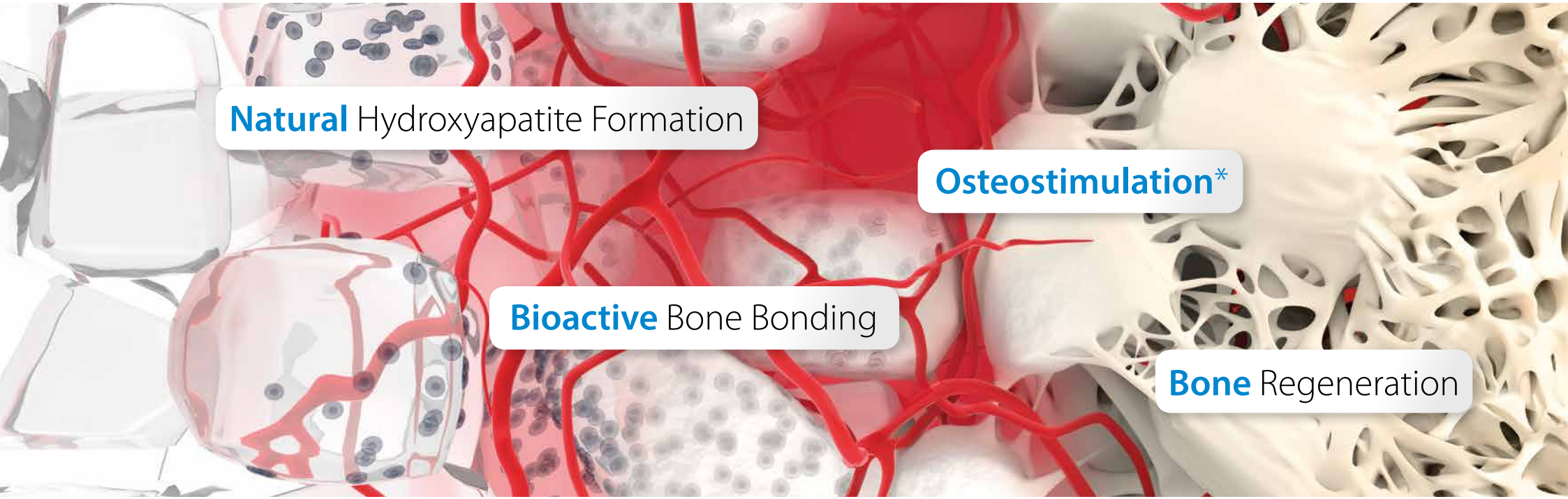
BonAlive®

Medical Education | *Spine & Neurosurgery*



*non-osteoinductive

BonAlive®
BIOMATERIALS LTD

OUR STORY

Glass into Bone – a Modern Mystery or Ancient Truth?

In the late 1960s an associate professor called Larry Hench travelled to an Army Materials Conference in Sagamore, New York, and seated himself next to a Vietnam veteran. Their discussions lead into the topic of bone recovery and methods of replacing bone with a man-made material that the body would not reject. The 45S5 Hench glass was soon born. The glass had tissue regenerative properties and bonded tightly to bone while being slowly biodegraded in the body.

A couple of decades after, in the 1980s, at the universities of Turku, Finland, the story of the Hench glass and its composition still puzzled scientists. What would happen if the composition were different, would it bring the same advantages or even new ones? Soon many different new bioactive glass compositions were developed and among them was the formula S53P4. As it turned out, as well as being strikingly osteostimulative*, S53P4 was found to have one new additional property that astounded its discoverers: the composition of 53% silica and smaller weights of sodium, calcium and phosphorus gave rise to surface reactions *in vitro* that appeared to be highly antibacterial by inhibiting bacterial growth – they had developed a material that could not be infected by bacteria.

The superior qualities of the glass did not just trigger excitement in the laboratory – the first patients were treated at the Turku University Hospital in 1991 with S53P4 implanted into a cavity in the frontal sinus. The post-operative results were more than anyone could hope for: this was the ultimate solution for filling defects in ear, nose and throat surgery as well as in the cranio-maxillofacial area. But could it do more?

Empowering Patient Healing

Today the story continues – the bioactive glass S53P4 is manufactured and provided worldwide by BonAlive Biomaterials Ltd in Turku, the birth city of the technology. The products come in different package sizes and compositions. One of the BonAlive® portfolio products, BonAlive® granules, is the only antibiotic-free biomaterial in the world with the claim to inhibit bacterial growth, with the official indication of bone cavity filling in the treatment of chronic osteomyelitis.

At BonAlive Biomaterials we take great pride in our story and we want to share it with the world. At the core of our activity lies patient healing. We want to make a change through safe and high-quality innovations that take us beyond the reliability of antibiotics in bone infection surgery. The pain and devastation that chronically infected bone can render in a patient's daily life, affecting family, work and spare time, is what drives us forward to constantly develop new technologies and applications of our products.

Also we do know that a product alone cannot solve problems in healthcare and that is why we want to be available for healthcare professionals in product support and education to ensure patient healing. We want to be the empowering force in patients healing, today and tomorrow.

Our purpose: To inspire the world with innovations that empower patient healing

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Our Innovative Solutions

We are entering a post-antibiotic era that is driven by the global threat of antibiotic resistance. At BonAlive Biomaterials, we are dedicated to employ new ways of controlling infection and restoring body function. Our commitment is to develop innovative solutions that empower patient healing.

To carry out our mission, we have developed two product lines of BonAlive® bioactive glass:

- Bone regenerative and moldable **BonAlive® putty**
- Bone regenerative and bacterial growth inhibiting **BonAlive® granules**

Clinical Evidence

BonAlive® is one of the most evidence-based technologies in the bone regeneration industry. The 20-year clinical history together with more than 20 published peer-reviewed clinical articles proves the efficacy, which is derived from prospective or prospective randomized clinical trials in benign bone tumor, trauma and spine surgery.

The innovative research and development continues. To strengthen this important task we are following the highest quality requirements for ISO 13485 and ISO 9001 certified class III medical devices and find it importat to work in close relationship with key medical centers throughout the world.

Medical Education Concept

We have compiled this brochure to provide you with the important facts about BonAlive®. We tell you how the bioactive glass works and present carefully chosen clinical cases showing why this is a very unique innovation.

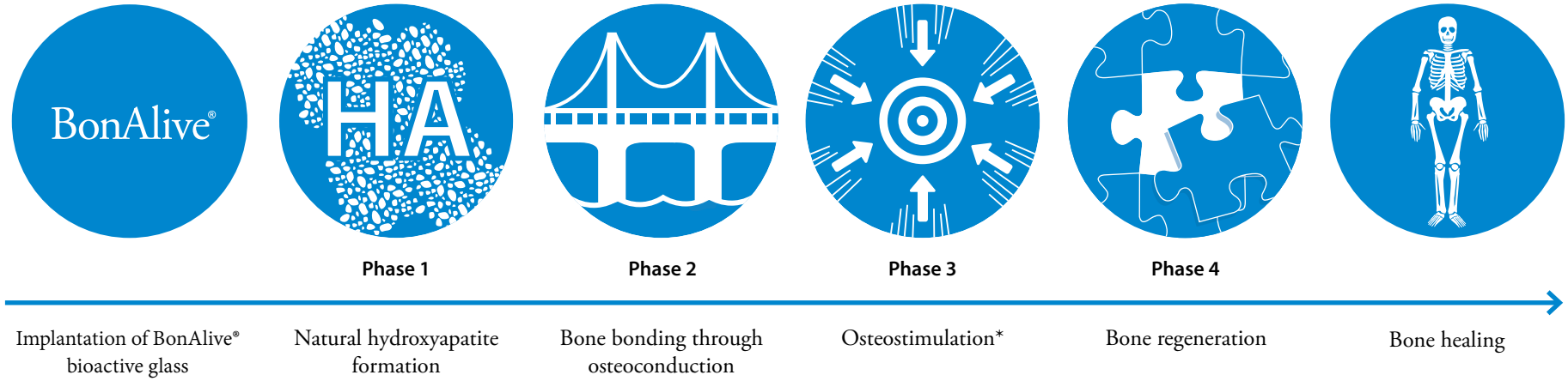
CONTENT

HOW BONALIVE® WORKS

"The bioactive glass surface is not only conductive but also osteoproductive in promoting migration, replication, and differentiation of osteogenic cells and their matrix production."

Virolainen et al. 1997

The following sequence presents the bone regeneration cascade of BonAlive® bioactive glass:



Composition of BonAlive® bioactive glass

- **Bioactive glass S53P4:** 53% SiO_2, 23% Na_2O, 20% CaO, 4% P_2O_5

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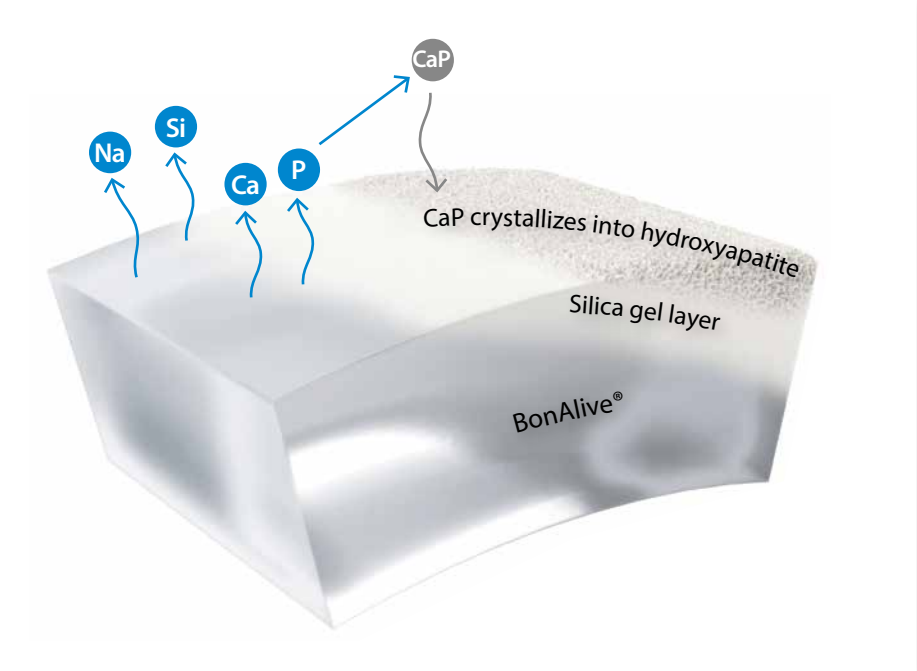
Phase 1: Natural Hydroxyapatite Formation

In contact with body fluids bioactive glass works by leaching out ions (Na, Si, Ca, P). This causes a localized breakdown of the silica network resulting in a silica gel layer with a net negative surface charge.

Following the formation of the silica gel layer, the Ca and P that has been released from the bioactive glass are attracted back to the surface and an amorphous calcium phosphate (CaP) layer forms on the glass surface. The CaP layer will subsequently crystallize into a natural hydroxyapatite (HA) layer.

