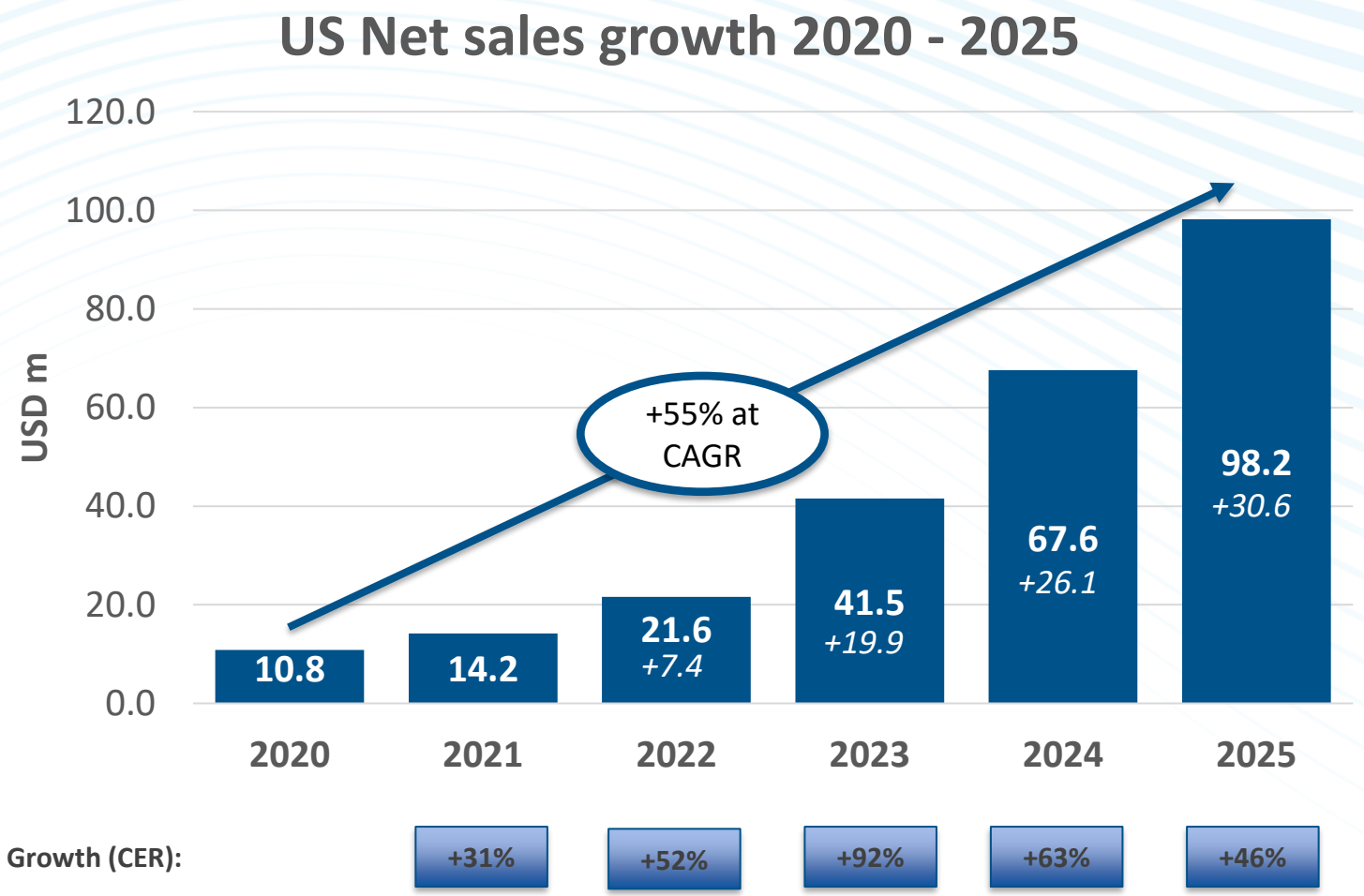
Cutting-edge technology with high-growth opportunities



- The commercial strategy and platform created in 2018 have established a solid growth momentum
- FDA Authorization of CERAMENT G and the market launch in US in Q4 2022 have further accelerated sales growth
- **44% CAGR** in 2020 to 2025
- Large remaining market potential talking for continued solid growth

