

## **TREATMENT OF SEPTIC NON-UNIONS WITH S53P4 BIOACTIVE GLASS**

**Presentation of 9 tibial septic non-unions  
from a series of 52 treated patients**



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## INTRODUCTION

The treatment of septic non-unions is a complex problem with high morbidity, prolonged and costly treatment with significant psycho-social implications. Good communication with the patient and individualized treatment objectives are therefore essential. With appropriate treatment and complete elimination of infection a good to excellent outcome can be expected.

The general problem with septic non-unions reside in the accurate assessment of the septic disease, interpretation and evaluation of the “delayed bone fracture healing” (6 months) vs. non-union (9 months). The surgery becomes challenging because of the extensive bone defect formations and the surgeon is confronted with a multitude of alternatives for the bone defect reconstruction and non-union treatment.

### **Options for bone reconstruction:**

- Autologous bone graft
- Masquelet technique
- Segmental bone transport (Ilizarov)
- Free autologous grafts (from iliac crest)
- Vascularized autologous grafts (e.g. fibula)
- Allogeneic (antibiotic impregnated) bone grafts
- Synthetic scaffolds – osteoconductive/inductive
- Prothesis

## THERAPY OF BONE INFECTIONS - SEPTIC DIAMOND CONCEPT

The critical factors of good fracture healing has been outlined by Giannoudis et al. in their article: “Fracture healing: the diamond concept” of bone fracture healing interactions (Injury. 2007 Sep;38 Suppl 4:S3-6). However, when treating patients with conditions involving bone infections the situation becomes more complex. In addition to the mechanical environment, osteoconductive scaffold, growth factors, osteogenic cells and vascularity as outlined in the diamond concept, the septic diamond concept needs to take a polytherapeutic approach. These patients have on average been isolated from society and they are hospitalized for long periods of time due to a typically prolonged duration of treatment. Furthermore, they have on average more comorbidities and complication rates and have often developed a resistance to antibiotics, which makes the efficacy of antibiotic therapy questionable. In addition, these patients have, in many cases, undergone 5-10 previous operations, hence they have poor soft tissue quality which compromises the prognosis of a successful clinical outcome.



## SURGICAL TECHNIQUE FOR SEPTIC NON-UNIONS AT DUISBURG

In our clinic we have gained experience in treating a wide range of septic non-unions with S53P4 bioactive glass (BonAlive® granules, BonAlive Biomaterials, Turku, Finland), including diaphysial septic non-unions, that extend up to 3cm in terms of segmental circular defects. The treatment of such defects has been possible due to a “neo-cortical” reaction that this bioactive glass seems to induce after implantation. Our technique of managing septic non-unions follows a 2-stage principal where the infection is cleared with antibiotics in the 1<sup>st</sup> stage surgery and bone reconstruction is performed in the 2<sup>nd</sup> stage.

### 1<sup>ST</sup> STAGE SURGERY

1. Clear infection with radical debridement and sequestrectomy. All infected parts of the bone and soft tissue must be removed.
2. Insert an antibiotic carrier (chain, beads, fleece) into the defect. During the operation take 5 – 6 microbiological samples with pieces of bone and soft tissue to detect the bacteria, in addition histological examination of bone samples is carried out. Soft tissue and wound closure is mandatory after completion of the 1<sup>st</sup> stage surgery.

### 2<sup>ND</sup> STAGE SURGERY

1. Enter the area of the septic non-union and perform radical debridement of the fibrotic and necrotic tissue in the non-union site. Debride until bleeding bone (paprika sign) is visible in the debrided cavity.
2. Open the proximal and distal medullary area by scraping.
3. Perform a decortication of the sclerotic bone in the close proximity of the bone gap in the non-union. This step is crucial to accelerate the osteogenesis in the area and to initiate the periosteal reaction.
4. If the medullary cavities are open it is possible to close them with a sponge, e.g. gentacoll. Materials that can induce a persistence of the infection or completely occlude the blood supply from the medullary room should not be used.
5. Apply the bioactive glass into the defect and pack tightly. Up to 20 cc of 100% bioactive glass can be used and for larger defects a mix with autograft (30–50%) is recommended. Only in 10% of the cases the bioactive glass is mixed with autologous bone in our practice.
6. It is difficult to access the non-union on the contralateral side to perform a decortication of the sclerotic bone because the surgical entry has been performed only from one side. To our experience, complete access is not necessary because when good healing is achieved in the revised area the rest of the non-union will heal uneventfully.

#### Types of defects:

Non-union with cortical defect



Non-union with cork screw defect



Non-union with cavitory defect



Segmental defect

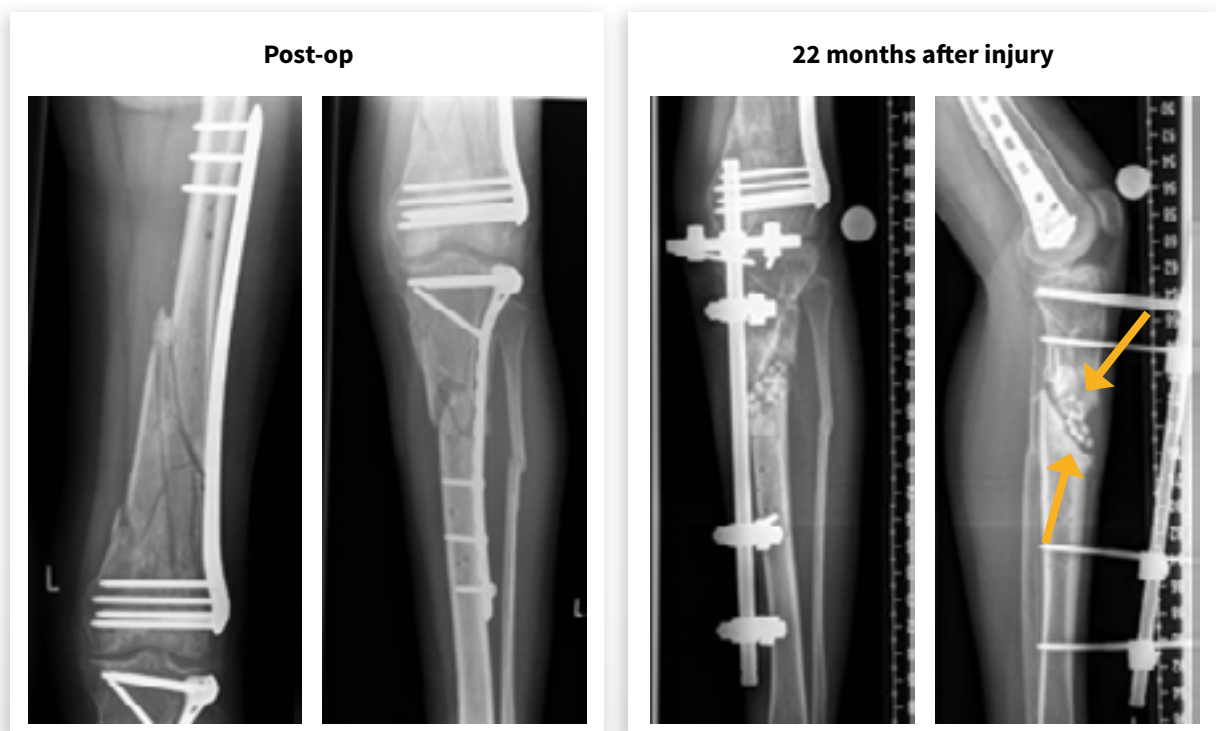


## PROXIMAL TIBIA (CASE 1)

**Patient:** 45-year-old female

**Preoperative status:** Type II° open proximal tibial fracture and distal femur fracture. Multiple revisions with autologous bone and BMP-2. Diagnosis of a septic non-union in the tibia 20 months after injury. Very sclerotic bone region next to the non-union.

**Bacterial culture:** *Staphylococcus capitis*



**Operation:** Extended decortication and drilling (24 months after injury) and insertion of intramedullary nail. Application of 10 cc bioactive glass mixed with autologous cancellous bone (20 cc) from ipsilateral posterior iliac crest 26 months after injury.