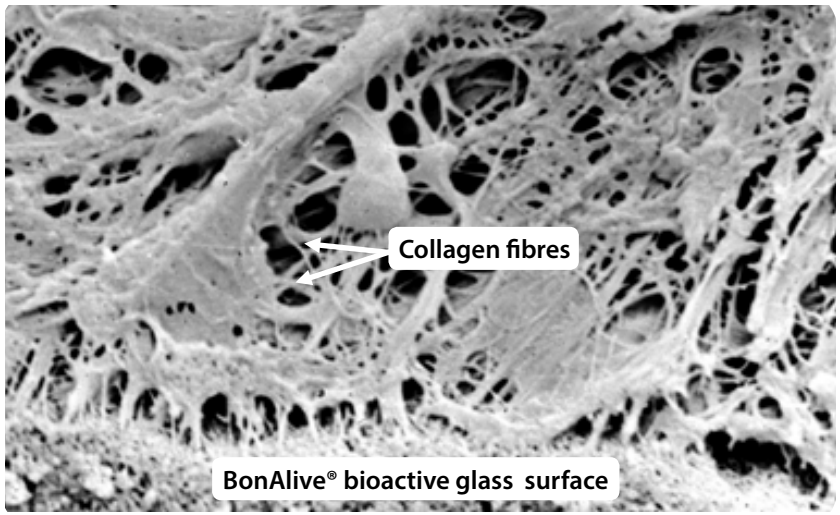


Formation of natural hydroxyapatite through surface reactions.

Phase 2: Bone Bonding through Osteoconduction

Following the formation of a hydroxyapatite layer on the surface of the bioactive glass, the bone bonding process is established. BonAlive® bioactive glass is **osteoconductive** in nature, providing a supportive material for the osteoblast cells during bone formation. The growing hydroxyapatite surface layer binds biological entities, such as blood proteins, growth factors, and collagen. The hydroxyapatite is chemically and structurally nearly identical to natural bone mineral, thus enabling the body tissues to attach to it. As a result of the osteoconductive process, bone grows onto and in between the bioactive glass granules.

Bone bonding with BonAlive® bioactive glass



Courtesy of Turku University Hospital, Finland

BonAlive® bioactive glass bonds to bone and stimulates new bone formation.

Phase 3: Osteostimulation*

BonAlive® bioactive glass has been proven to activate a biological process that stimulates bone regeneration in a fashion far superior to traditional osteoconductive materials.

The mechanism of bone regeneration with bioactive glass is based on both **surface-mediated** (natural hydroxyapatite surface) and **solution-mediated** (release of Si and Ca) processes. The effect is seen on a cellular level as promotion of particular cell stages of the osteogenic cell lineage through specific gene activation. This active role in osteogenesis has been defined as osteostimulation*.

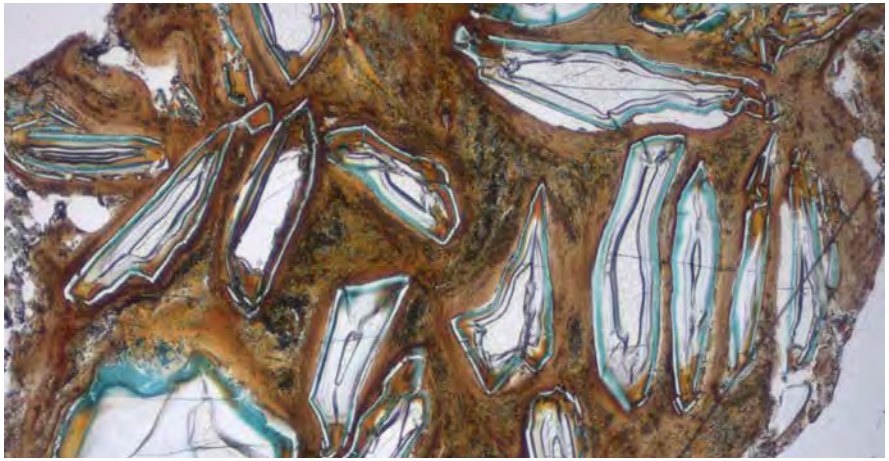
In vitro and preclinical studies with BonAlive® bioactive glass give evidence that it acts as an osteostimulative* material through the recruitment and differentiation of osteogenic cells. Also, BonAlive® bioactive glass has proven to activate genes in osteogenic cells to increase the remodeling rate of bone.

Definition of osteostimulation*:

"Activation of genes responsible for bone formation in osteogenic cells"

Virolainen et al. 1997

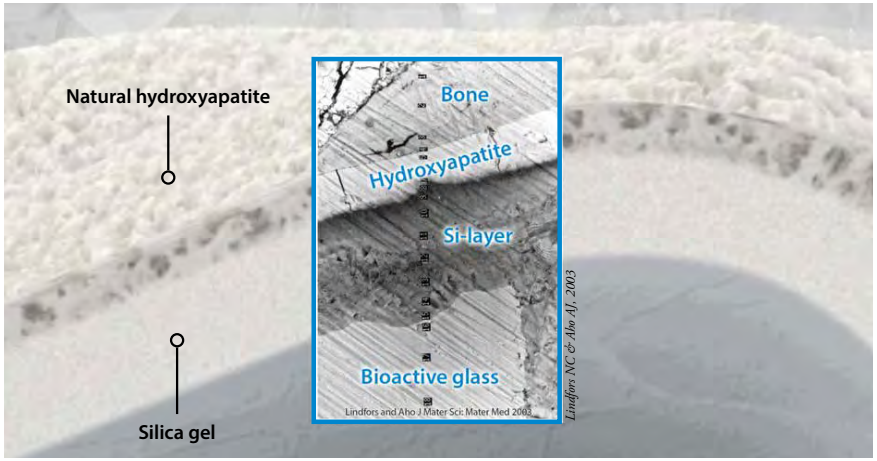
Histology 3 months post-op



Courtesy of Päijät-Häme Central Hospital, Finland

Histological 20µm-thick section from the mastoid area at 3 months after BonAlive® bioactive glass implantation (human biopsy). The natural hydroxyapatite layer that has been formed on the BonAlive® bioactive glass conducts and stimulates new tissue formation in the grafted area. Tissue formation can be clearly visualized around the BonAlive® bioactive glass in the microscopy image.

Reaction layers of BonAlive® bioactive glass



Lindfors NC & Aho AJ, 2003

A BonAlive® bioactive glass cross-section shows the characteristics of the reaction layers.

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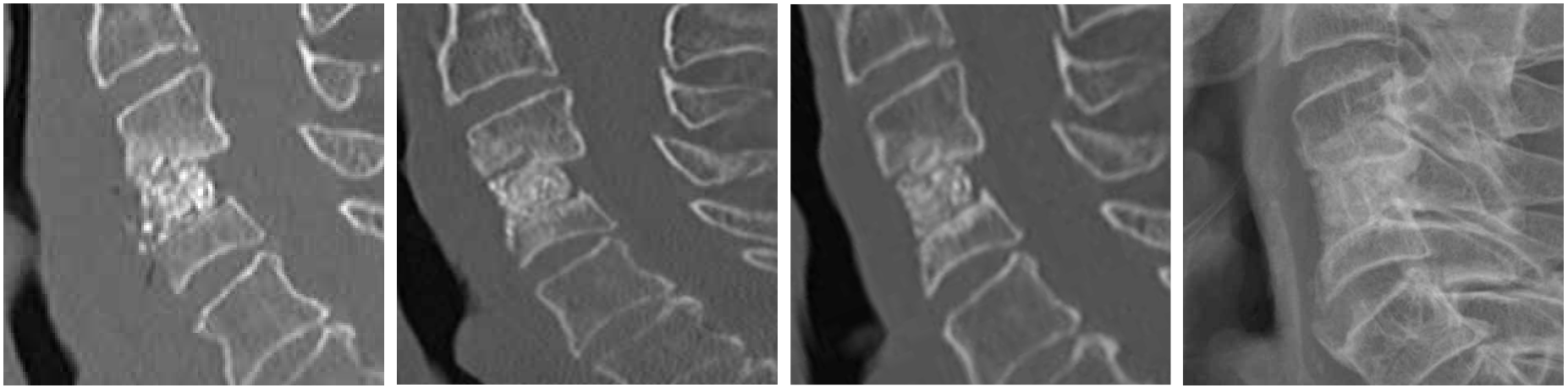
Phase 4: Bone Regeneration

After the bone bonding and osteostimulative* phases, the process of bone regeneration and remodeling continues the pathway of consolidating the bone and restoring the anatomy.

Bone formation with BonAlive® bioactive glass

3-day post-op CT | 3-month post-op CT | 8-month post-op CT | 28-month post-op X-ray



Courtesy of Dr. Janek Frantzén Turku University Hospital, Finland

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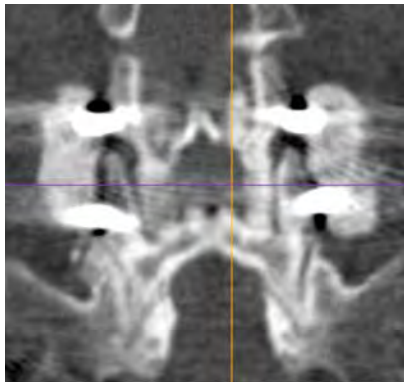
RESORPTION, REMODELING AND VISUALIZATION

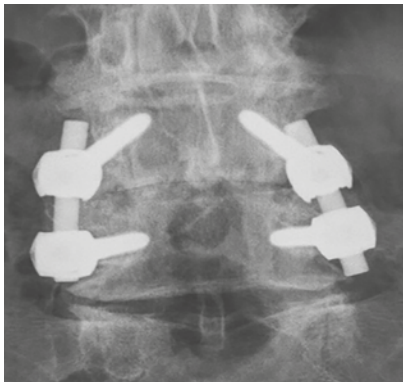
BonAlive® bioactive glass is a fully resorbable biomaterial that remodels completely into bone over a period of years to allow sufficient time for bone regeneration. The BonAlive® bioactive glass can be visualized with imaging during surgery and progression of the healing. Resorption, remodeling and bone regeneration can be followed post-operatively due to the radio-opaque nature of the BonAlive® bioactive glass.