[1] Net sales in CER calculated on average fx rates for the period 2020-2025

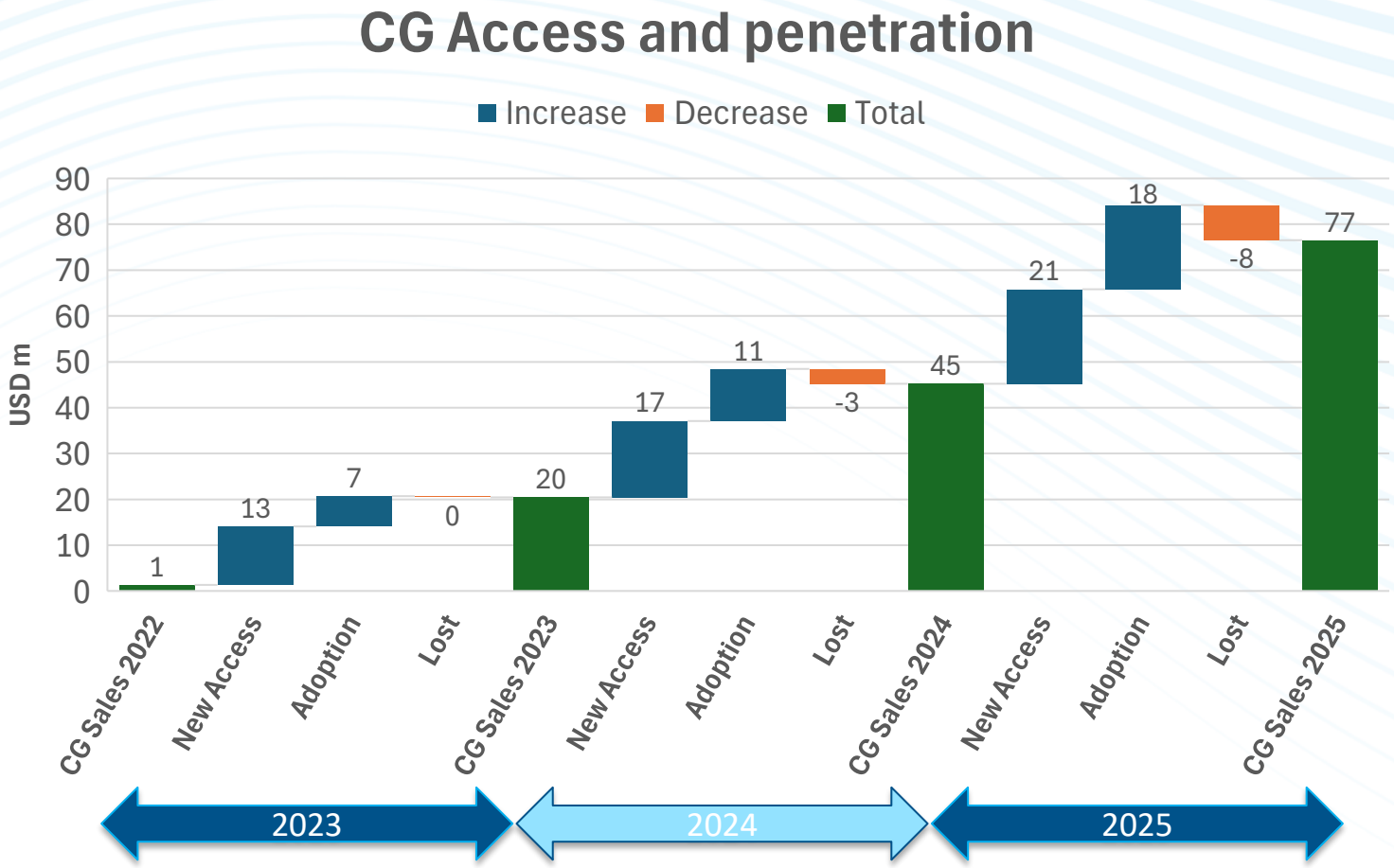
US accelerating sales growth



- The early traction created with CERAMENT BVF, expanding hospital access and distributor network created a solid platform ahead of the launch of CERAMENT G
- Incremental sales growth accelerating as CERAMENT G was lunched in October 2022.