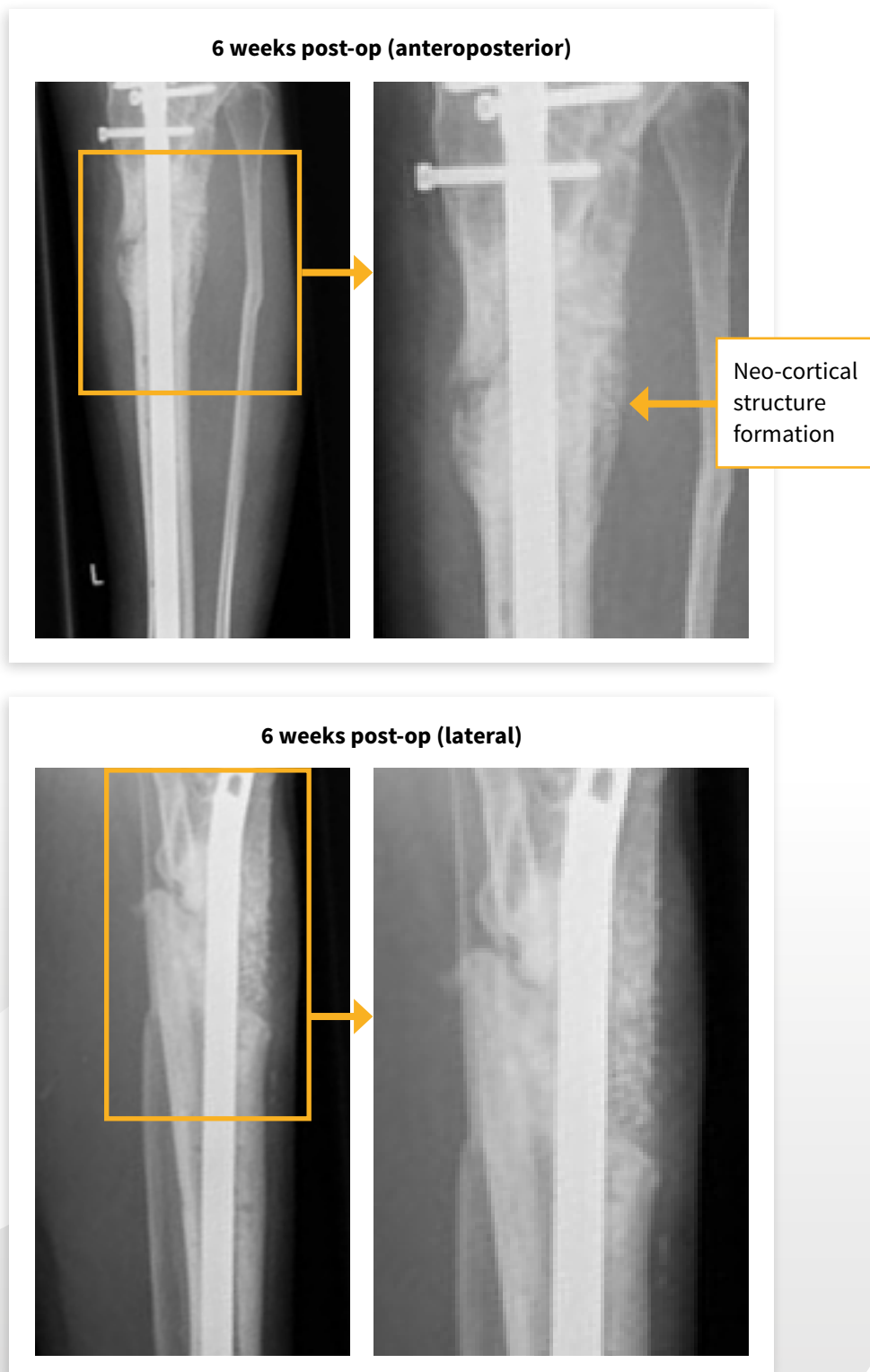
**24 months after injury**



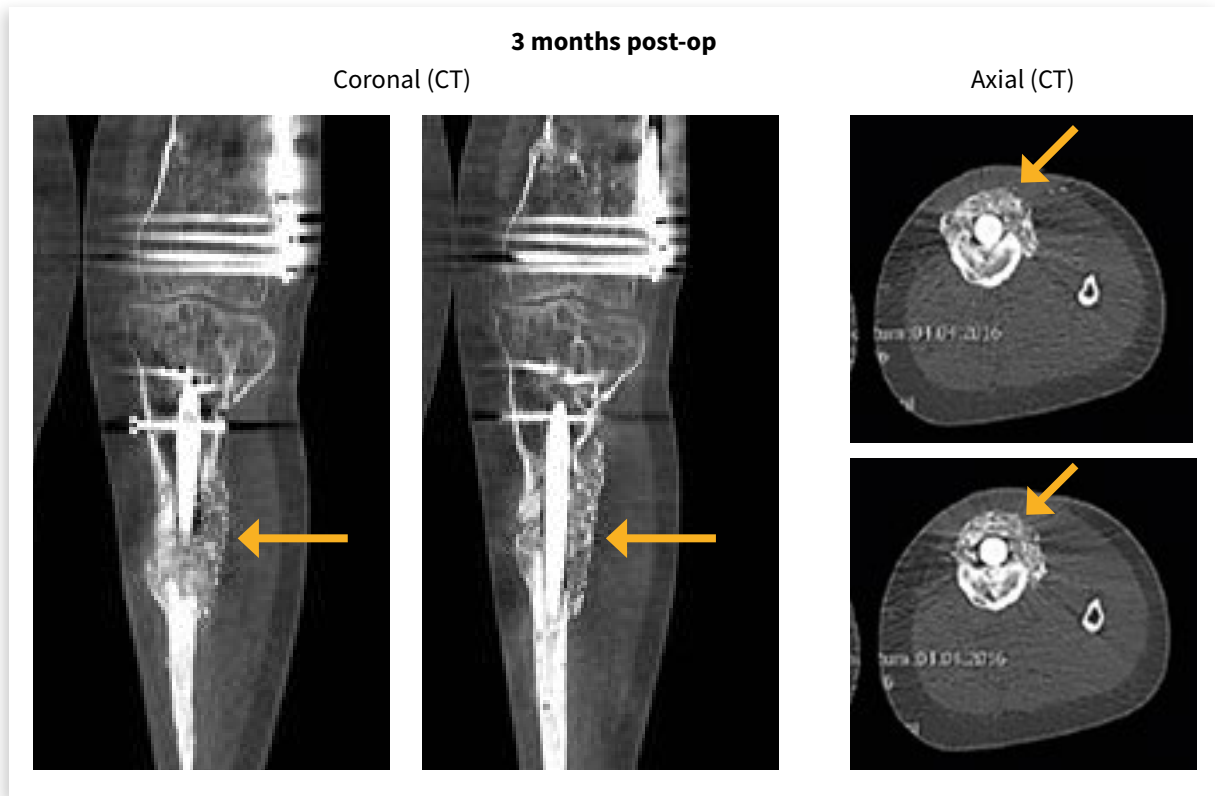
**Post-op after bioactive glass implantation**



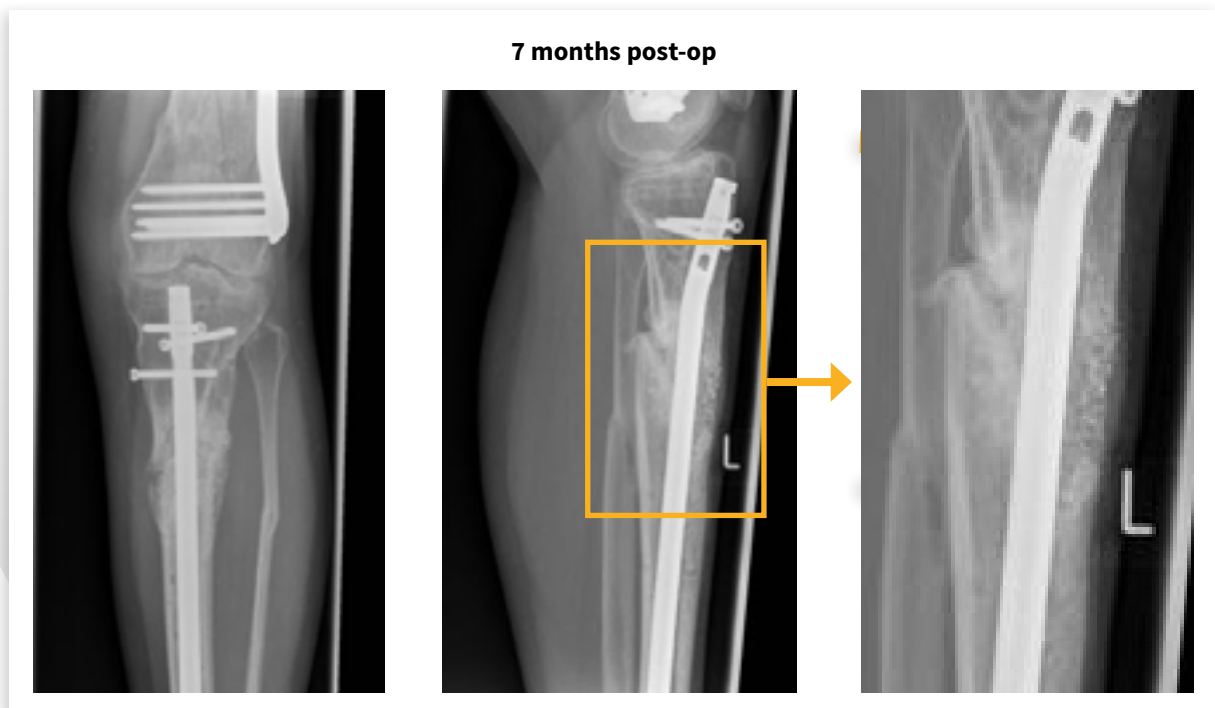
**Clinical outcome:** Bone formation visible with new callus formation 6 weeks after surgery.



**Clinical outcome:** New cortical bone formation and progression of bone remodeling visible in the CT images.



**Final clinical outcome:** 7 months after application of bioactive glass a complete consolidation could be observed.



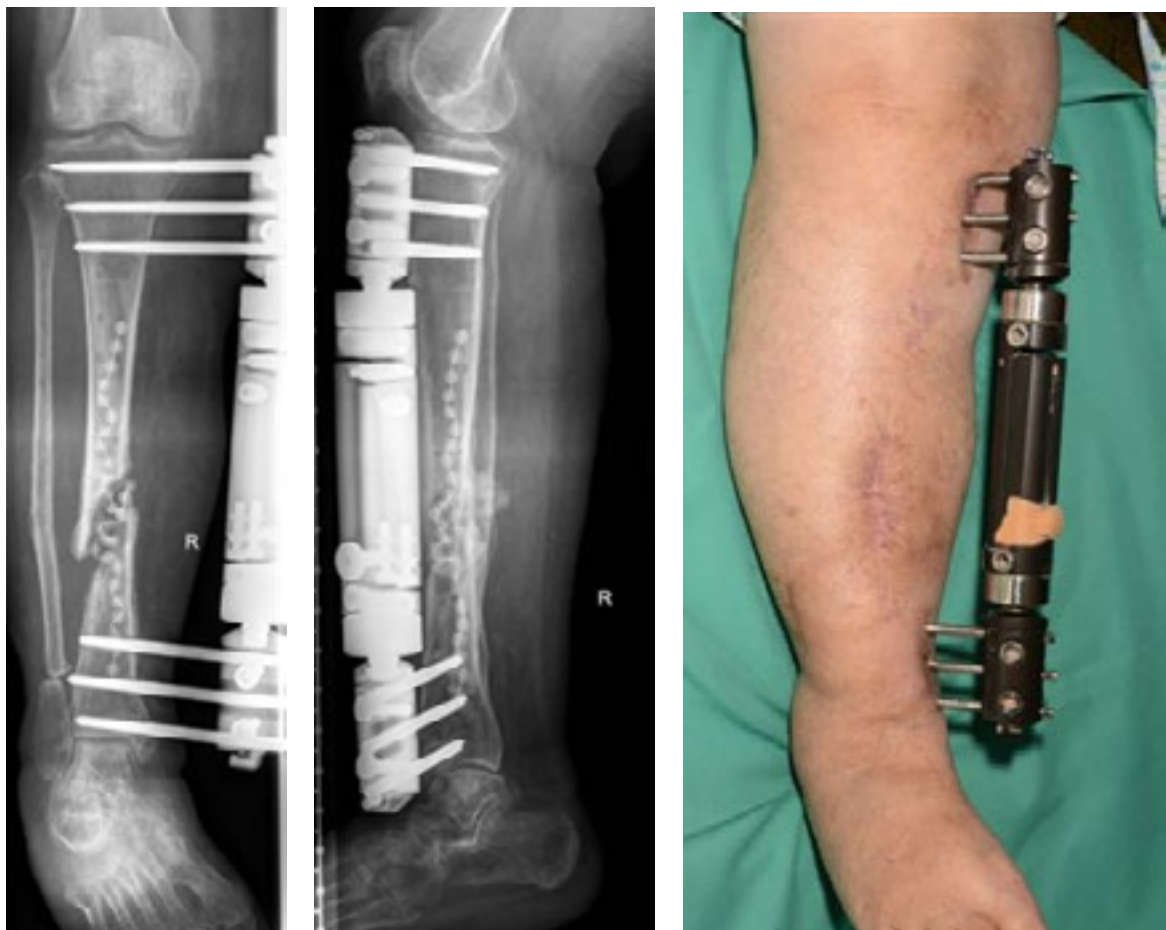
## DIAPHYSEAL TIBIA (CASE 2)

**Patient:** 69-year-old female

**Preoperative status:** Closed tibial fracture, initial ORIF, shortening of the leg, multiple revisions with autologous bone and several external fixators. Diagnosis of tibial osteomyelitis 7 months after injury. Nearly two years of treatment with failure of all performed treatment measures. Sent to BG Duisburg for amputation. Use of bioactive glass in limb salvage trial.

**Bacterial culture:** *Staphylococcus aureus*, which had become resistant during the treatment.

**Status of patient after first revision and insertion of antibiotic releasing beads**



**Operation:** Two years and four months after accident, reaming and application of gentamycin coated nail (Synthes Tibia Expertnail; Length: 255mm, Diameter: 13mm). The remaining bone defect was the shape of a corkscrew (8cm long) in the tibial diaphysis. Two months after the nail fixation, implantation of 10 cc bioactive glass with equal amount of autologous bone.

**2 years and 4 months after injury**



**Post-op after implantation of  
bioactive glass**



**Clinical outcome:** Positive progression of healing with new bone and cortex formation at 6 months postoperatively. Full consolidation can be observed at 1.5 years postoperatively with CT.