BonAlive® putty

Post-op CT



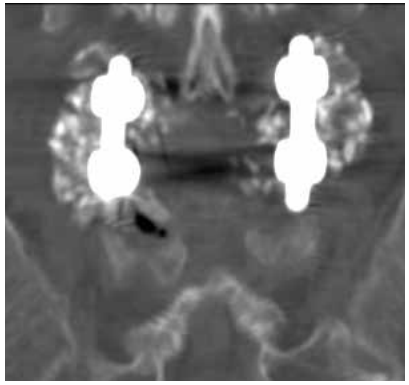
6-month post-op X-ray



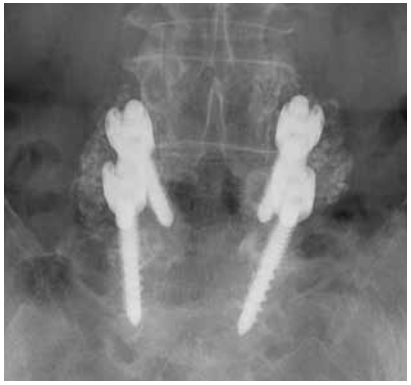
Courtesy of Brisbane Private Hospital, Australia

BonAlive® granules

Post-op CT



3-month post-op X-ray



Courtesy of Turku University Hospital, Finland

BonAlive® putty

BonAlive® putty has specifically been designed to possess ideal handling properties for spine and neurosurgical procedures. It is a ready-to-use and highly moldable biomaterial, that regenerates bone effectively.

BonAlive® putty contains bioactive glass S53P4 that is osteoconductive and osteostimulative*. In addition, it contains a water-soluble synthetic binder which is a blend of polyethylene glycols (PEGs) and glycerol that acts as a temporary binding agent for the bioactive glass. After implantation the binder is absorbed within a few days, leaving behind only the bioactive glass, thus permitting tissue infiltration between the granules to facilitate the regeneration of bone.

Main Properties

- Highly moldable, allowing it to be easily mixed with autograft and packed in e.g. interbody fusion cages
- Can be injected into the interbody space before cage implantation
- Stays in place, i.e. does not dissolve or wash away during the implantation

Indication

- Filling of bony voids and gaps

Official Product Claim

- Osteostimulative*

Composition

- **Bioactive glass:** 53% SiO_2, 23% Na_2O, 20% CaO, 4% P_2O_5
- **Synthetic binder:** Polyethylene glycols (PEGs) and glycerol

Recommended for mixing with autologous bone in spinal fusion procedures

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BonAlive® putty has not been verified to inhibit bacterial growth.

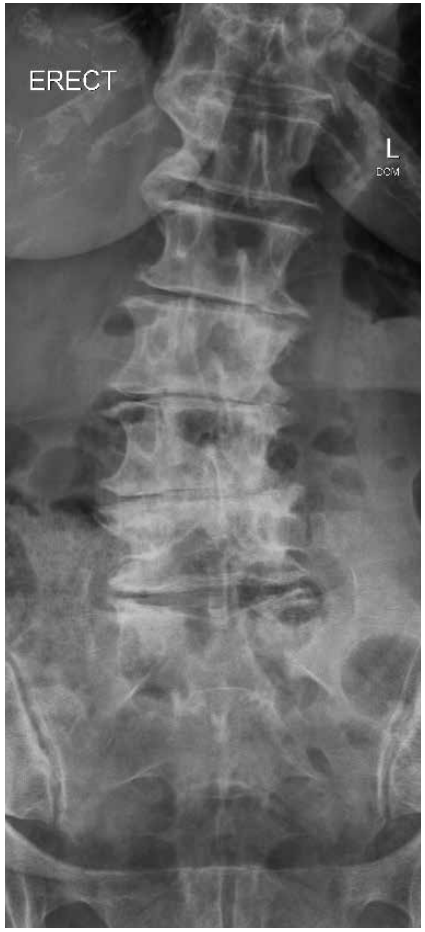
putty

SPINE FUSION WITH MEDIAL APPROACH (CASE 1)

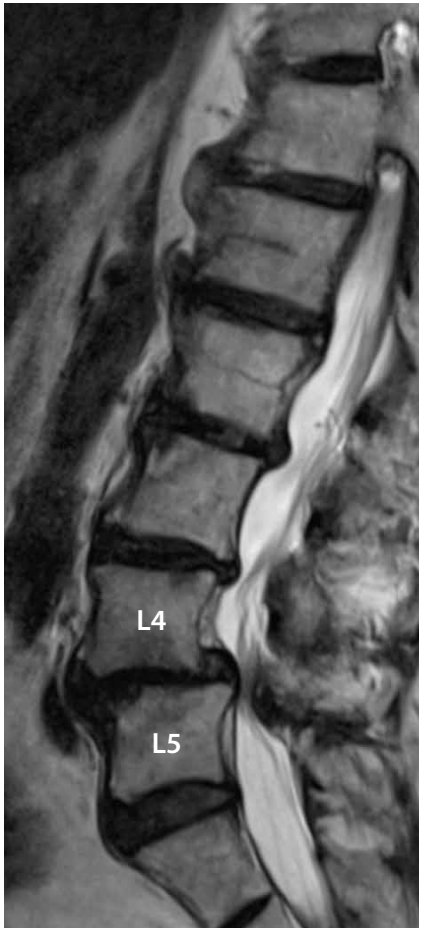
Patient: 82-year-old patient with deteriorating back and leg pain and with difficulty in walking. Symptoms suggestive of neurogenic claudication. The patient received temporary relief with an epidural steroid injection.

Operation: L4/L5 posterolateral instrumented fusion with BonAlive® putty and decompressive laminectomy.

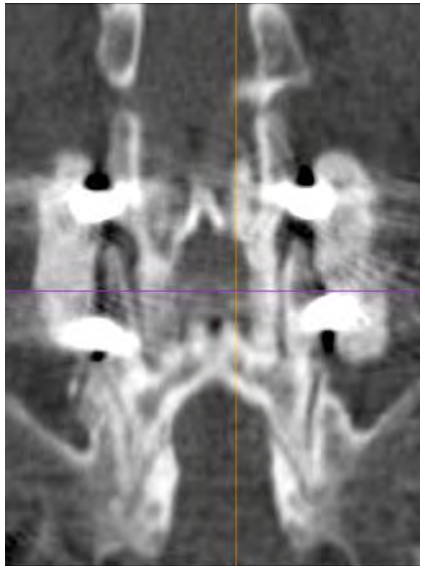
Pre-op X-ray (anteroposterior)



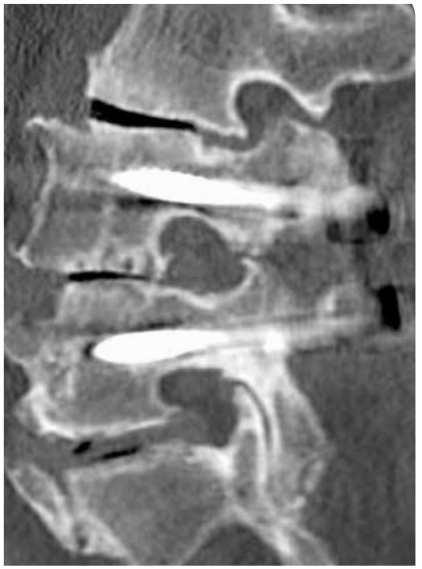
Pre-op MRI T2 (sagittal)



Post-op CT (coronal)



Post-op CT (sagittal)



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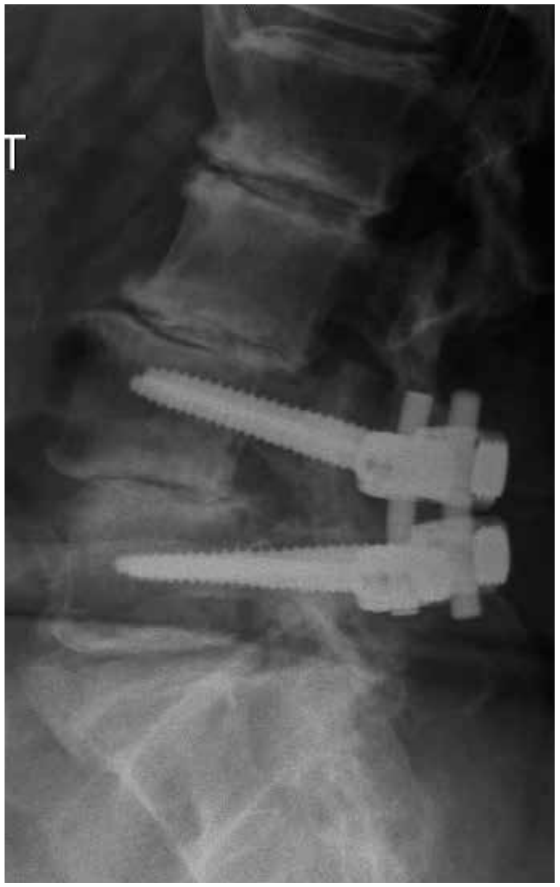
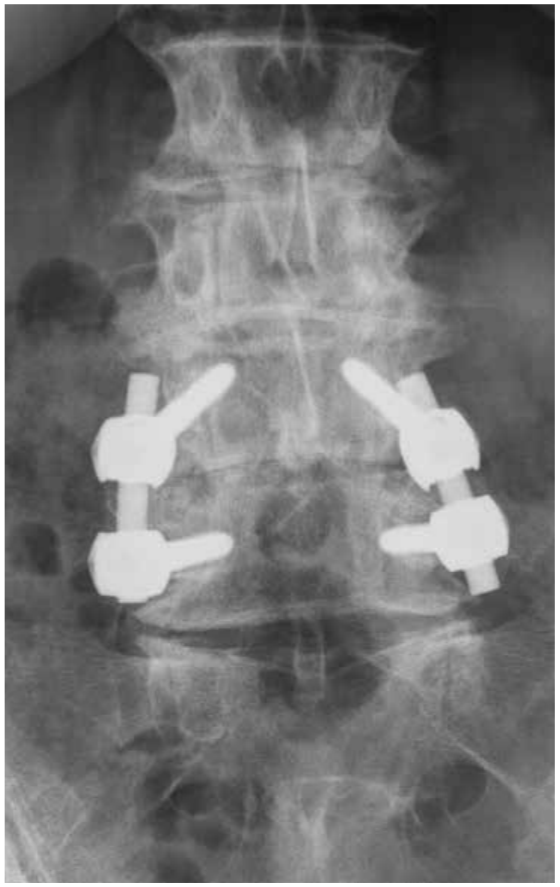
Clinical outcome: Resolution of leg pain and significant improvement in walking tolerance. Mild ongoing low back pain. Subjectively very satisfied.