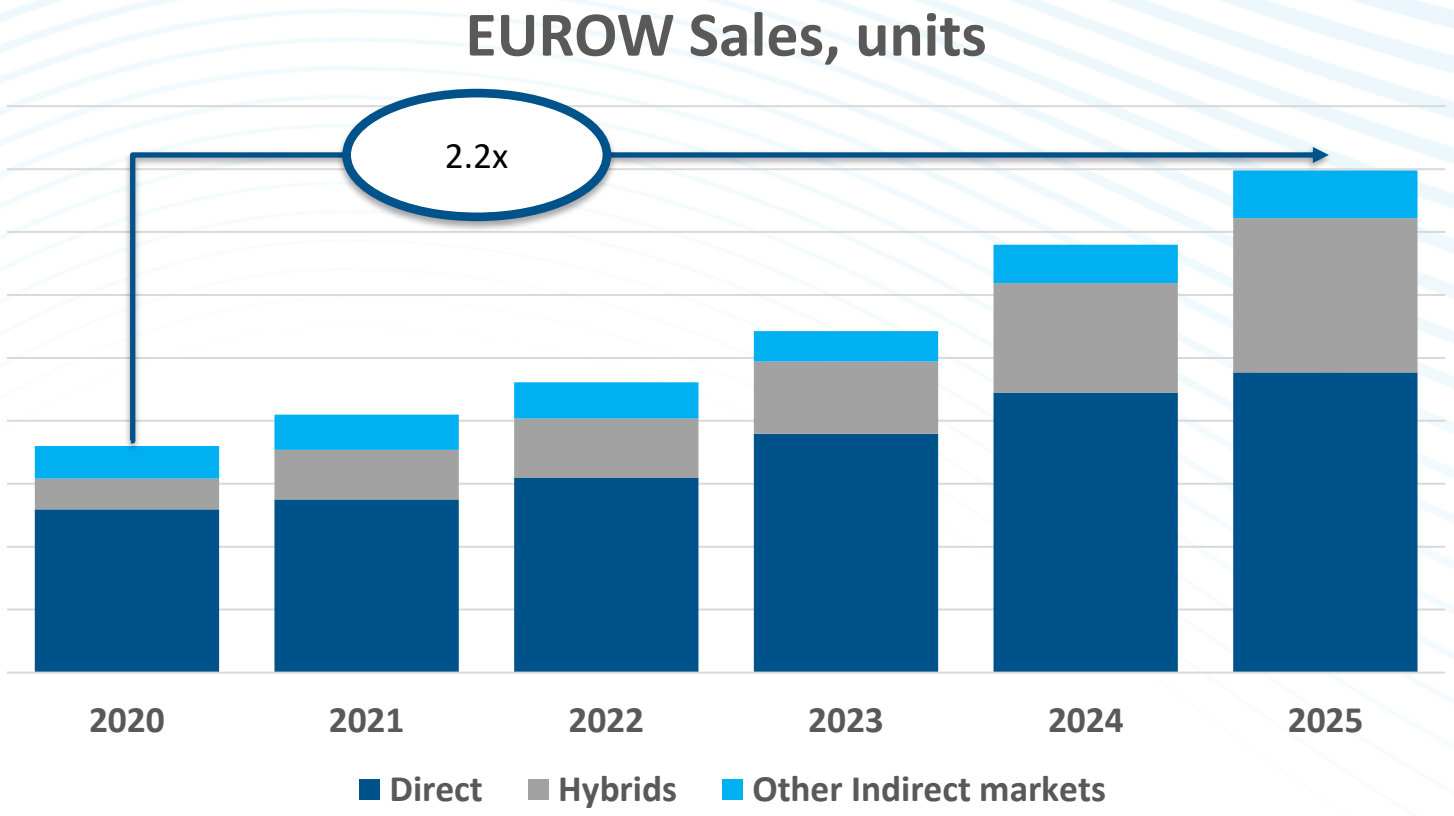
[1] Incremental growth in Italic style

CERAMENT G a second gear in market penetration



- Both New Access and Adoption accelerates Y o Y
- Strong retention of approximately 85%
- Multiple of “Lost” accounts are Surgeons moving to other indication areas or moving from a hospital with CERAMENT listed to a hospital where CERMENT is not listed
- A segment-based approach will continue support adoption, extending surgeons use of various applications within their field of expertise, for many years to come