**4 months post-op**



**6 months post-op**



**1.5 years post-op**

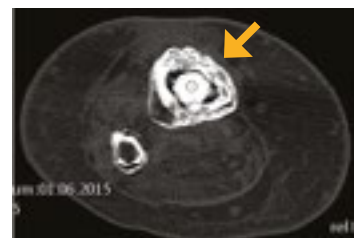
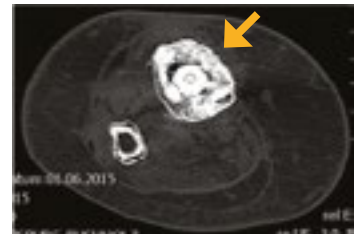
**Coronal (CT)**



**Sagittal (CT)**



**Axial (CT)**



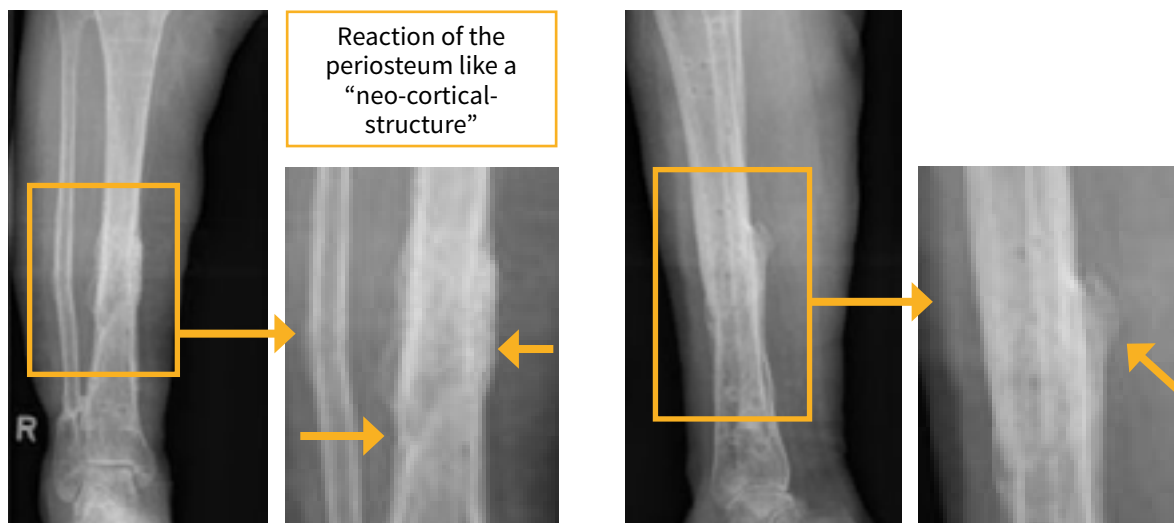
**Final clinical outcome:** Removal of the nail and insertion of temporary precautionary antibiotic loaded beads. 1.5 years postoperatively the leg was fully load bearing.

**1.5 years post-op**



AP view

Lateral view



## DIAPHYSEAL TIBIA (CASE 3)

**Patient:** 70-year-old male

**Preoperative status:** Type I° open distal tibial and fibula fracture, diagnosis of tibial osteomyelitis 4 months after injury.

**Bacterial culture:** *Staphylococcus aureus* and *Streptococcus agalactiae*

Pre-op images

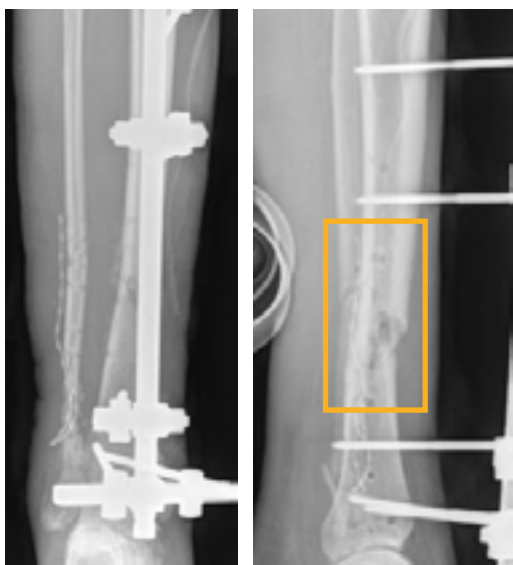


Post-op images



4 months post-op after injury

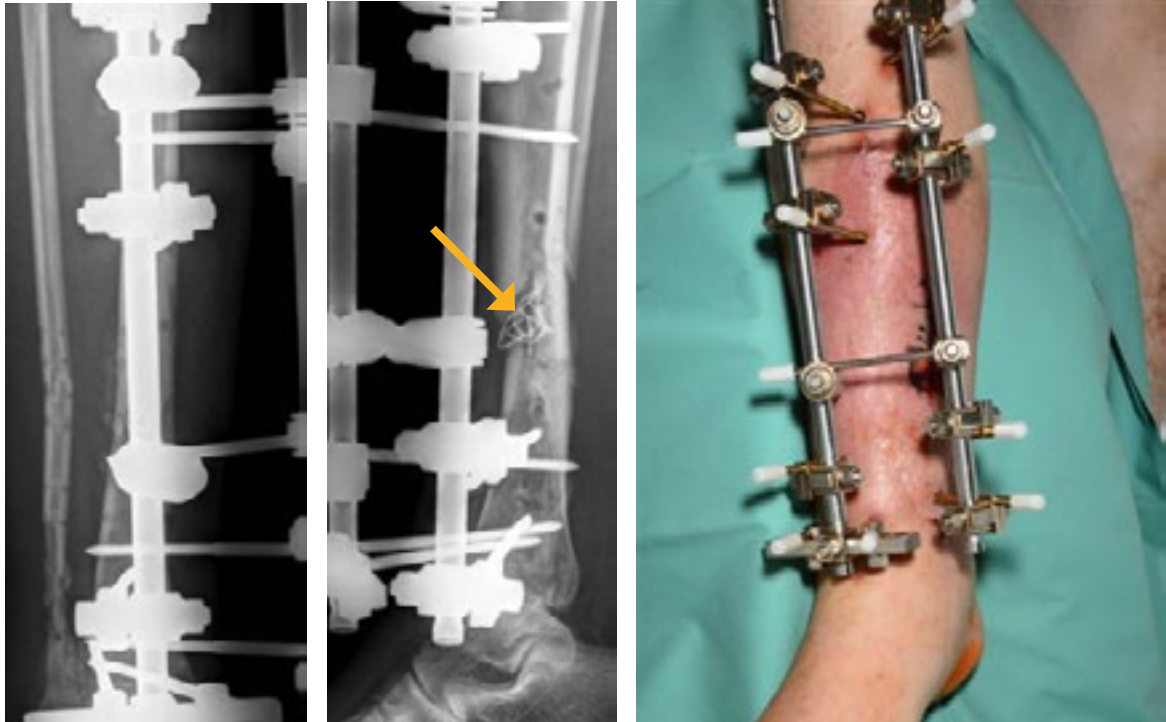
Diagnosis of tibial osteomyelitis



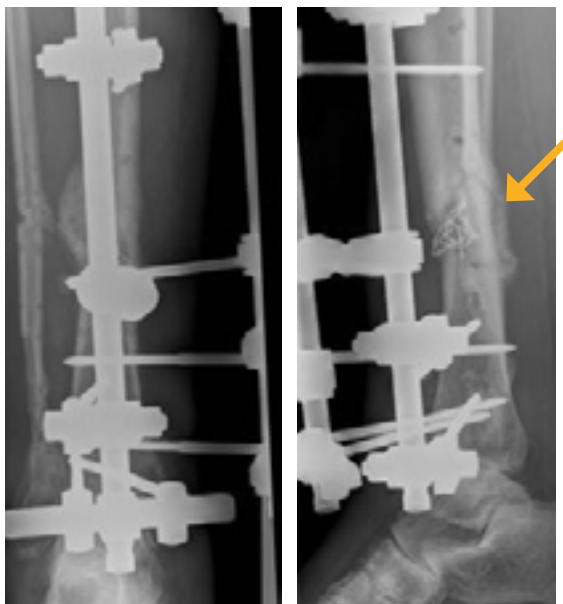
Problem with soft tissue



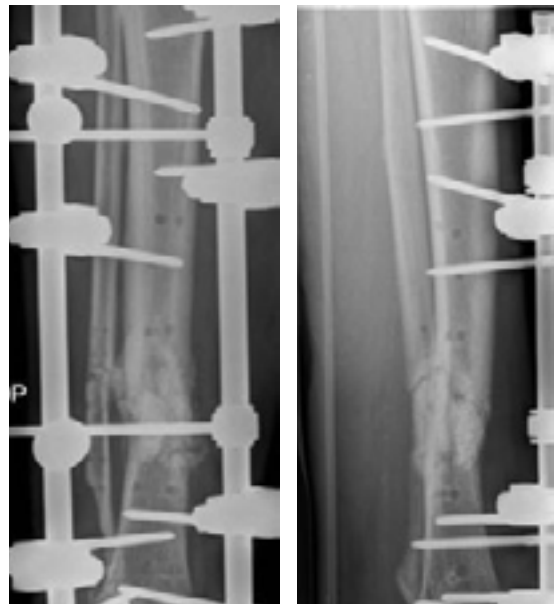
5 months post-op after injury



Multiple revisions, persistence of bacteria



Implantation of 10 cc bioactive glass



**Clinical outcome:** New bone and callus formation was observed 3 months postoperatively.

**3 months post-op**



**5 months post-op**



**Final clinical outcome:** 11 months after treatment with bioactive glass, a full consolidation of the septic non-union was achieved and the patient was free of infection. The limb was fully load bearing.

**11 months post-op**



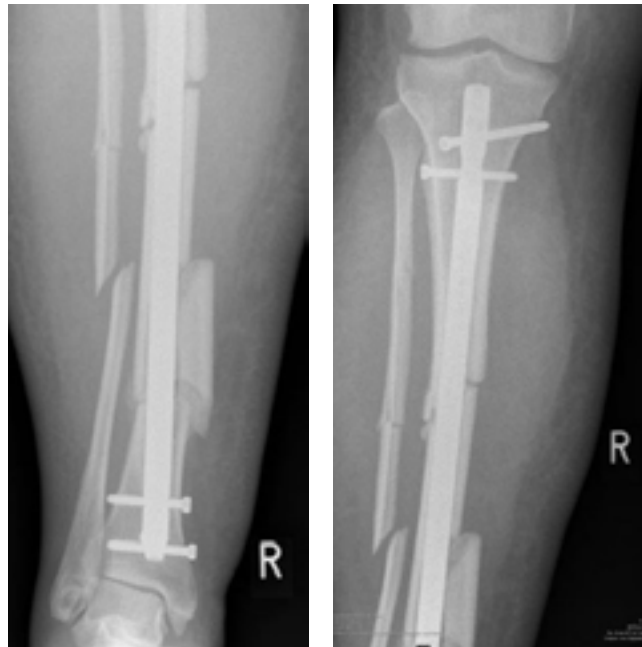
## DIAPHYSEAL TIBIA (CASE 4)

**Patient:** 56-year-old female

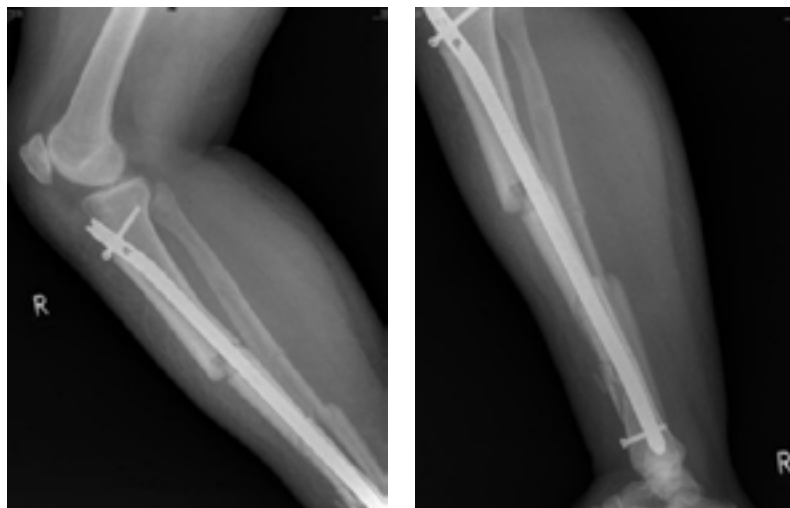
**Preoperative status:** Type II° open proximal tibial fracture, closed distal fracture. Diagnosis of tibial osteomyelitis 9 months after injury.