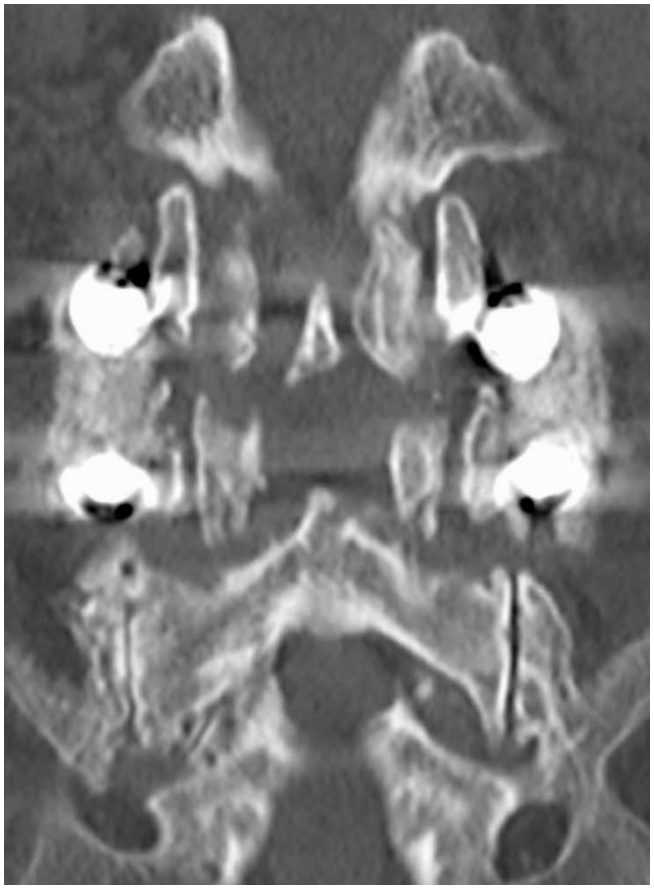
6-month post-op X-ray (lateral)



6-month post-op X-ray (anteroposterior)



6-month post-op CT (coronal)



Courtesy of Dr. Paul Licina Brisbane Private Hospital , Australia

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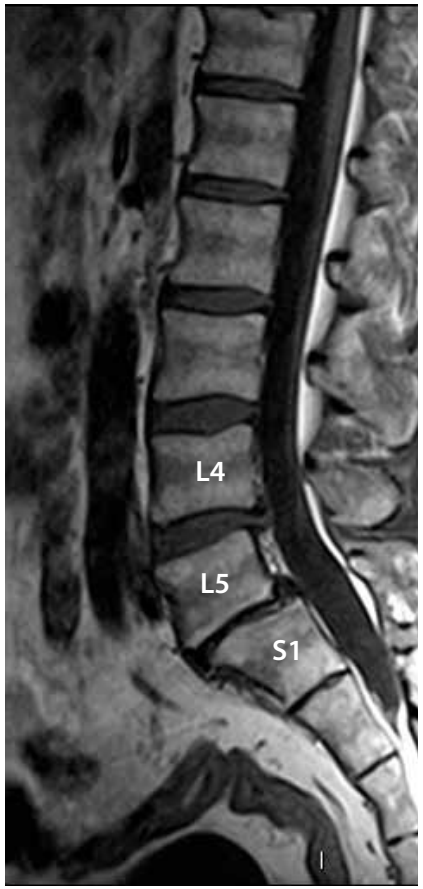
POSTEROLATERAL FUSION (CASE 2)

Patient: 44-year-old patient suffering from low back pain for 2.5 years. Increasing radicular pain to the right leg for more than one year before surgery.

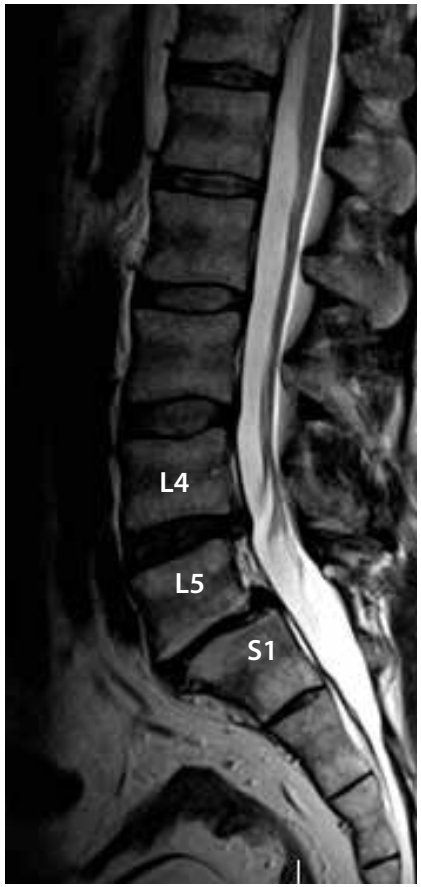
The patient received physiotherapy and occupational therapy at work. Preoperatively Oswestry 30, SLR 60/80 L5 and S1 pain, instability symptoms. Sensory defect on S1 dermatome right side. Lumbar MRI showed an L5/S1 lytic spondylolisthesis of 8 mm, increasing in the functional X-rays. L4/L5 degeneration and a central disc herniation and fluid in the facet joints.

Operation: Decompressive laminectomy L5, L4–S1 transpedicular fusion. Posterolateral fusion using autograft and BonAlive® putty as a bone graft expander.

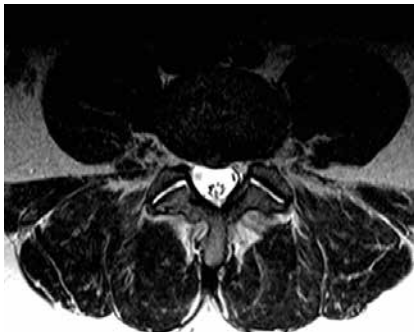
Pre-op MRI T1 (sagittal)



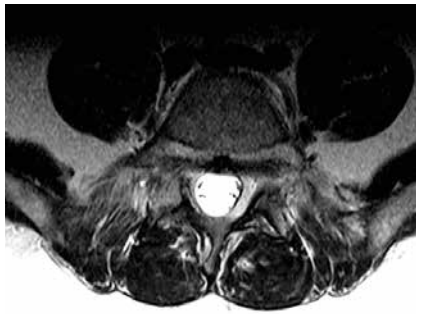
Pre-op MRI T2 (sagittal midline)



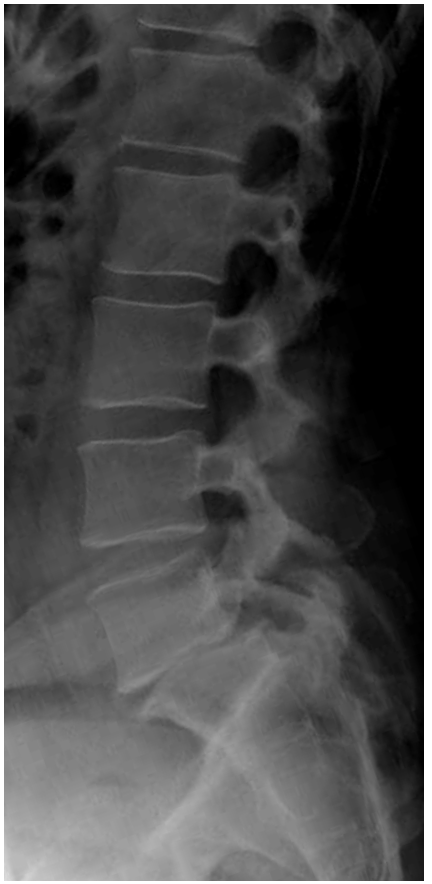
Pre-op MRI T2 (axial L4/L5)



Pre-op MRI T2 (axial L5/S1)



Pre-op X-ray



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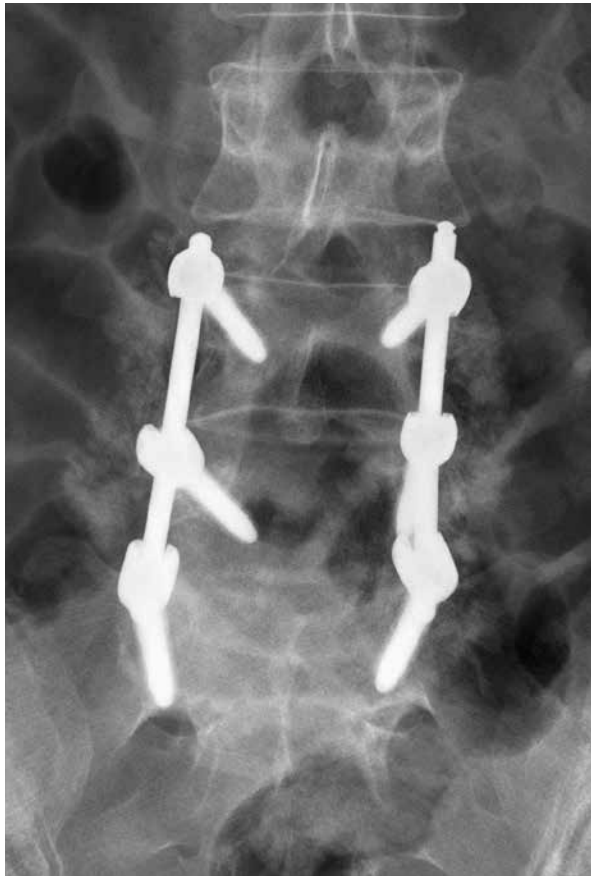
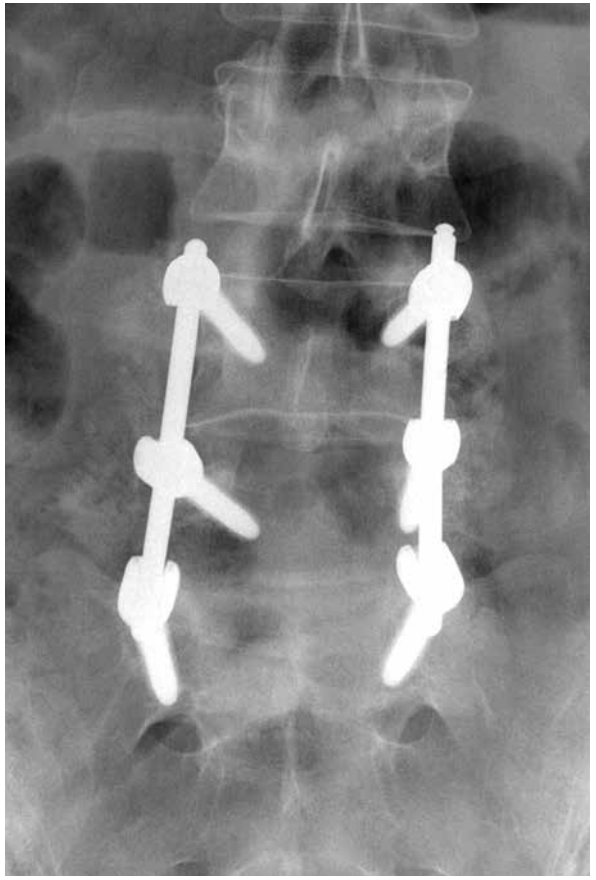
Clinical outcome: Intraoperative O-arm® images showed that the instrumentation was placed correctly. Outpatient clinic visits at 3 months and 12 months post-op. The patient returned to work 4 months post-op. At the one-year follow-up the patient was pain free and had returned to normal activities. Some numbness in right leg. No revisions, excellent outcome.