Stable growth partly masked behind differences in business models

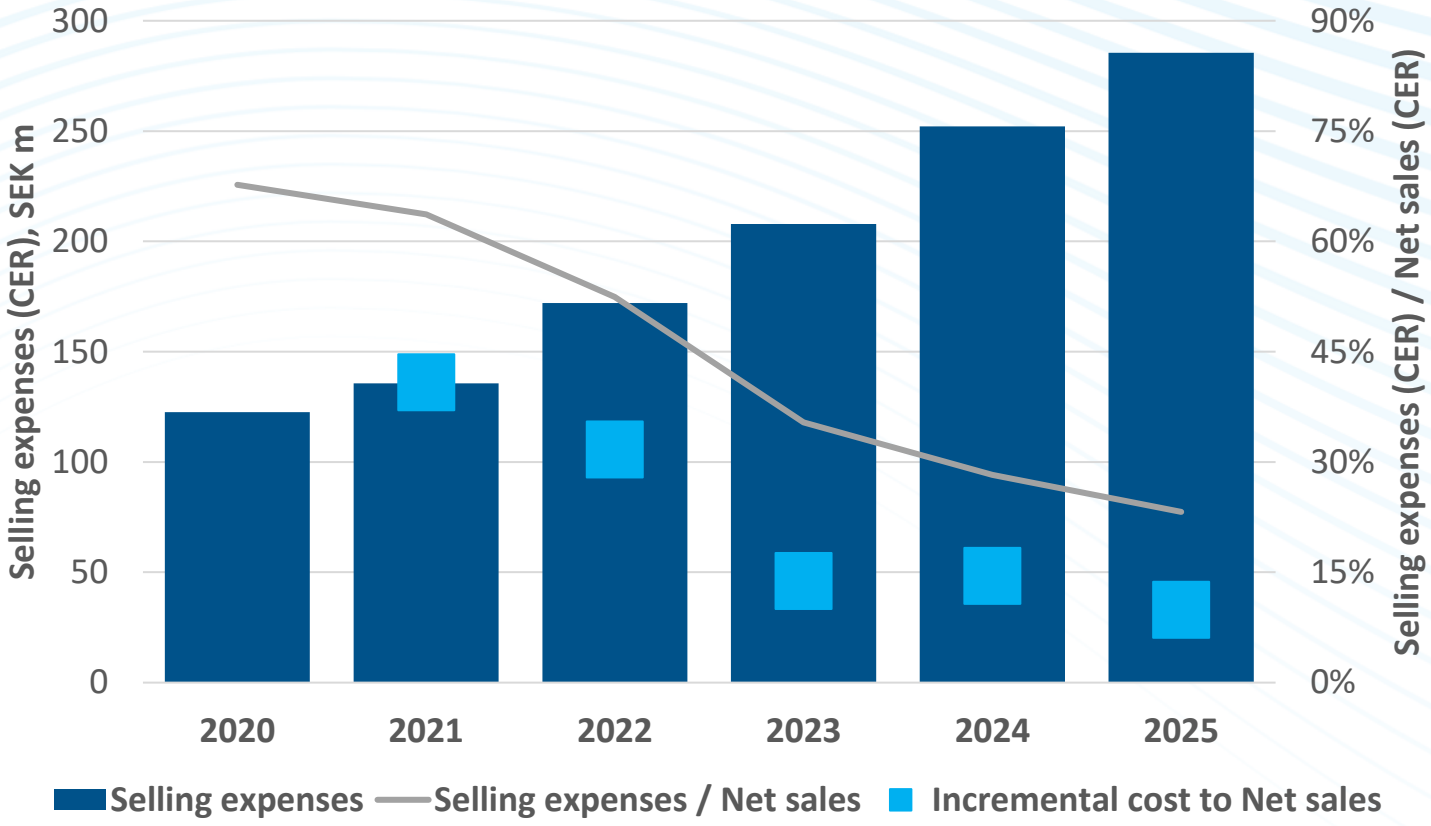


The actual unit data is not shared as we do not want to share this data with competitors

- Solid trajectory with a 13% CAGR[1] in direct markets despite headwinds in UK and Germany in 2025
- Investments in hybrid markets showing solid early traction and a 38% CAGR[1]
- The EUROW booster launched in late 2024 adding additional FTEs investing in growth, especially in Hybrid markets
- Other distributor markets includes future hybrid potentials
- Strong potential in continued gradual Geographic expansion