**Bacterial culture:** *Staphylococcus epidermidis*

**Post-op after primary surgery**



**5 months post-op**



**Complication:** Low grade infection with non-union observed at 9 months post-op.

**8 months post-op**



**Revision surgery**

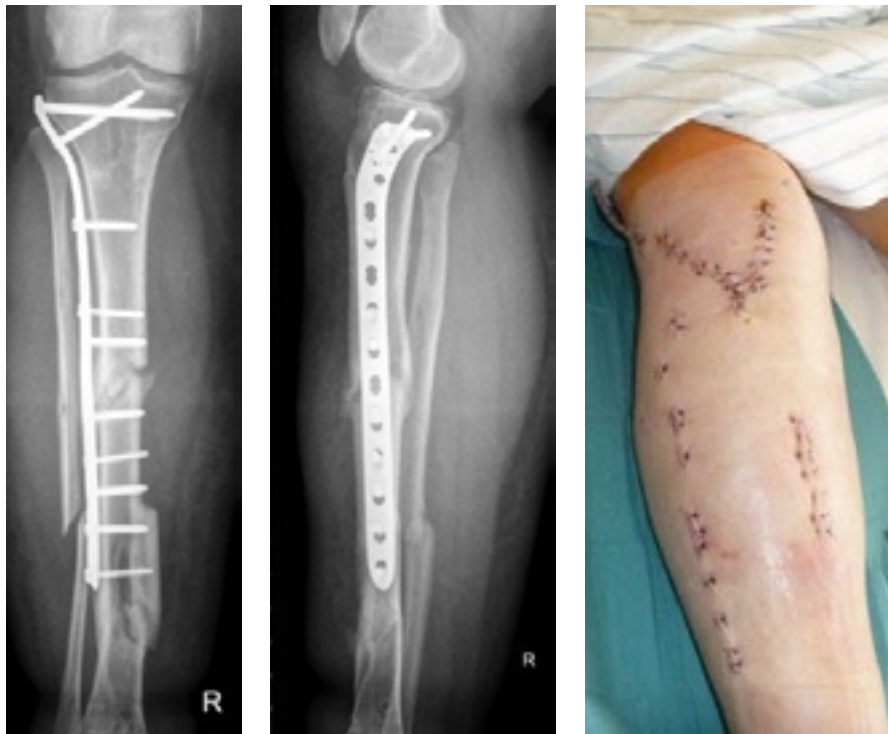


**2 weeks after revision**



**Operation:** Debridement and implantation of 10 cc bioactive glass 2 weeks after revision surgery.

**Post-op after implantation of bioactive glass**



**14 weeks post-op**



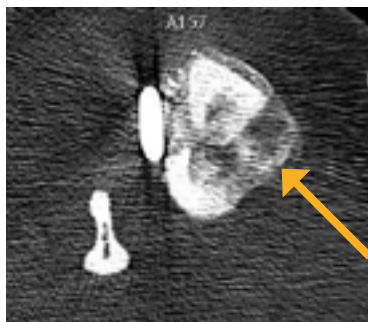
**6 months post-op**



**Final clinical outcome:** Consolidation and load bearing with cortical bone and callus formation visible with CT at 10 months post-op.

**10 months post-op (CT)**

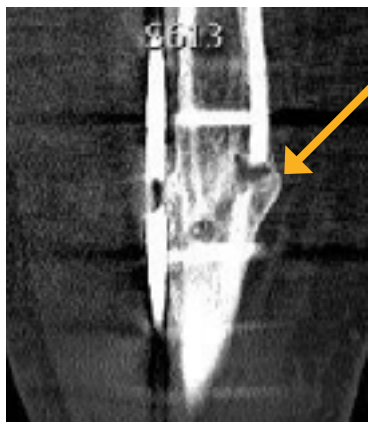
Axial (CT)



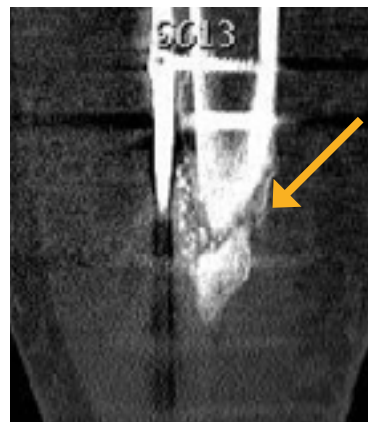
Axial (CT)



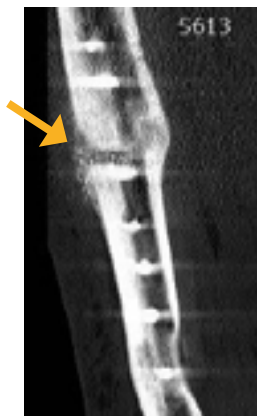
Coronal (CT)



Coronal (CT)



Sagittal (CT)



Sagittal (CT)



## DISTAL TIBIA (CASE 5)

**Patient:** 45-year-old male

**Preoperative status:** Closed tibial fracture, diagnosis of tibial osteomyelitis 8 months after injury. Patient suffered from compartment syndrome.

**Bacterial culture:** Multi-drug resistant *Staphylococcus haemolyticus*

Post-op after injury



**Operation:** The external fixation was changed to a medial plate, however at 6 months after the accident there was still delayed bone healing and poor soft tissue healing.

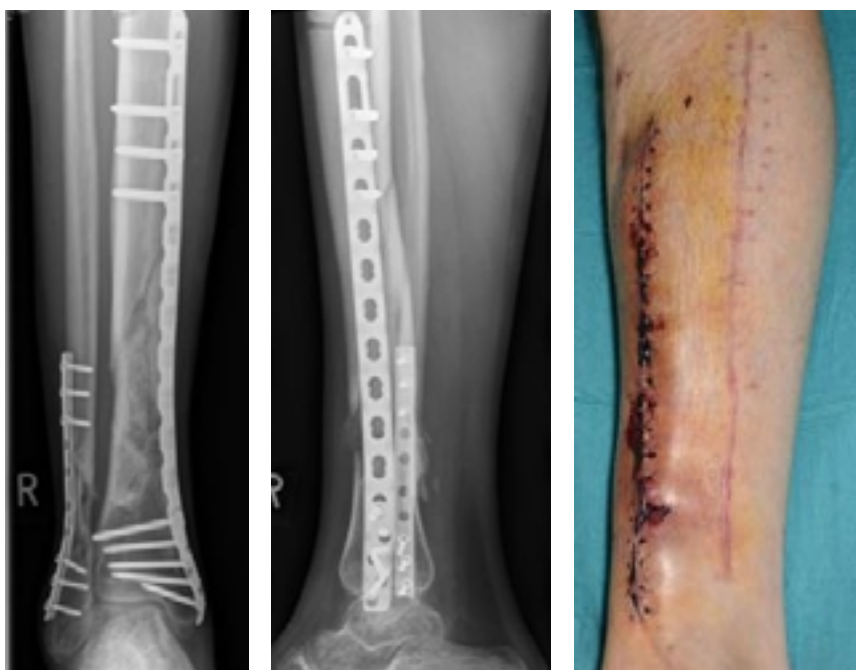
**1 month after injury**



**3 months after injury**



**6 months after injury**

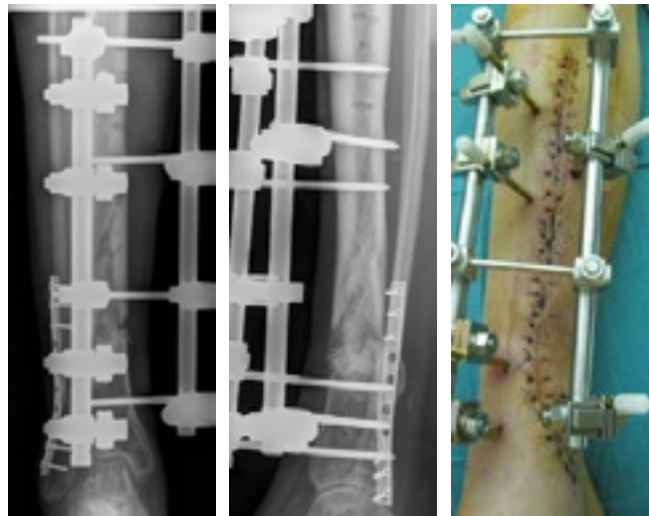


**Operation:** One stage procedure, removal of the plate, debridement and sequestrectomy, implantation of 5 cc bioactive glass in the septic focus.

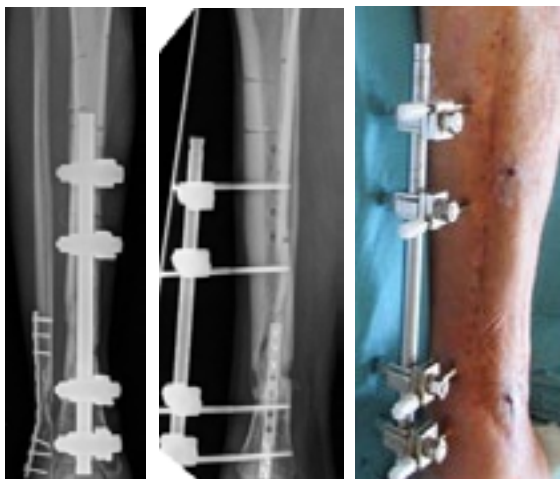
**Post-op**



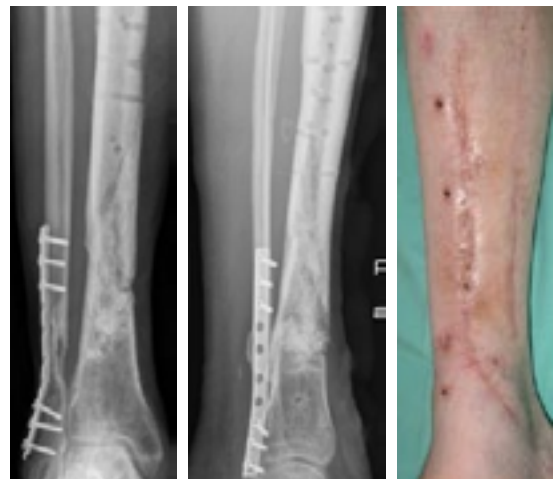
**2 weeks post-op**



**5 months post-op**



**7 months post-op**



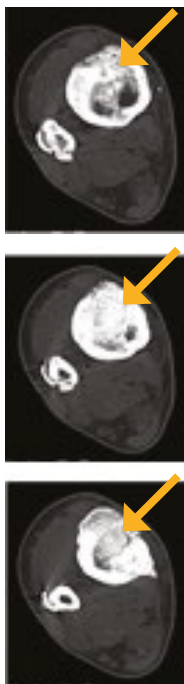
**Final clinical outcome:** New cortical bone formation was clearly visible 15 months after implantation of bioactive glass and full consolidation was achieved after 16 months as seen with CT. The limb was fully load bearing.