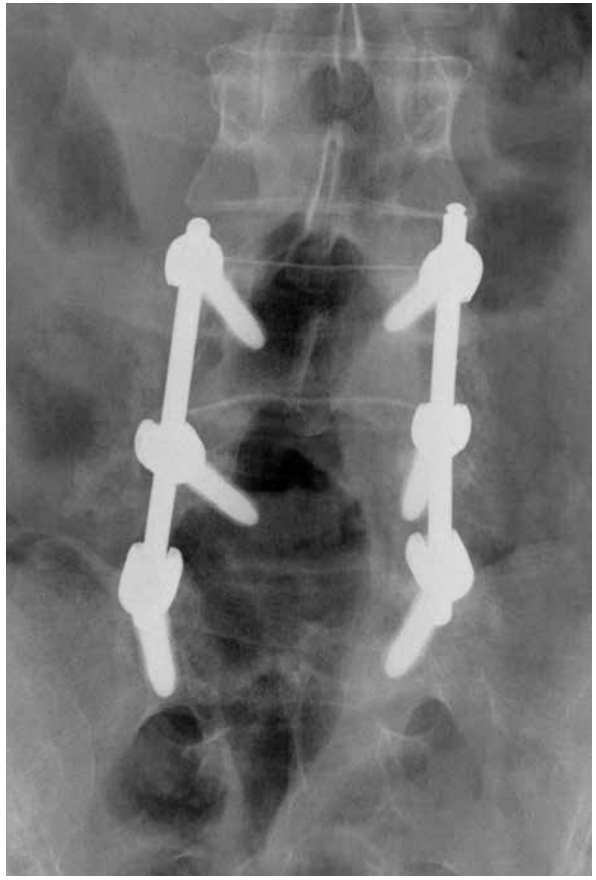
3-day post-op X-ray



3-month post-op X-ray



12-month post-op X-ray



Courtesy of Dr. Janek Frantzén Turku University Hospital, Finland

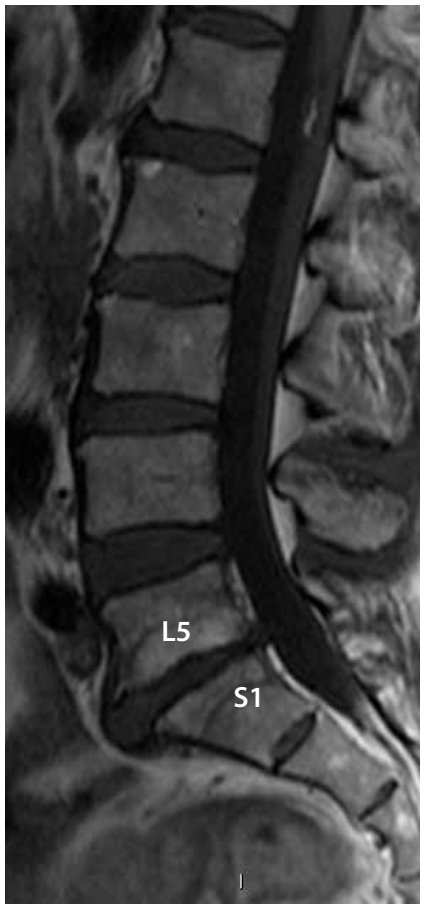
POSTEROLATERAL FUSION WITH MINIMAL-INVASIVE SURGERY (CASE 3)

Patient: 54-year-old patient suffering from low back pain for 2 years. Worsening radicular pain in the left leg (L5). The patient received physiotherapy and changes to tasks required at the patient's place of work were made to alleviate symptoms. Preoperatively instability symptoms. Sensory defect on L5 dermatome left side. Lumbar MRI showed L5/S1 disc degeneration and Modic I changes. A small central disc herniation and fluid in the facet joints.

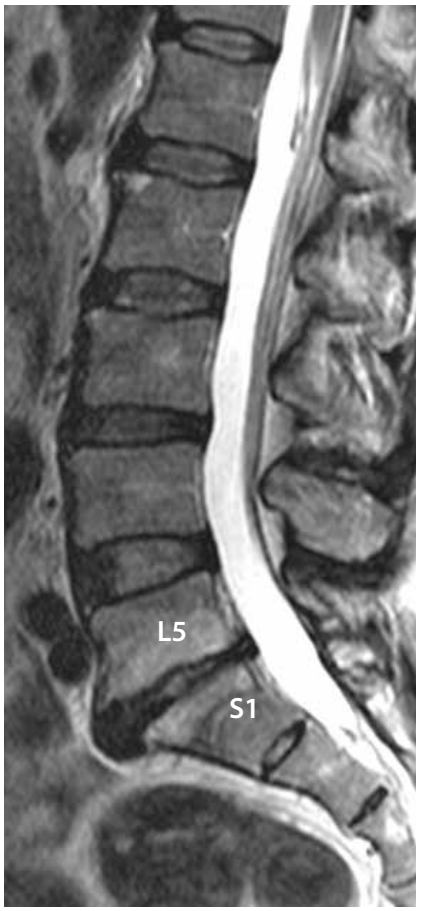
Operation: Transpedicular fusion L5/S1. Posterolateral (left) and intercorporal fusion using autograft and BonAlive® putty as bone graft expander.

putty

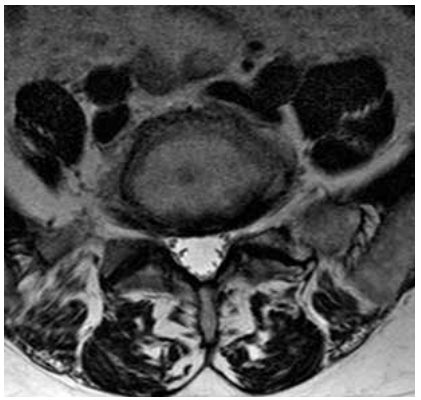
Pre-op MRI T1 (sagittal)



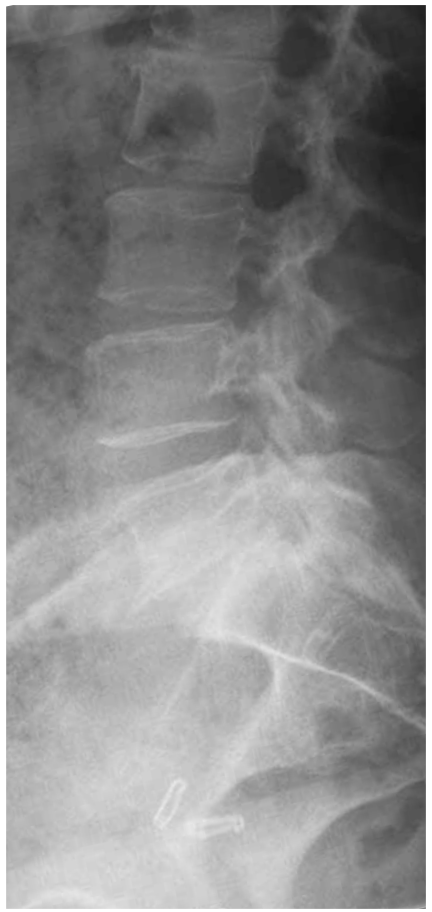
Pre-op MRI T2 (sagittal)



Pre-op MRI T2 axial L5/S1

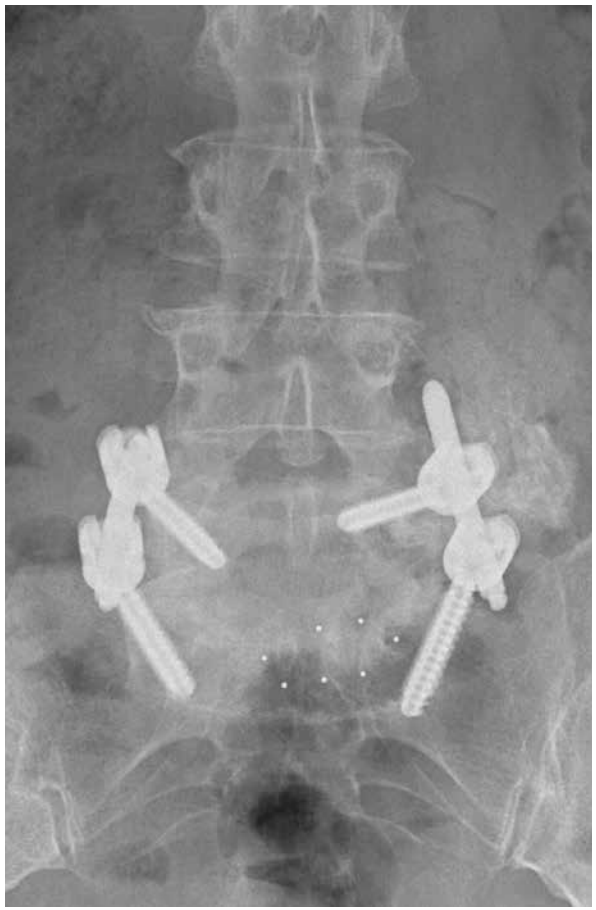


Pre-op X-ray

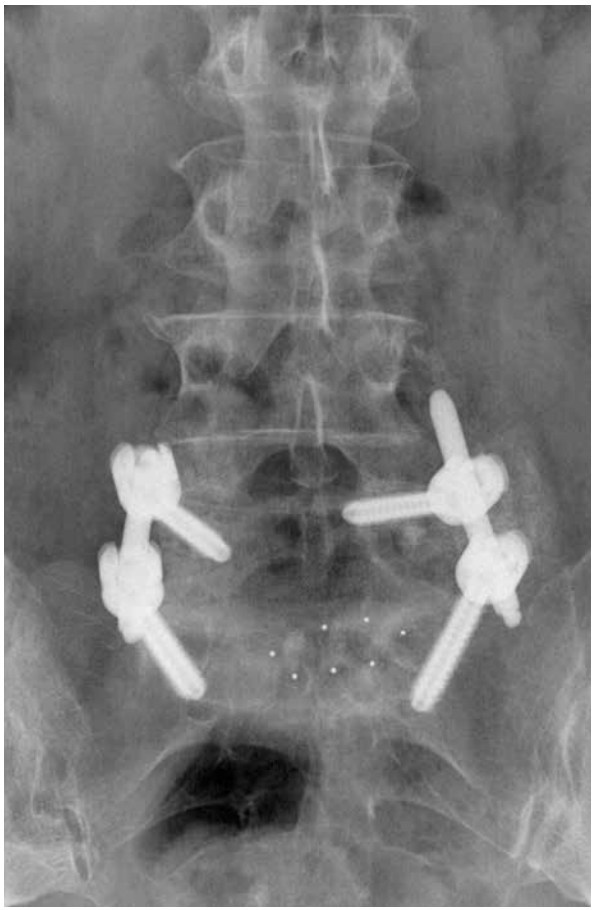


Clinical outcome: Intraoperative O-arm® images showed that the instrumentation was placed correctly. Postoperatively for one month the patient complained of left sided paresthesia and radicular pain on the left side (L5). Outpatient clinic visits at 3 months and 12 months post-op. At one-year follow-up the patient had returned to full time work. No revisions, excellent outcome.