[1] Compound Annual Growth Rate (CAGR) in units sold

Commercial investments building for the future

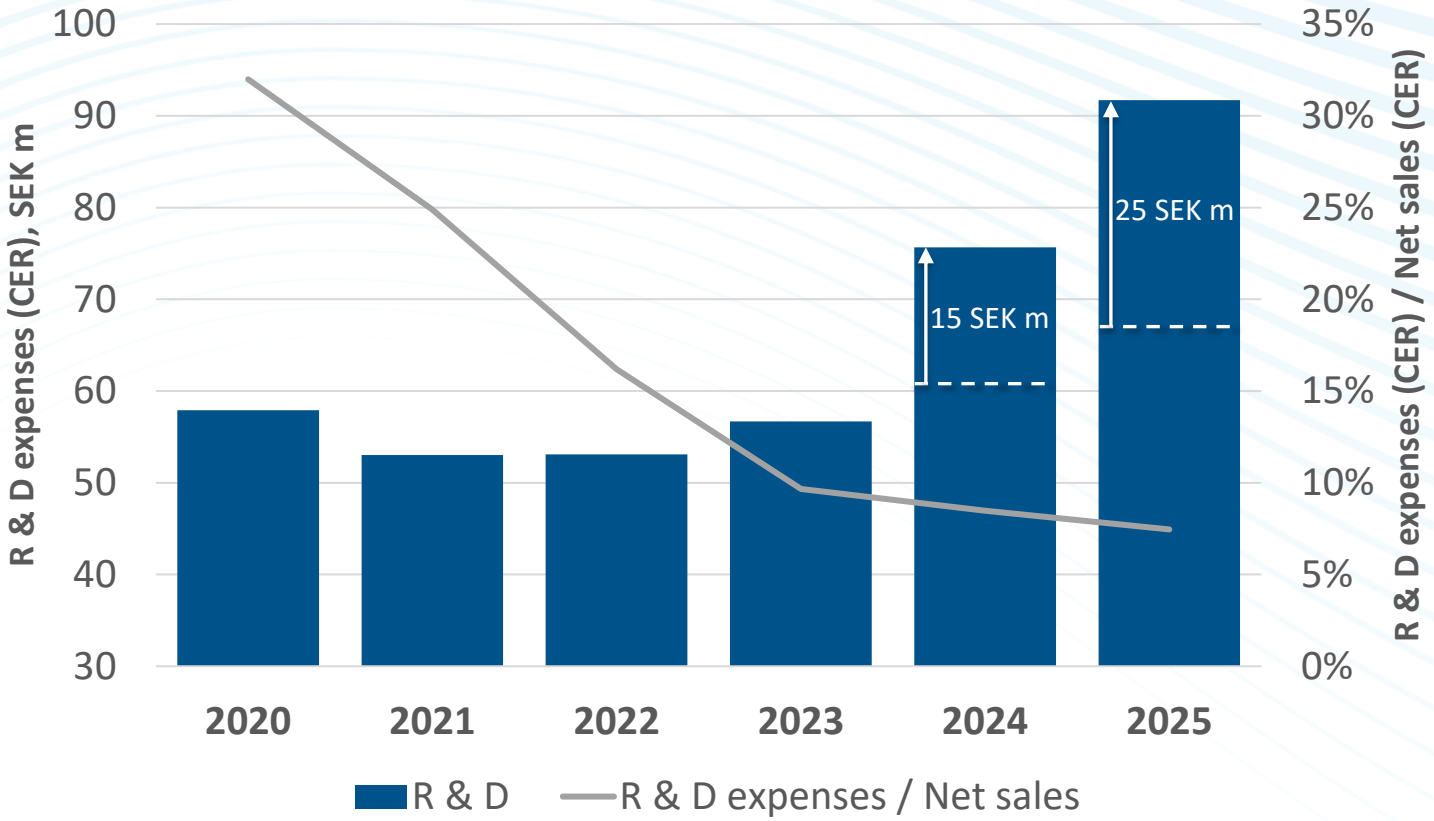


Average FTEs in Sales and Marketing:	50	51	49	58	67	85

- Continuous commercial investments made supporting sustainable sales growth
  - A 19% CAGR in selling expenses compared with a 44% CAGR in Net sales
- Adding 15 FTEs in EUROW sales since 2022 of which 10 in 2025
- Adding 15 FTEs in EUROW sales since 2022 of which 10 FTEs in 2025
  - Average ROI estimated to 18 months
  - Peak sales estimated 5 years post starting date

When referring to currency translation in constant exchange rates ("CER"), Net sales has been converted from the transactions' currencies into SEK and costs have been converted from the foreign subsidiaries' accounting currencies (which in all material aspects corresponds to the transaction currency) into SEK. Conversion has been made using average currency rates for the period January 1, 2020, to December 31, 2025.