**15 months post-op**



**16 months post-op**

**Axial (CT)**



**Coronal (CT)**



**Sagittal (CT)**



## DISTAL TIBIA (CASE 6)

**Patient:** 79-year-old female

**Preoperative status:** Closed tibial fracture in the distal diaphysis with the Pilon tibiale affected. Diagnosis of low grade tibial osteomyelitis 2 months after injury.

**Bacterial culture:** multiresistant *Staphylococcus epidermidis*



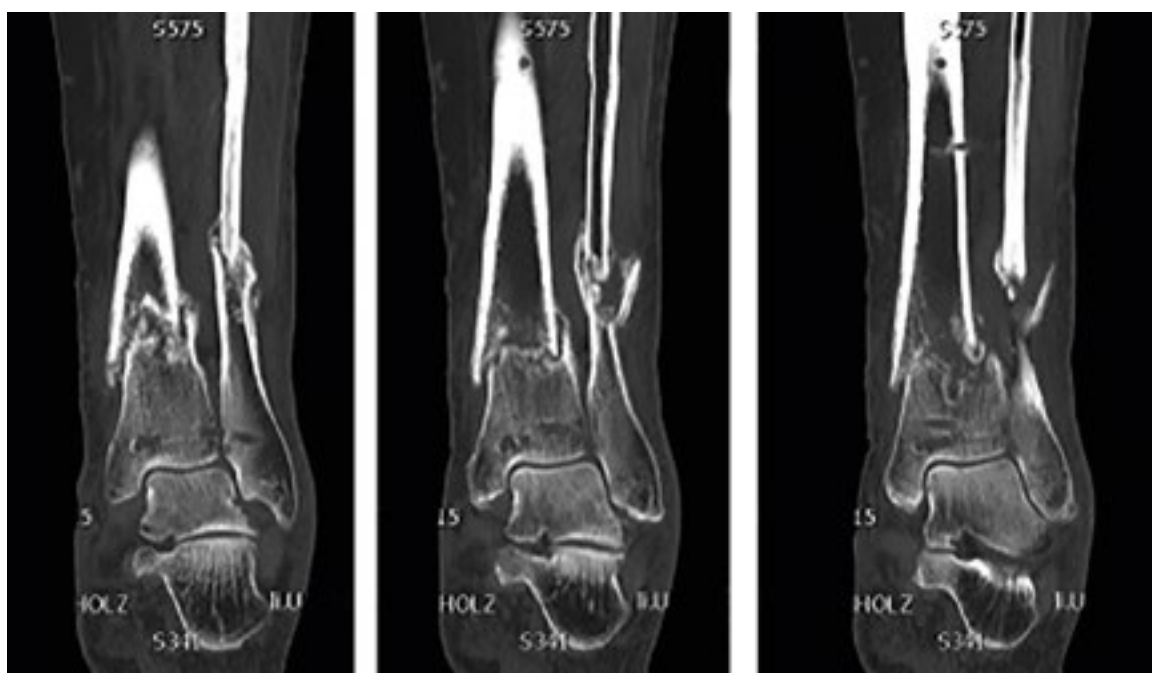
2 weeks post-op



8 weeks post-op

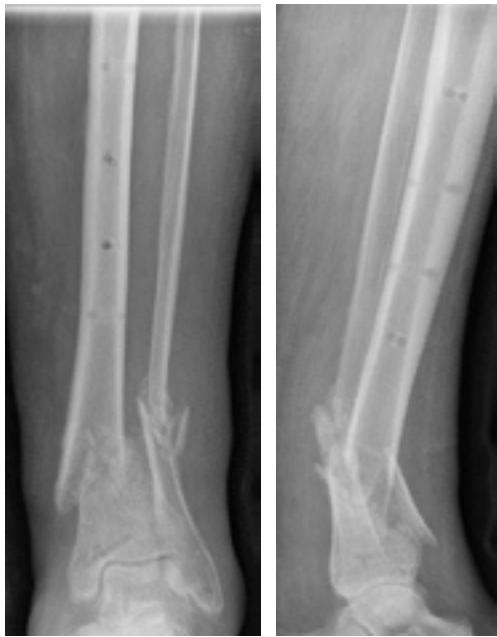


8 weeks post-op, Coronal (CT)

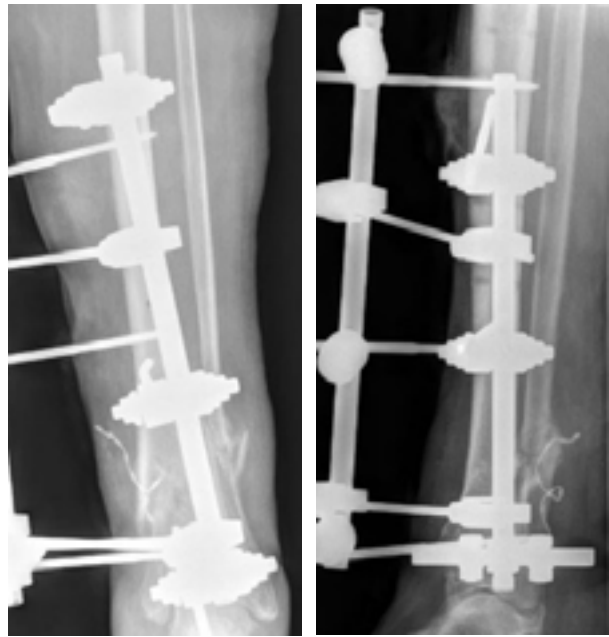


**Operation:** Fixation and implantation of 20 cc bioactive glass 4 months post-op.

**10 weeks post-op**



**4 months post-op**



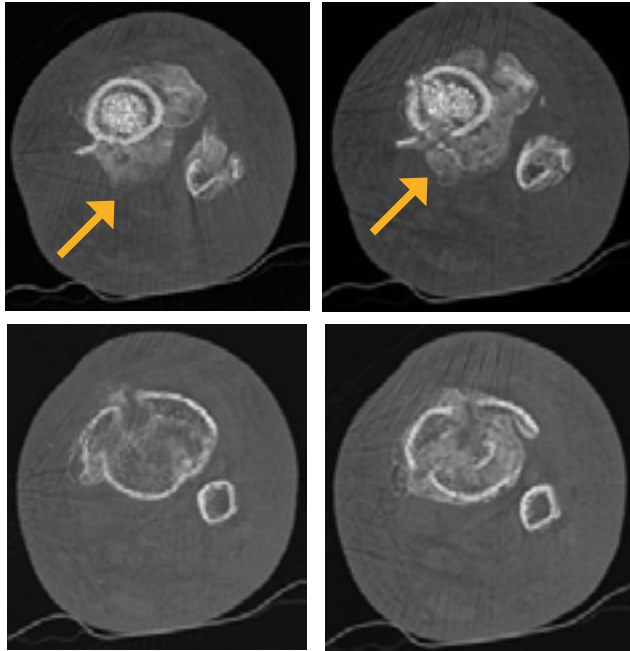
**Post-op after bioactive glass implantation**



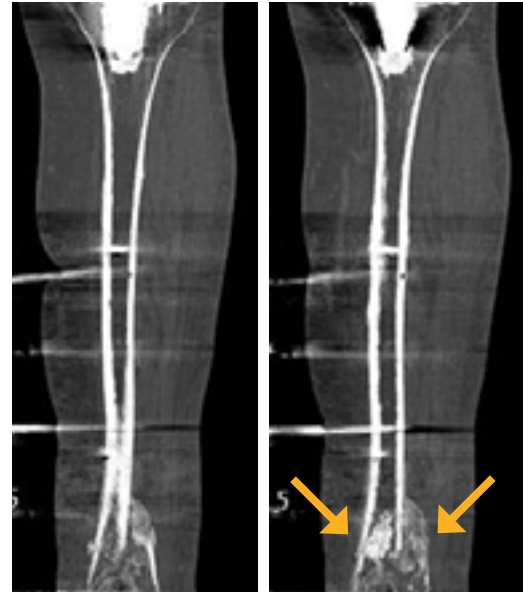
**Clinical outcome:** Increased bone formation 4 months after treatment, good bone healing and consolidation 7 months after treatment. Limb fully load bearing at 7 months.

**2 months post-op**

Axial (CT)



Coronal (CT)



**4 months post-op**



**7 months post-op**



## DISTAL TIBIA (CASE 7)

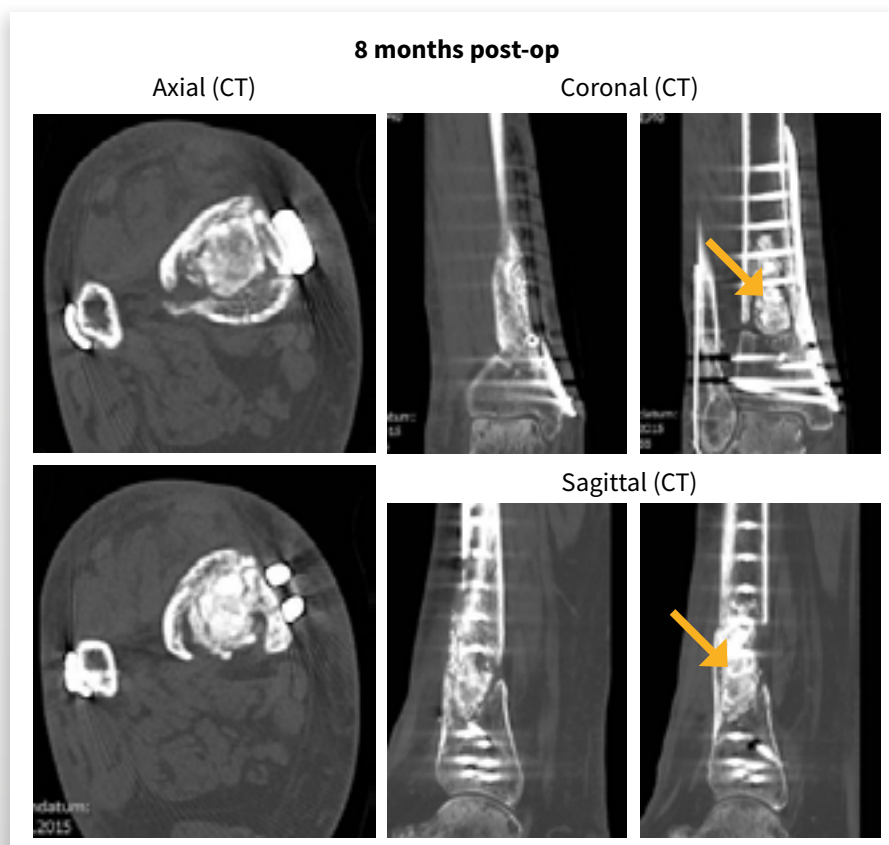
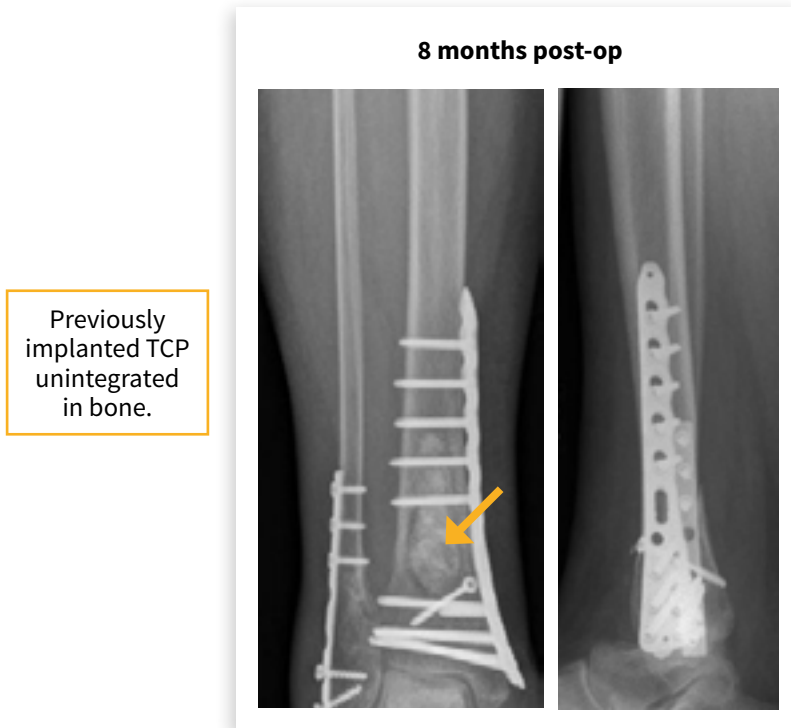
**Patient:** 73-year-old female