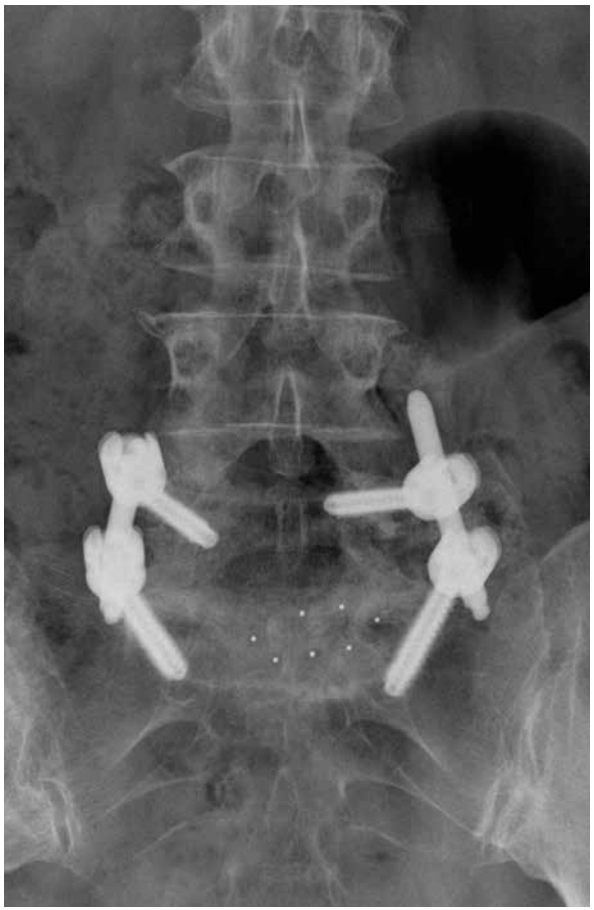
3-day post-op X-ray



3-month post-op X-ray



12-month post-op X-ray



Courtesy of Dr. Janek Frantzén Turku University Hospital, Finland

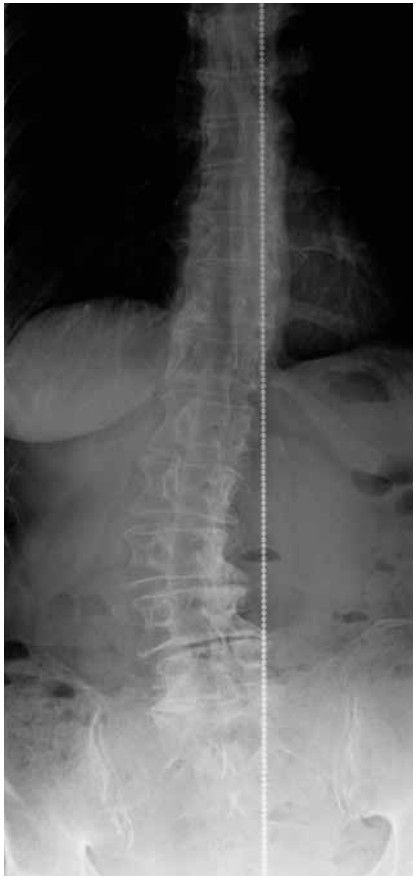
SCOLIOSIS SURGERY (CASE 4)

Patient: 66-year-old patient with a degenerative scoliosis Cobb's degrees 22. Low back pain, radicular symptoms to left L4 dermatome. VAS Pain 8–9/10.

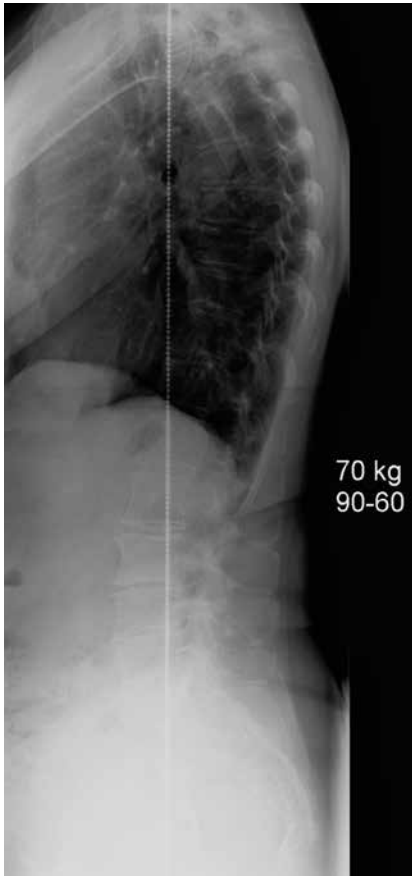
Lumbar MRI showed advanced lumbar degeneration and right convex scoliosis. Left-sided L3/L4 foraminal compression of the nerve roots.

Operation: Decompressive laminectomy L2–L5. Two osteotomies. Transpedicular fusion Th10–S1. Posterolateral fusion using autograft and BonAlive® putty as a bone graft expander.

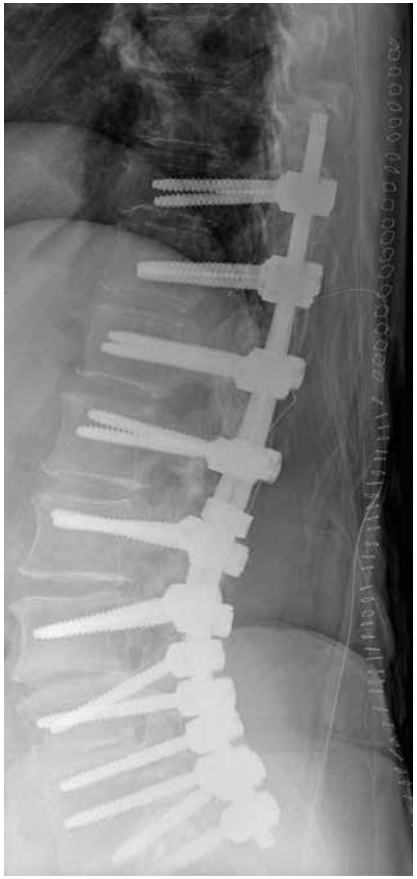
Pre-op X-ray (anteroposterior)



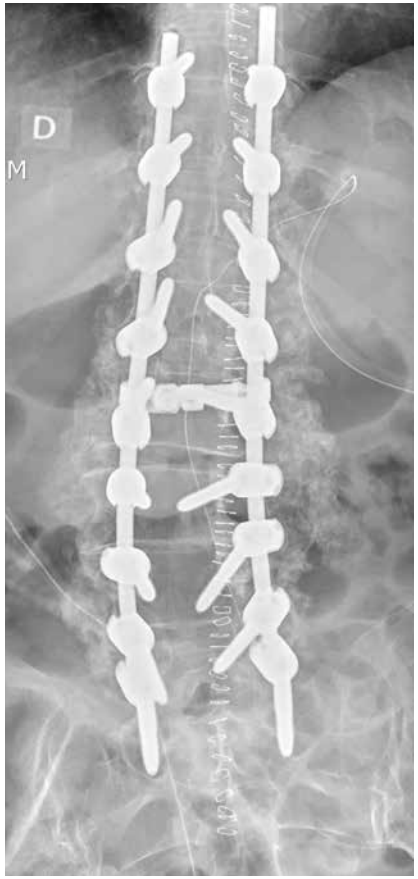
Pre-op X-ray (sagittal)



3-day post-op X-ray



3-day post-op X-ray



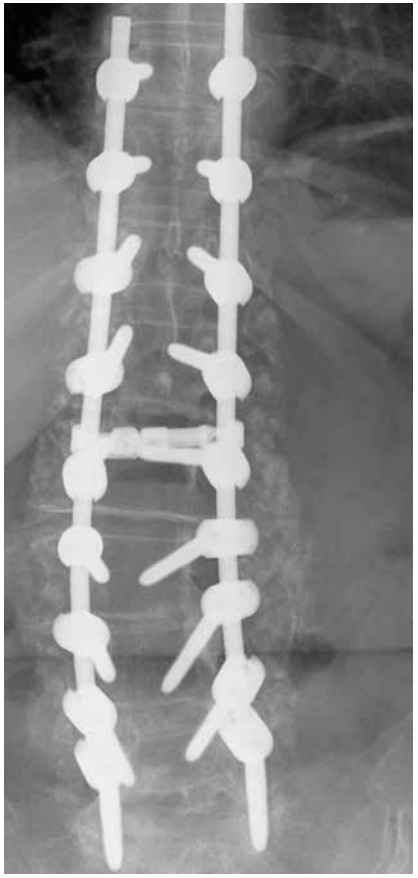
putty

Clinical outcome: Intraoperative O-arm® images showed that the instrumentation was placed correctly.

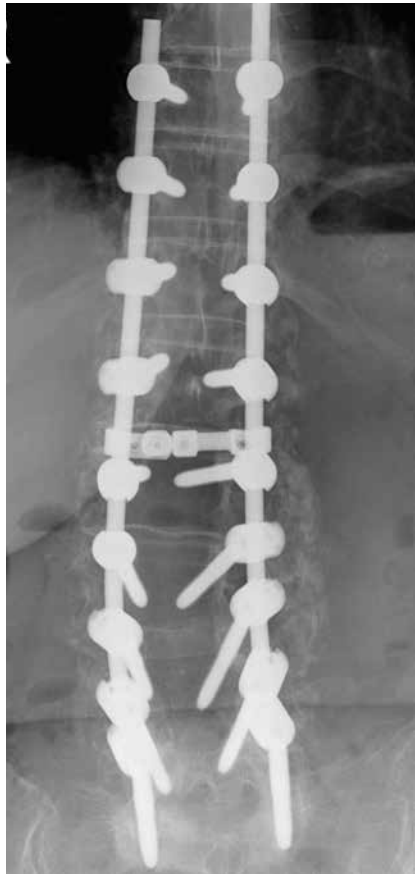
Recovered well until 6 months postoperatively, whereafter the patient had kyphotic change in posture.

At the one-year follow up the bony fusion was well developed. Removal of the hardware was performed at 20 months post-op, however a pseudoarthrosis was suspected at L5/S1. Re-operation at this level is planned. Fair outcome.