Investing in future growth opportunities

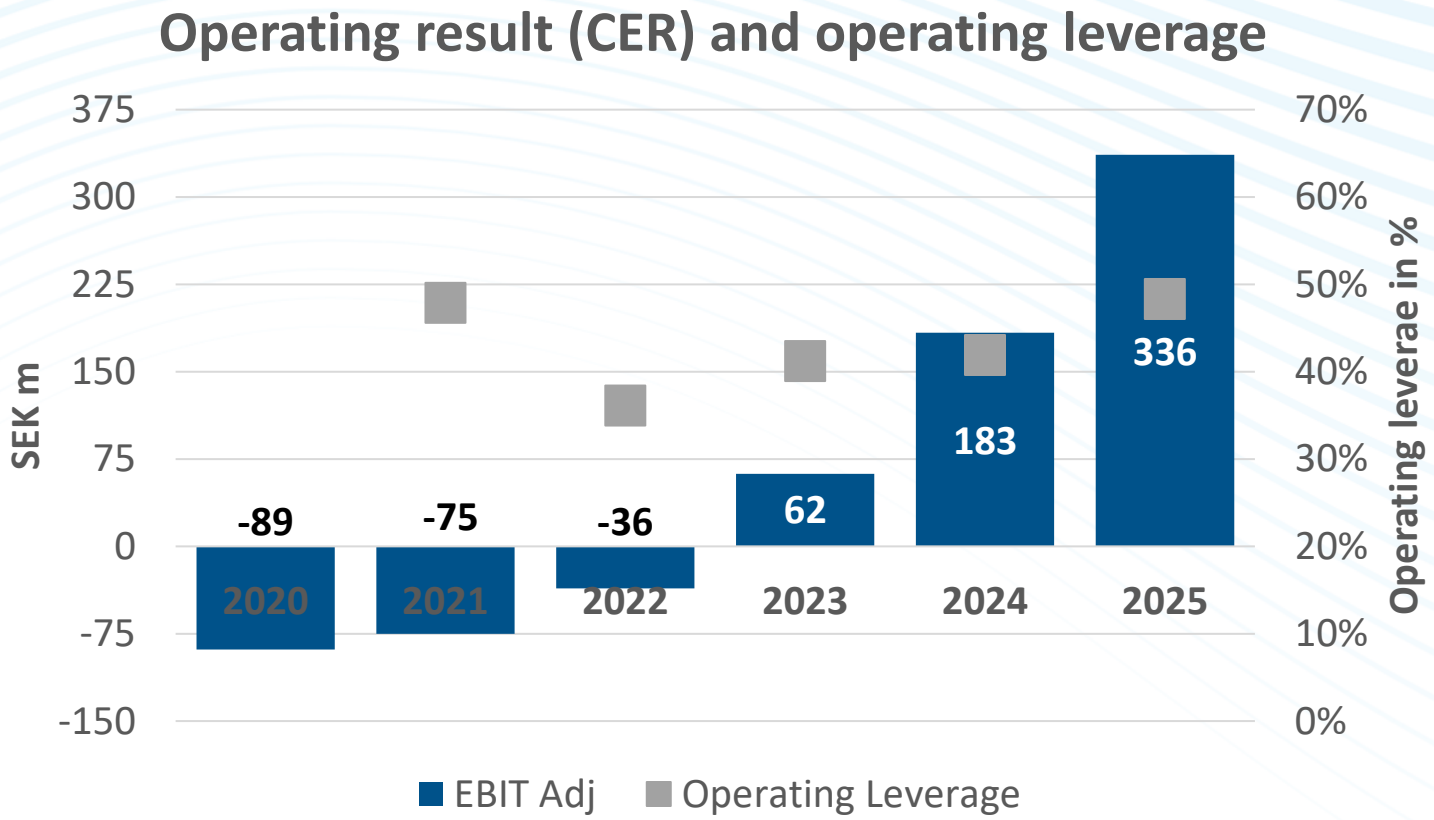


- The R & D baseline ensuring current regulatory approvals as well as clinical studies within existing labels remaining on a relatively stable level

- R & D expenses increasing in the latest two years (15 + 25 SEK m) as investments in future revenue streams accelerates.
  - CERAMENT V
  - CERAMENT in Spine
  - New Markets
  - Product development

When referring to currency translation in constant exchange rates ("CER"), Net sales has been converted from the transactions' currencies into SEK and costs have been converted from the foreign subsidiaries' accounting currencies (which in all material aspects corresponds to the transaction currency) into SEK. Conversion has been made using average currency rates for the period January 1, 2020, to December 31, 2025.

Disciplined execution ensuring strong operating leverage[1]