**Preoperative status:** Closed distal tibial fracture with Pilon tibiale affected. The patient had previously received a plate and a Tricalcium phosphate (TCP) bone substitute at another hospital. Diagnosis of tibial osteomyelitis 10 months after injury (only with Histology). Problem with soft tissue.

**Bacterial culture:** No detection of bacteria



**Complication:** Diagnosis of non-union and non-osteointegrated TCP bone substitute clearly visible on CT.



**Operation:** 10 months after injury, revision surgery with thorough debridement of the septic focus and implantation 20 cc of bioactive glass.

**Post-op after implantation of bioactive glass**



**4 weeks post-op**



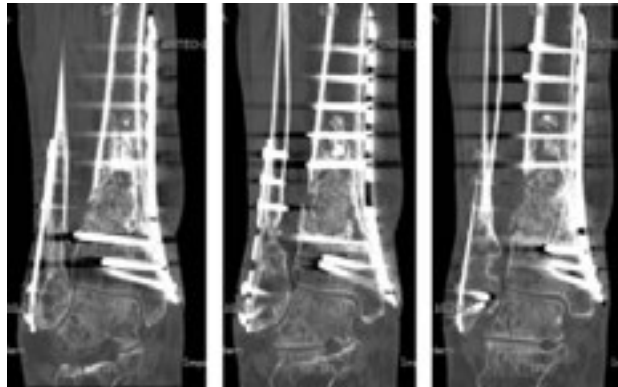
**10 weeks post-op**



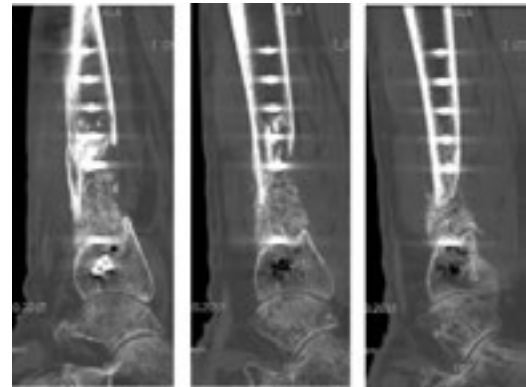
**Clinical outcome:** Gradual formation of new bone structure after 4 months and complete consolidation visible after 12 months post-op seen with CT.

**4 months post-op**

Coronal (CT)

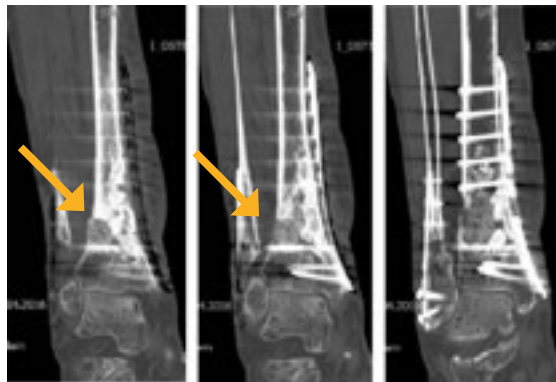


Sagittal (CT)

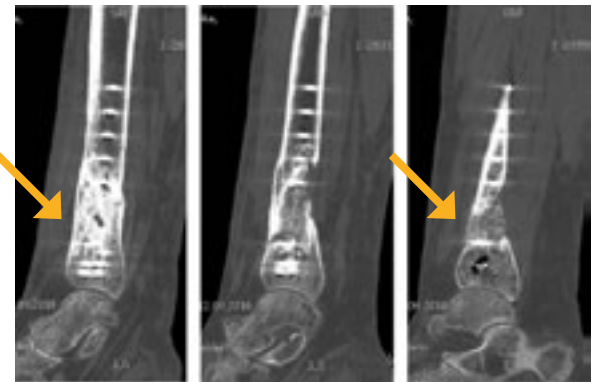


**12 months post-op**

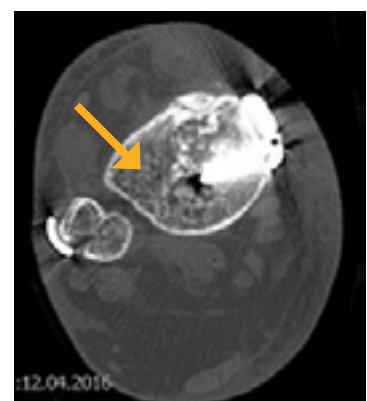
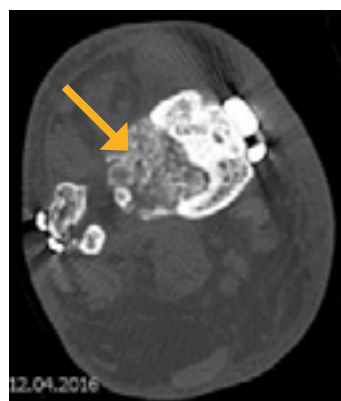
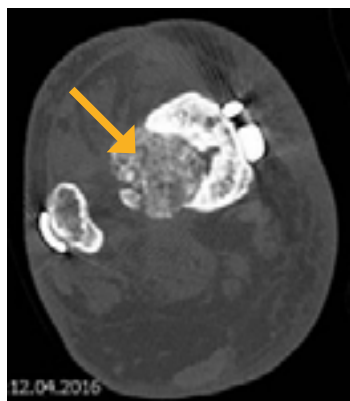
Coronal (CT)



Sagittal (CT)



Axial (CT)



## DISTAL TIBIA (CASE 8)

**Patient:** 72-year-old male, supramalleolar osteotomy was performed.

**Preoperative status:** Fracture of the plate 5 months post-op after the injury. 7 months post-op there was swelling, pain and reddening. Diagnosis of tibial osteomyelitis (non-union) 8 months after the initial injury.

**Bacterial culture:** *Staphylococcus epidermidis*

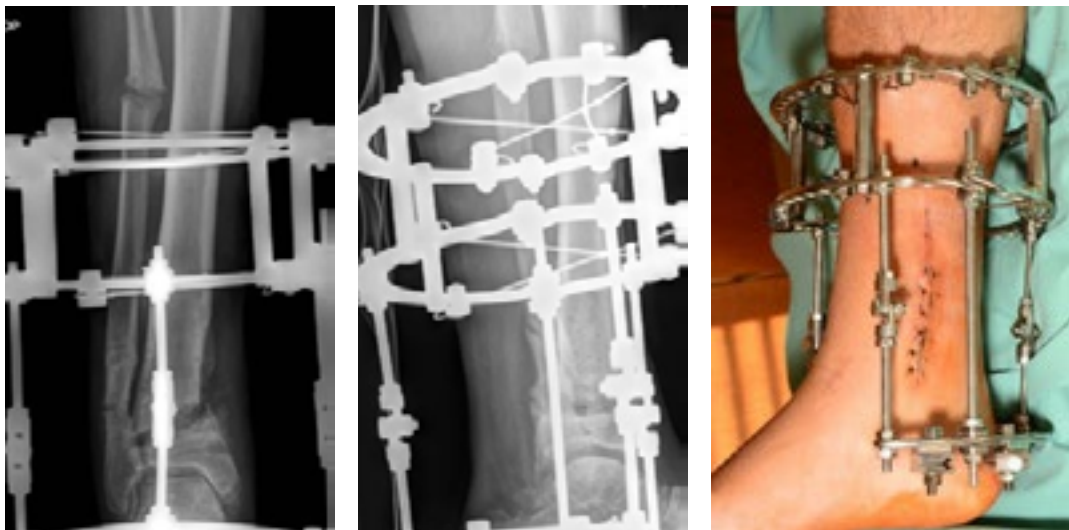
**6 months after injury**



**7 months after injury**



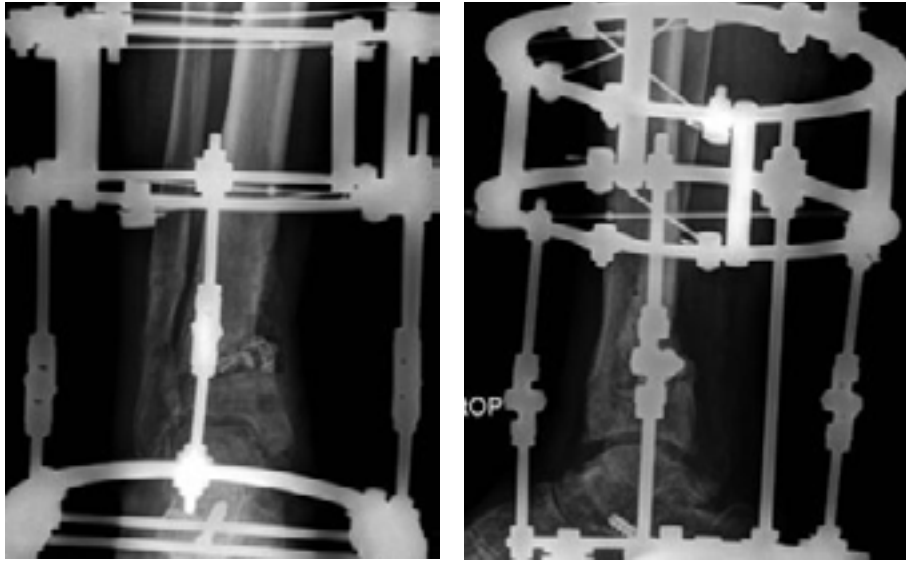
**Revision surgery 7 months after injury**



**Complication:** Persistence of infection and new bacteria encountered. Three further revisions with debridement performed.