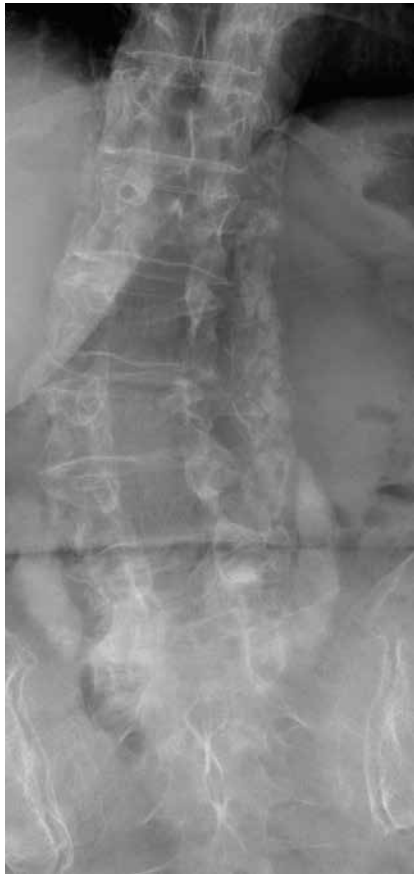
3-month post-op X-ray (anteroposterior)



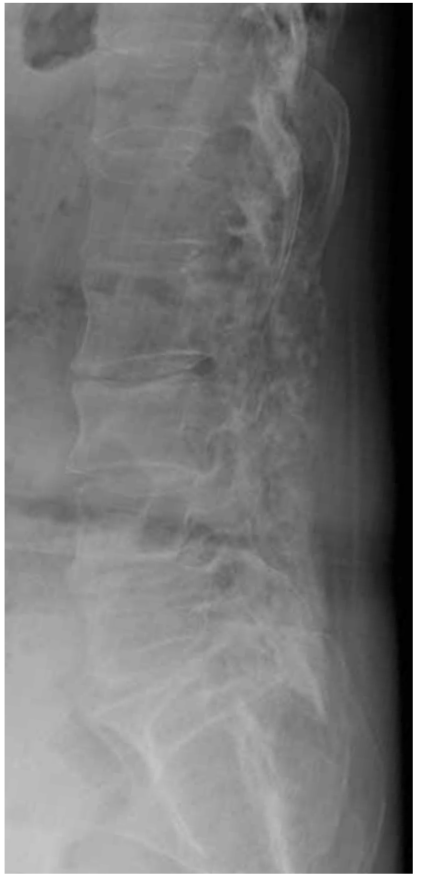
12-month post-op X-ray (anteroposterior)



20-month post-op X-ray (anteroposterior)



20-month post-op X-ray (lateral)



Courtesy of Turku University Hospital, Finland

BonAlive® granules

Antimicrobial resistance is a critical global health issue. Over several decades, to varying degrees, bacteria causing common infections have developed resistance to each new antibiotic, and antimicrobial resistance has evolved to become a world-wide health threat. Therefore, new alternative antibiotic-free technologies are needed to overcome the increasing problems involving resistance.

BonAlive® granules (bioactive glass S53P4) is a CE-marked class III medical device that is used in surgical procedures to regenerate bone. With its unique feature of inhibiting bacterial growth locally without antibiotics, the BonAlive® granules technology has become an essential tool to resolve complications involving bone infections.

The broad spectrum efficacy that BonAlive® granules presents has been studied with more than 50 common gram-positive and gram-negative bacteria species, including multi-drug resistant MRSA and MRSE. This makes BonAlive® granules a powerful tool in demanding surgery where a reliable technology is needed for bone regeneration. The clinical efficacy and performance has been proven during the past 20 years in CMF, ENT, spine and neurosurgery as well as in orthopedic surgery.

Indications

- Bone cavity filling
- Bone cavity filling in the treatment of chronic osteomyelitis

Official Product Claim

- Inhibition of bacterial growth
- Osteostimulative*

Composition

- **Bioactive glass S53P4:** 53% SiO_2, 23% Na_2O, 20% CaO, 4% P_2O_5

Offical product claim: inhibition of bacterial growth

*non-osteoinductive

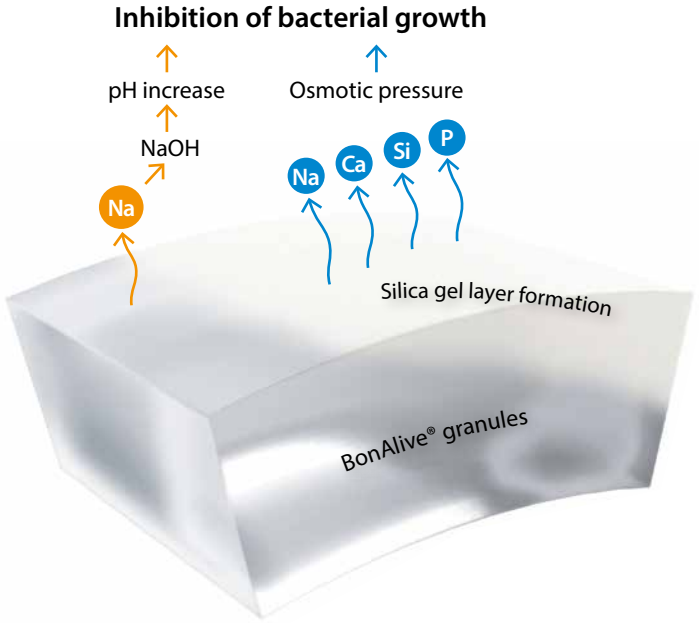
HOW BONALIVE® GRANULES WORKS

The following sequence presents the bacterial growth inhibiting and bone regeneration cascade of BonAlive® granules:

Inhibition of Bacterial Growth

Immediately in contact with body fluids BonAlive® granules reacts and leaches out ions (Na, Ca, Si, P) leading to an alkaline environment (high pH) and increased osmotic pressure. This mechanism has been shown to effectively inhibit bacterial growth.

See p. 4–7 for continued mechanism of action for BonAlive® bioactive glass.



*non-osteoinductive

INHIBITION OF BACTERIAL GROWTH

One of the most striking features of BonAlive® granules is its ability to inhibit bacterial growth. This phenomenon has been evidenced with more than 50 clinically relevant aerobic and anaerobic bacterial species through *in vitro* studies, and indirectly by empirical observation of patient data over the past 20 years.

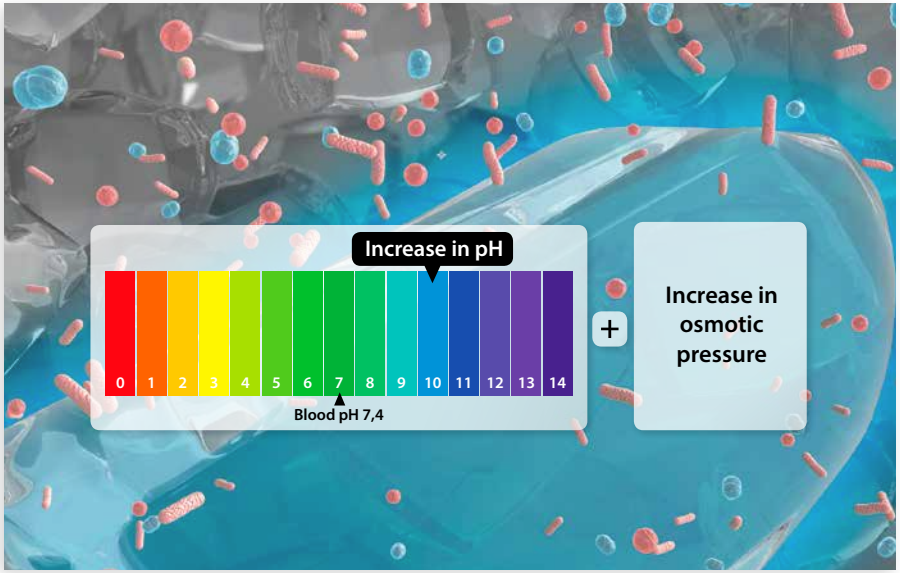
Chronic bone infections play a large role in surgery as the infection can be difficult to eradicate and might require several operations. Antibiotic resistance has become an increasing threat and new tools that are not based on antibiotics can bring significant benefits in fighting chronic bone infections. The efficacy of BonAlive® granules towards methicillin-resistant (MR) *Pseudomonas aeruginosa*, *Staphylococcus aureus* (MRSA), *Staphylococcus epidermidis* (MRSE) has been tested and proven effective.

Mechanism

The bacterial growth inhibiting effect of BonAlive® granules is based on two simultaneous processes that occur when the bioactive glass reacts with body fluids.

1. Sodium is released from the surface of the bioactive glass and induces an **increase in pH** (alkaline environment), which is not favorable for the bacteria.
2. The released Na, Ca, Si and P ions give rise to an **increase in osmotic pressure** due to an elevation in salt concentration, i.e. an environment where the bacteria cannot grow.

These two mechanism will together effectively inhibit the adhesion and colonization of bacteria on the granule surface.



Broad Spectrum Efficacy

BonAlive® granules is effective in inhibiting bacterial growth of more than 50 common bacteria species (including MRSA and MRSE).

Gram positive bacteria

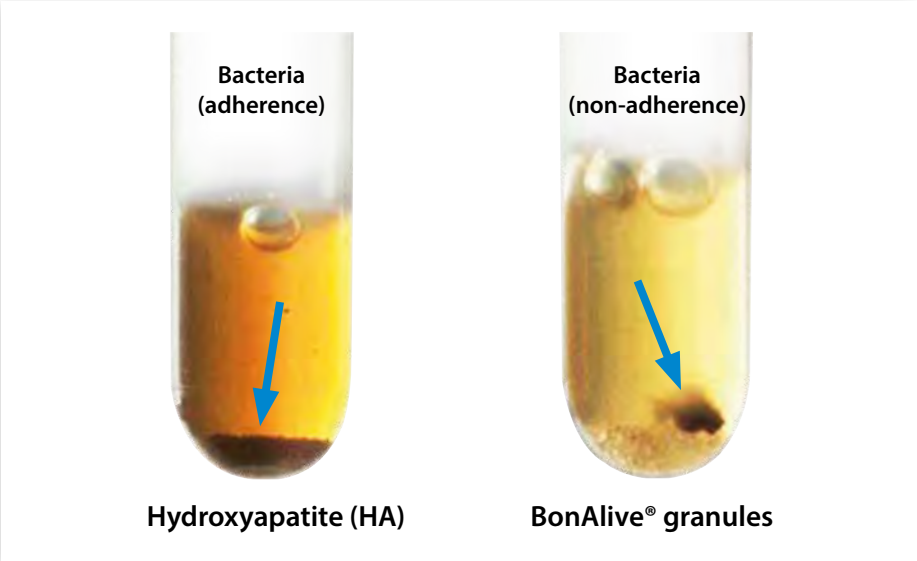
- *Bacillus cereus*
- *Bifidobacterium adolescentis*
- *Clostridium difficile*
- *Clostridium perfringens*
- *Clostridium septicum*
- *Corynebacterium ulcerans*
- *Enerobacter cloacae*
- *Enterococcus faecalis*
- *Enterococcus faecium*
- *Eubacterium lentum*
- *Listeria monocytogenes*
- *Micrococcus sp.*
- *Mycobacterium tuberculosis*
- *Peptostreptococcus anaerobius*
- *Peptostreptococcus magnus*
- *Propionibacterium acnes*
- *Propionibacterium propionicus*
- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Staphylococcus hominis*
- *Staphylococcus lugdunensis*
- *Streptococcus agalactiae*
- *Streptococcus mutans*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- *Streptococcus sanguis*