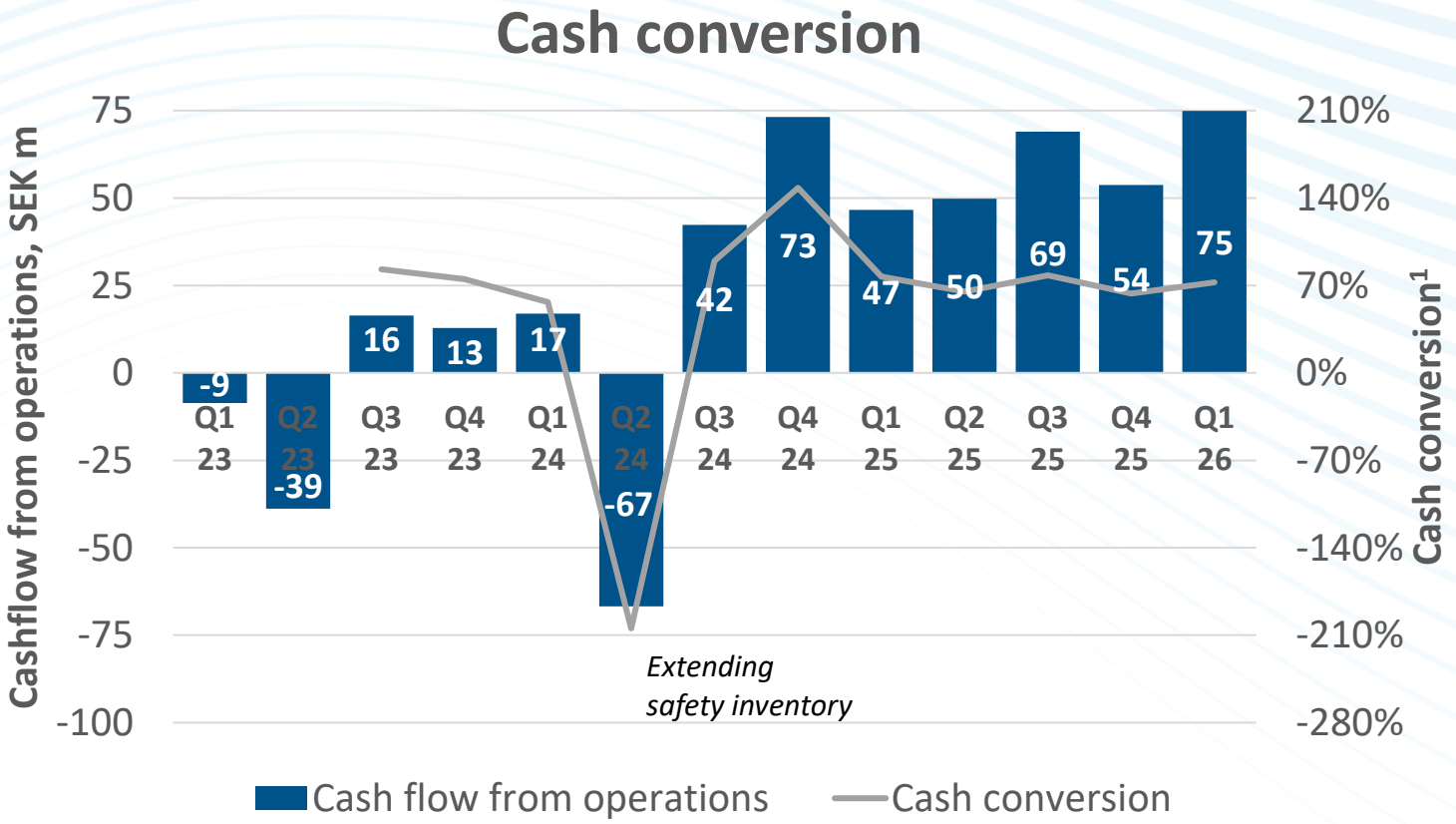


- Operating result accelerating with the successful launch of CERAMENT G in the US
- Commercial investments over the years continue to deliver strong operating leverage.
  - Strong sales growth in combination with a scalable business model
  - Disciplined cost management
- The stability in operating leverage gives a strong indication of long-term operating margins

1) Operating leverage is calculated as yearly improved Adjusted operating result (CER) in percentage of yearly gross profit improvement (CER)

When referring to currency translation in constant exchange rates ("CER"), Net sales has been converted from the transactions' currencies into SEK and costs have been converted from the foreign subsidiaries' accounting currencies (which in all material aspects corresponds to the transaction currency) into SEK. Conversion has been made using average currency rates for the period January 1, 2020, to December 31, 2025.

Strong cash conversion drives financial health and enables flexibility



- Strong cashflow from operations and business scalability enables deliberate business development in focused market segments and geographies, innovation pipeline and market penetration
- Tax losses carried forward will continue to have favorable impact on cash conversion well into 2028
- Creating headroom for capital allocation

[1] Cash conversion calculated as Cashflow from operations in relation to Adj. Operating result (CER)

Unlocking a large untapped potential

BONESUPPORT™

Delivering strong shareholder value

- Penetration in early phase in all main segments with great market potential ahead
- Scalable business model with strong operating leverage and cash conversion, large investments made driving future growth
- Several triggers in short- to mid term
  - SOLARIO study
  - CERAMENT V submission
  - Geographic expansion outside existing markets
  - Antibiotic eluting product for Spine