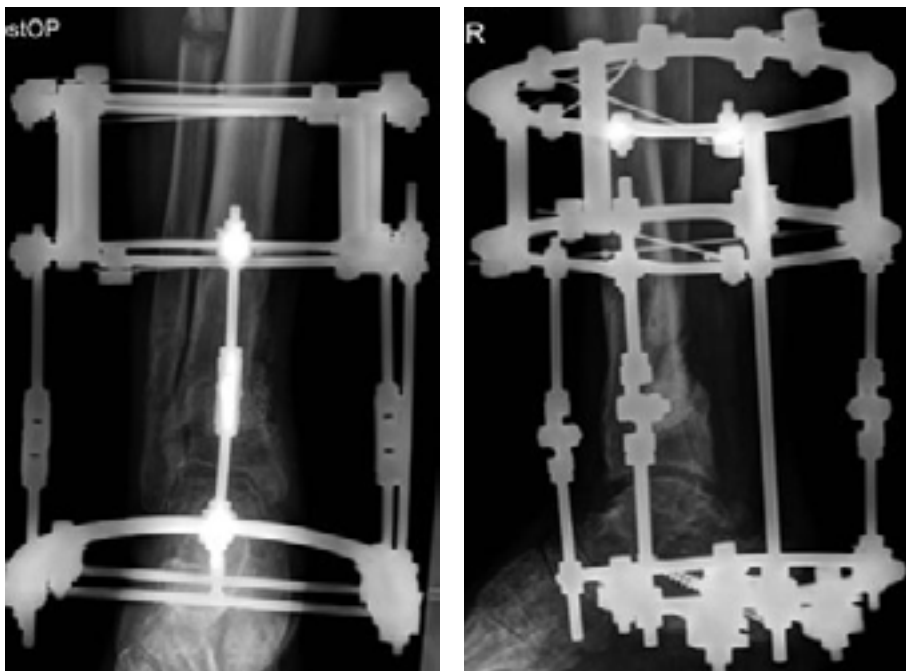
**Bacterial culture:** *Enterococcus faecalis* and *Staphylococcus caprae*

**Revision surgery 9 months after injury**

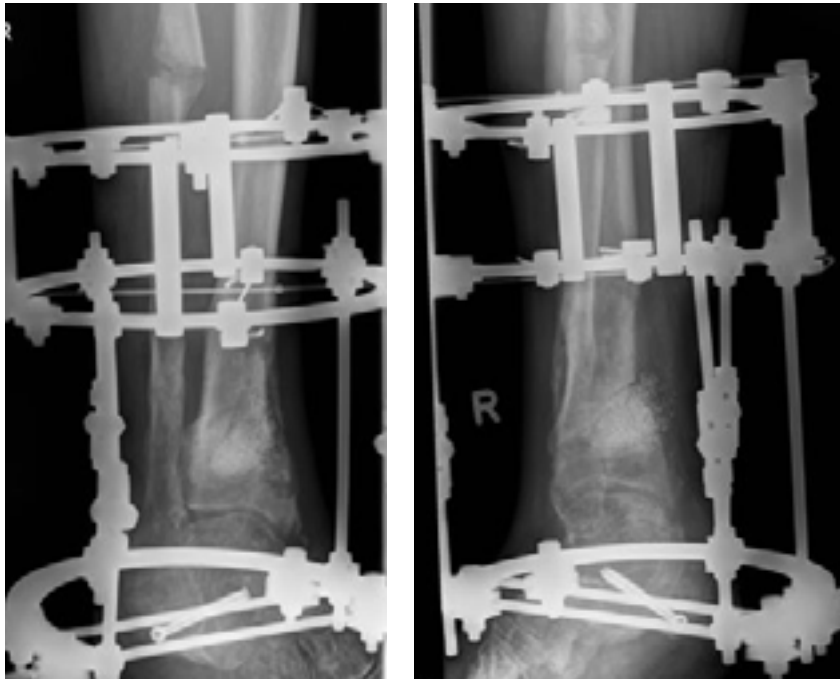


**Operation:** Revision surgery 10 months after injury and implantation of 20 cc bioactive glass.

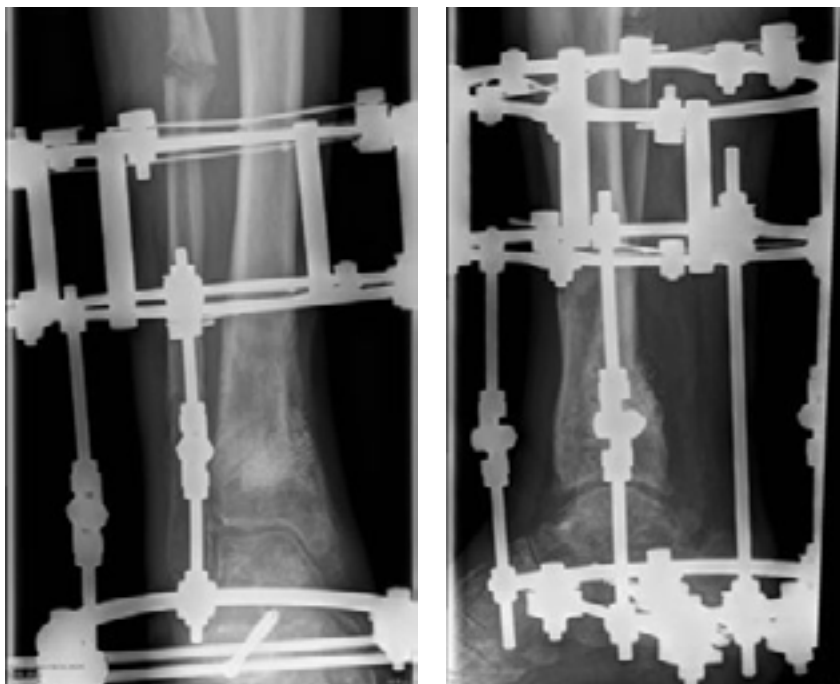
**Post-op after bioactive glass implantation**



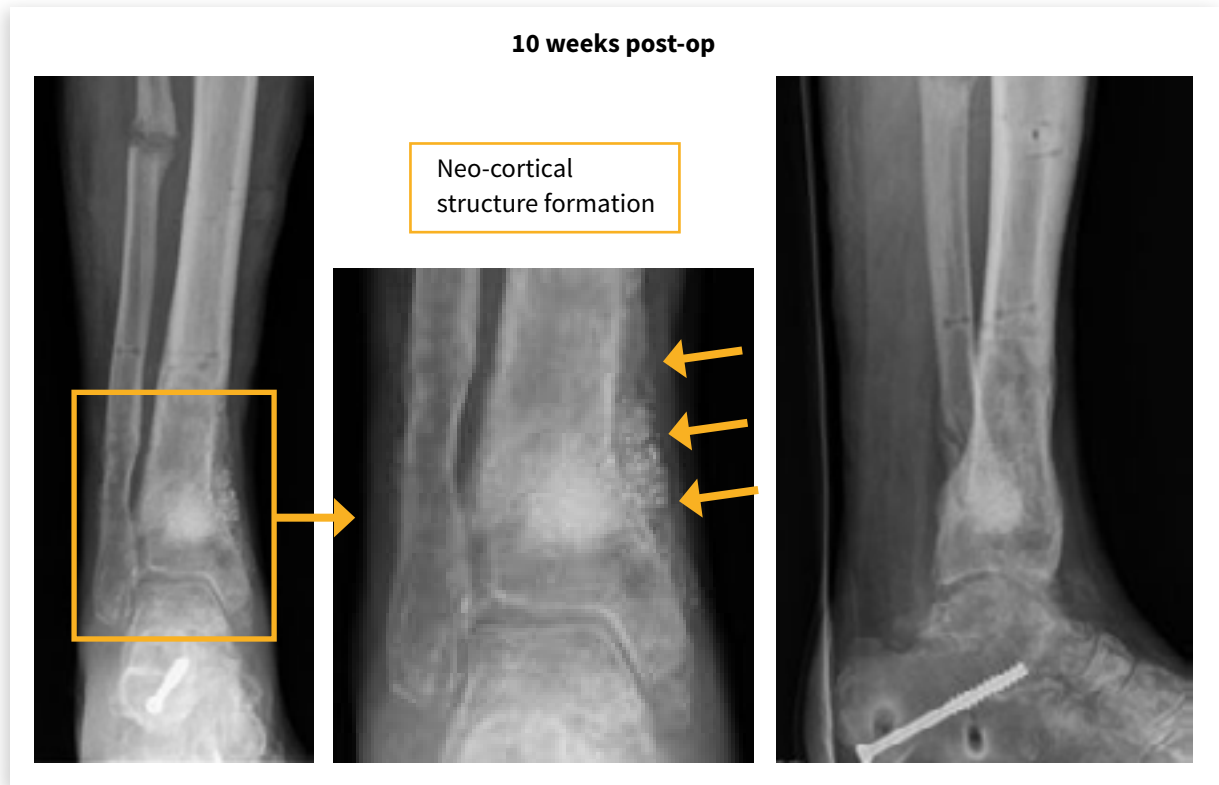
**5 weeks post-op**



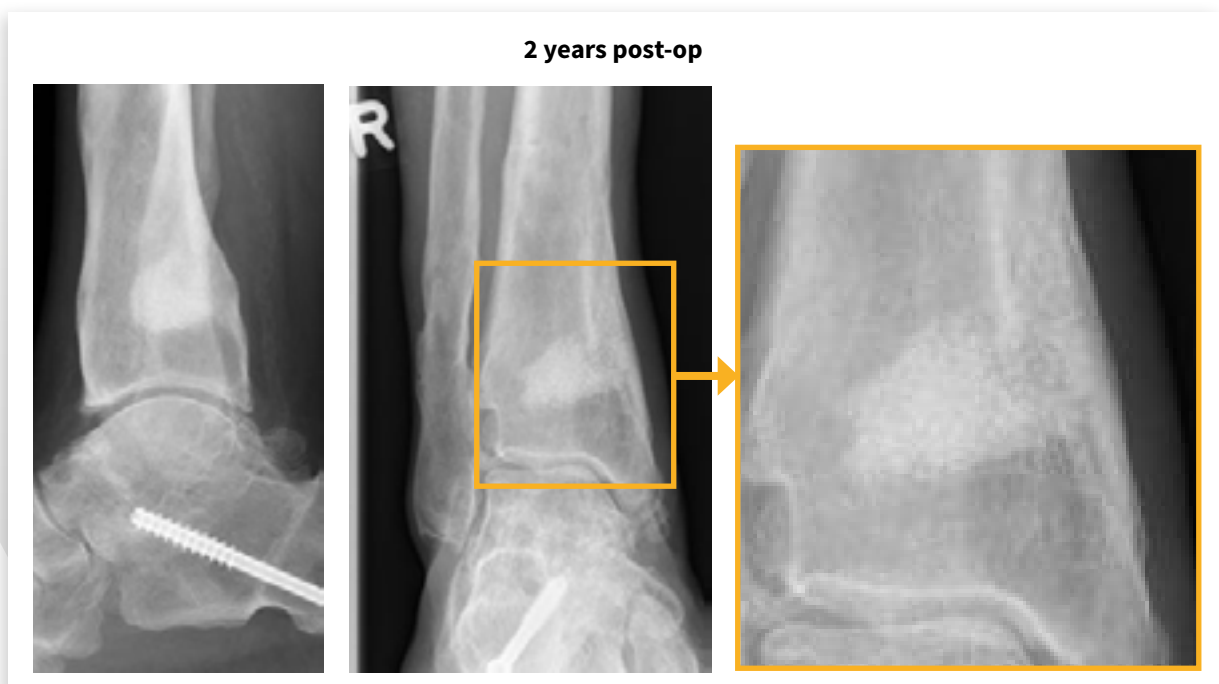
**8 weeks post-op**



**Clinical observation:** Periosteal reaction resembling a “neo-cortical-structure” was visible 10 weeks after treatment.



**Final clinical outcome:** Complete integration of bioactive glass into the bone structure and full consolidation could be observed at 2 years post-op.



## DISTAL TIBIA (CASE 9)

**Patient:** 61-year-old male.

**Preoperative status:** Closed distal tibia fracture with affected Pilon tibiale. Infection of the tibial plate 3 months after Open Reduction Internal Fixation (ORIF).

**Bacterial culture:** *Staphylococcus aureus* and *Staphylococcus epidermidis*

**1 month post-op after ORIF**

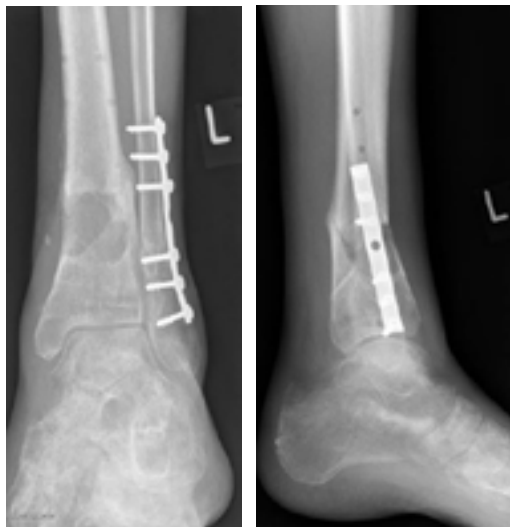


**Revision surgery 3 months post-op due to infection**



**Operation:** Removal of the antibiotic releasing beads after 6 weeks and implantation of 20 cc bioactive glass. Bone formation can be observed 2 months and 4 months after treatment.

**Pre-op**



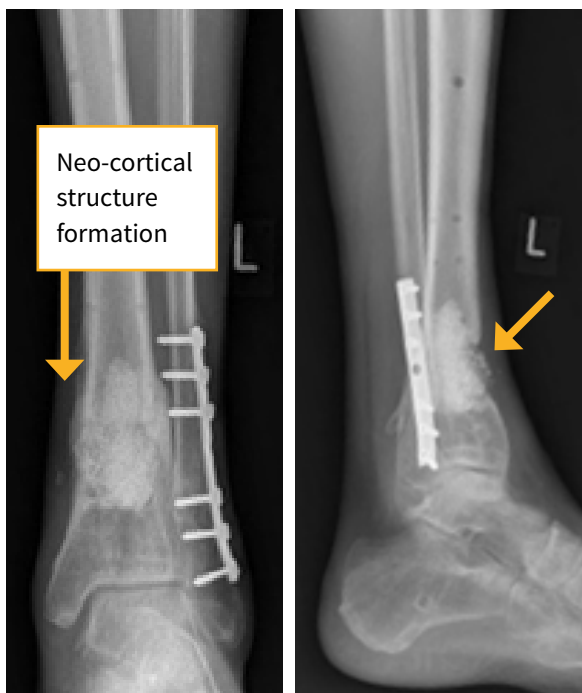
**Post-op**



**2 months post-op**



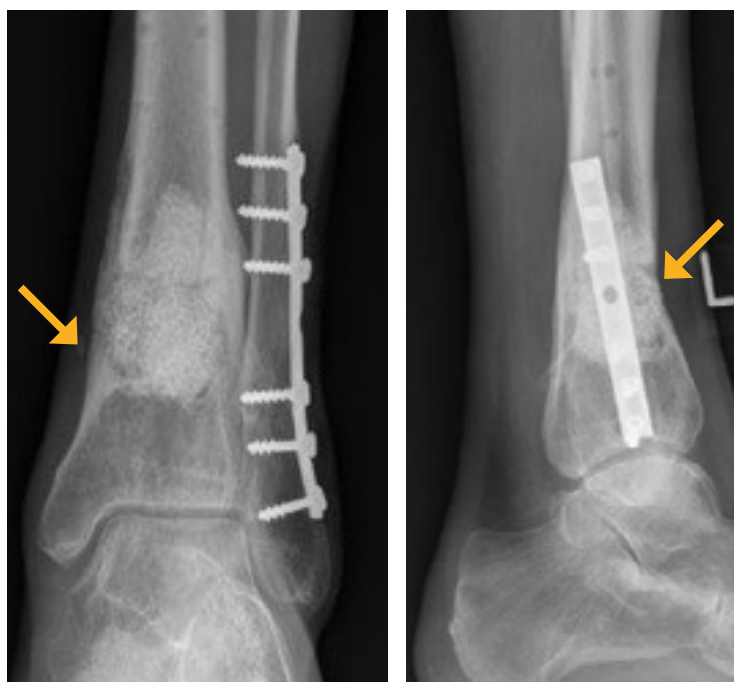
**4 months post-op**



**6 months post-op**

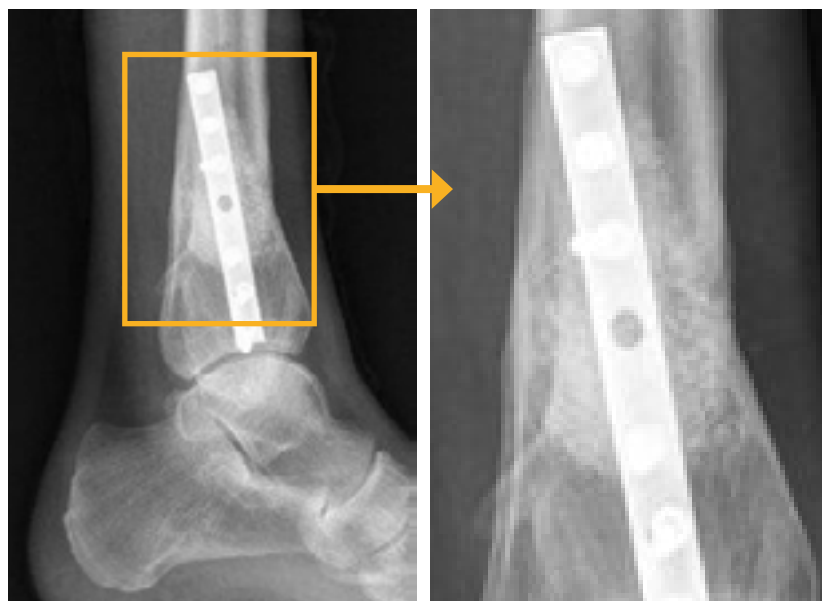


**8 months post-op**



**Final clinical outcome:** Periosteal reaction resembling a “neo-cortical-structure” is visible in the anterior region where bioactive glass has been implanted.

**14 months post-op**

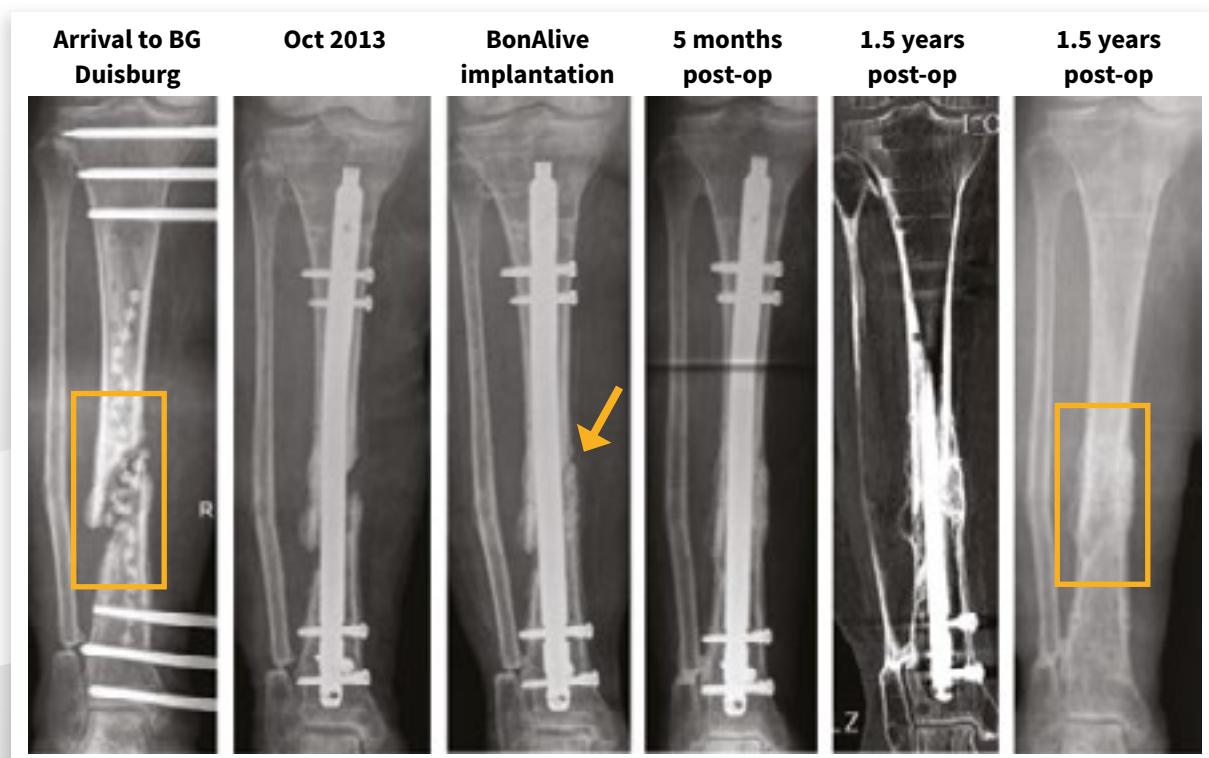


## CONCLUSIONS

- S53P4 bioactive glass (BonAlive® granules) is a promising biomaterial for the regeneration of bone in septic non-unions in the long bones.
- Compared with other biomaterials, especially good results have been obtained in healing complicated septic non-unions in the tibial diaphysis.
- Bioactive glass is very easy to use and it works in older patients as well.
- In the beginning of integration process of bioactive glass, an “onions-skin pattern” known as periosteal reaction can be observed in many of the clinical cases.
- Bioactive glass seems to have an effect that stimulates the formation of a “neo-cortical” structure towards the soft tissues in the implanted area.
- In 90% of the cases in our clinic bioactive glass has been used without the addition or mixing with autograft bone.
- Bioactive glass is used without the addition of local antibiotics, even in patients with extensive bone infections.

***“The combination of thorough debridement and decortication of the non-union according to the Septic Diamond Concept, together with the “reaction chamber technique” of S53P4 bioactive glass can effectively resolve the most challenging septic non-unions.”***

Dr. med. M. Glombitza  
Chief of Septic Surgery Department  
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## REFERENCES

### MECHANISM OF ACTION

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## OUR PURPOSE

**– To inspire the world with innovations  
that empower patient healing –**



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