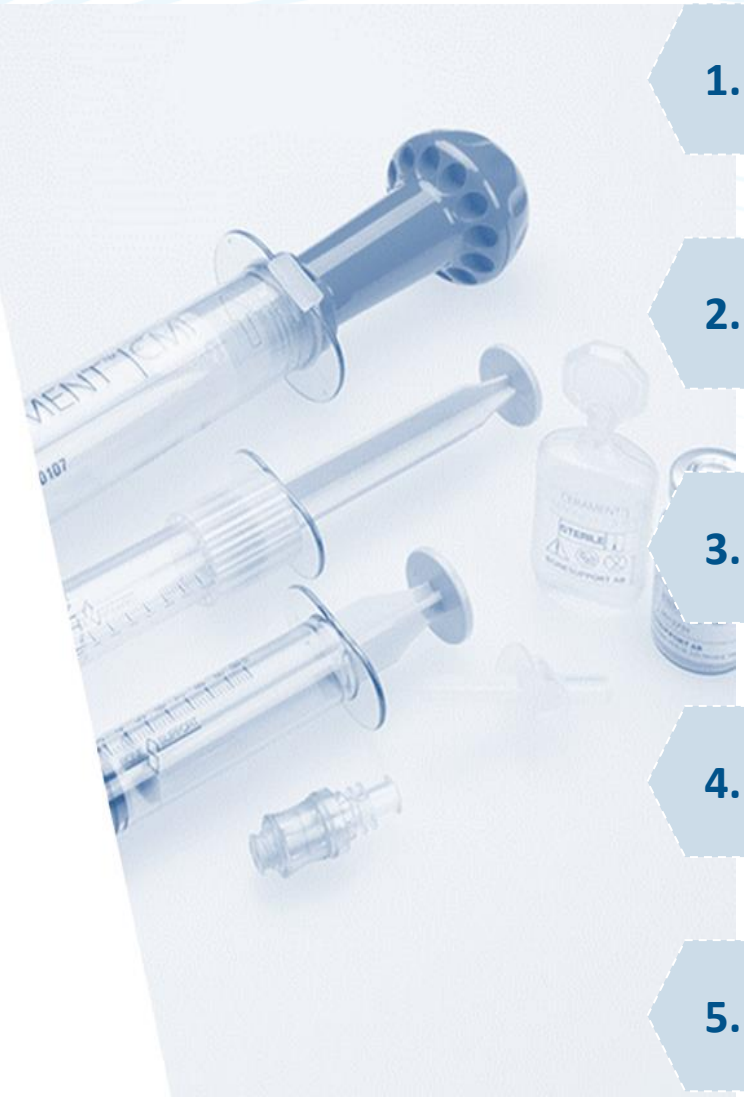
BONESUPPORT™

Capital Markets Day 2026

Wrap up and Q&A

Torbjörn Sköld, CEO

Concluding remarks



1. The **BONESUPPORT strategy is proven** – our next evolution is **segment specific execution** to unlock full potential of CERAMENT

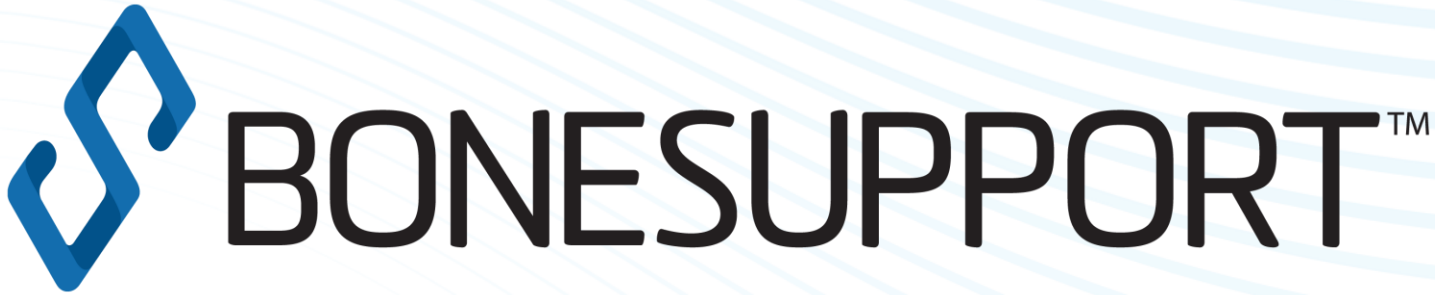
2. Our **U.S. market opportunity is larger** (460K vs. 380K procedures) than previously assessed, underlining the long-term growth potential of CERAMENT

3. We **continue to invest in evidence** with special emphasis on Arthroplasty where a multicentre RCT will be initiated in 2027 on antibiotic eluting CERAMENT

4. **Spine offers high unmet need** for on label antibiotic eluting CERAMENT – multicentre study to start 2027, with regulatory (FDA) submission no later than 2031

5. Our **penetration is in early phase**, our **business model is scalable** with strong cash conversion profile

BONESUPPORT



Q&A

BONESUPPORT™