Gram negative bacteria

- *Acinetobacter baumannii*
- *Bacteroides fragilis*
- *Bacteroides thetaiotaomicron*
- *Chryseobacterium (former Flavobacterium) meningosepticum*
- *Enterobacter aerogenes*
- *Enterobacter amnigenus*
- *Escherichia coli*
- *Fusobacterium necrophorum*
- *Fusobacterium nucleatum*
- *Haemophilus influenzae*
- *Klebsiella pneumoniae*
- *Moraxella catarrhalis*
- *Neisseria meningitidis*
- *Pasteurella multocida*
- *Porphyromonas gingivalis*
- *Prevotella intermedia*
- *Prevotella melaninogenica*
- *Proteus mirabilis*
- *Pseudomonas aeruginosa*
- *Salmonella typhimurium*
- *Shigella sonnei*
- *Veillonella parvula*
- *Yersinia enterocolitica*

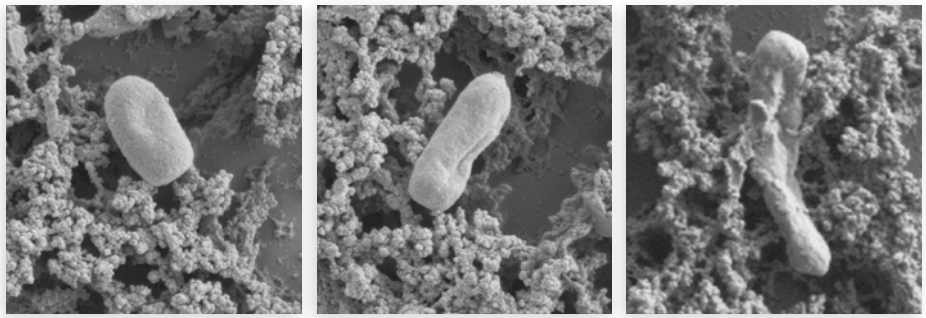
Methicillin-resistant bacteria

- *Pseudomonas aeruginosa*
- *Staphylococcus aureus* (MRSA)
- *Staphylococcus epidermidis* (MRSE)



Stoor et al. 1996

Bacteria test with pigmented *Porphyromonas gingivalis* shows that bacteria cannot adhere and grow on BonAlive® granules surface.

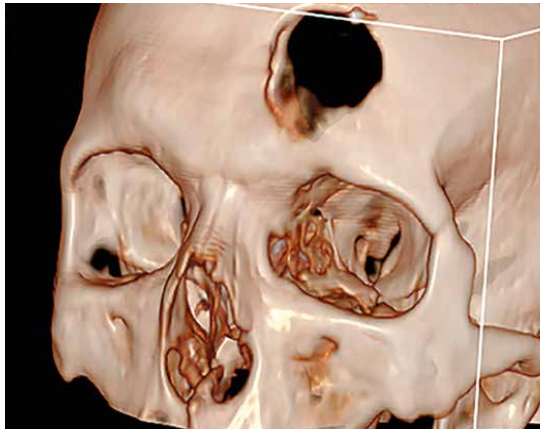


Courtesy of Prof. Lorenzo Drago, University of Milan, Italy

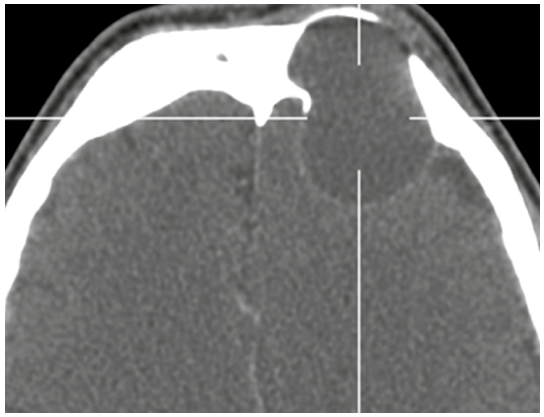
The images illustrate the impact of S53P4 bioactive glass on methicillin-resistant *Staphylococcus aureus, Klebsiella pneumoniae* and *Acinetobacter baumannii*. The inhibition of bacterial growth can be seen as changes in the morphology of the bacteria; deformation of the cells and hole formation in the cell membranes.

SEVERE MUCOPYOCELE IN FRONTAL SINUS AREA (CASE 1)

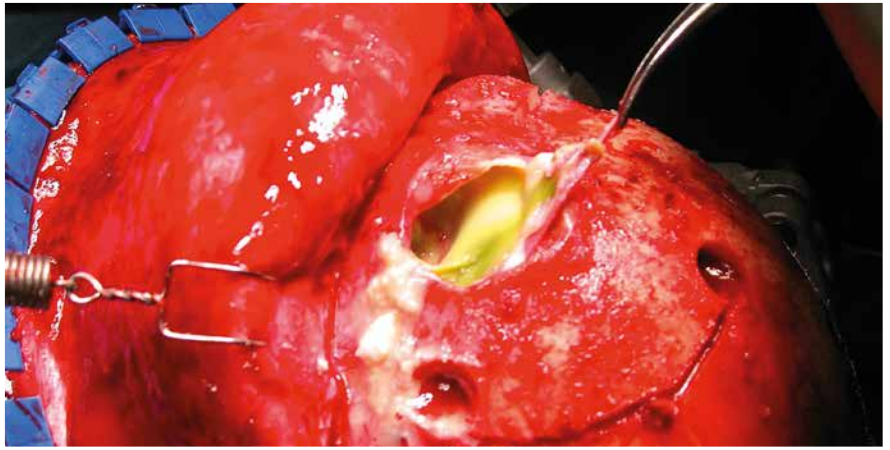
Patient: 59-year-old patient who developed an increasing soft and tender expansion on the left forehead. The patient suffered from headache and diplopia in the left gaze. While soldering, he had been hit in the left frontal area of the head by a small metal fragment. Preoperatively the patient was treated with azithromycin 500 mg/week and methylprednisolone 5 mg/day.



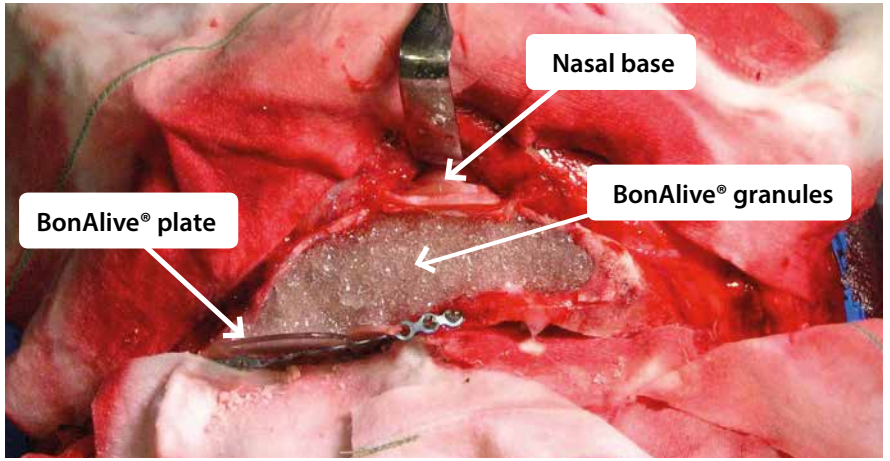
3D illustration showing the effects of complicated mucopyocele in frontal sinus, orbita and frontal lobe.



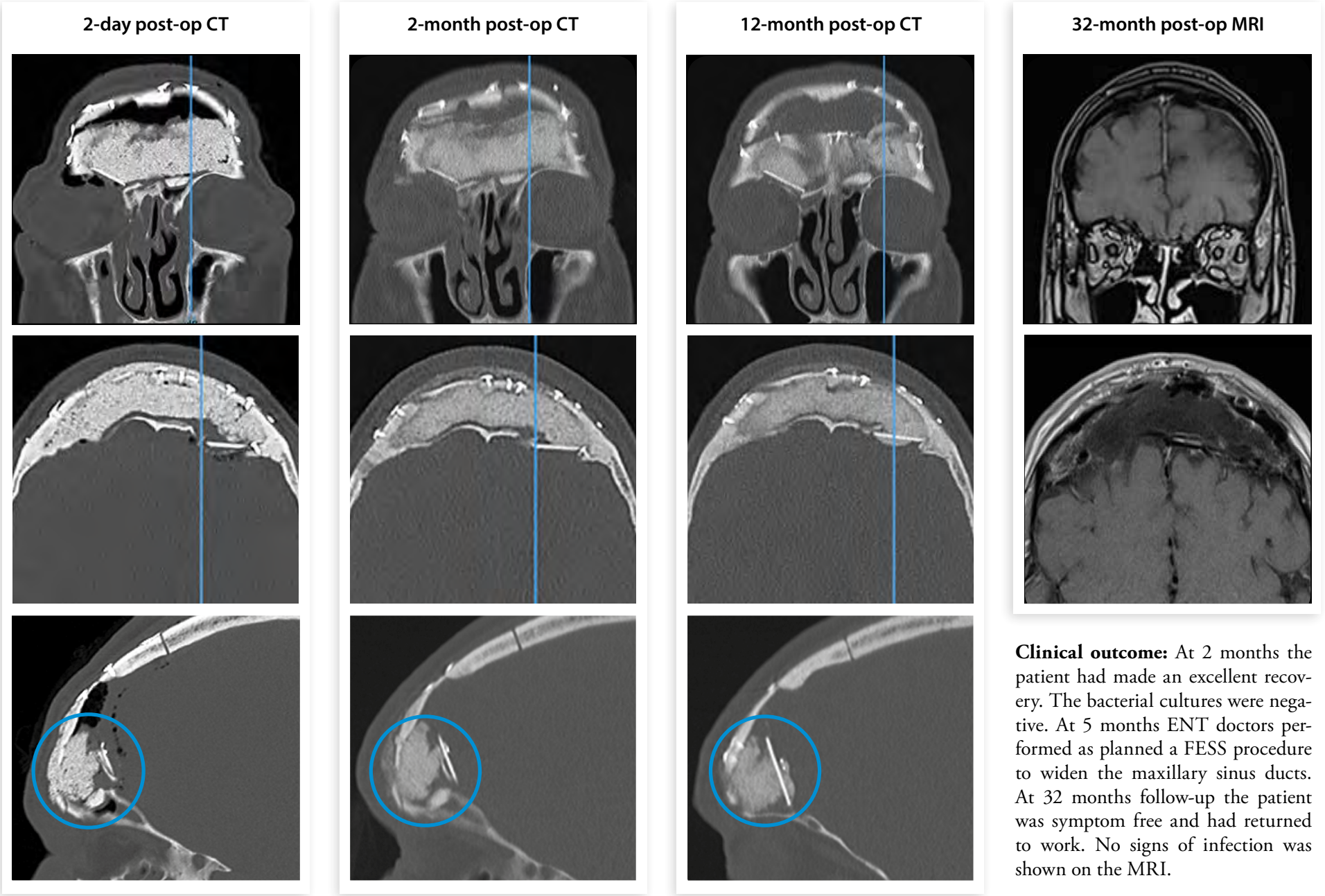
CT illustration showing mucopyocele in frontal sinus, orbita and frontal lobe.



Mucopyocele intraoperatively presenting a large amount of pus. The area was thoroughly debrided from necrotic and infected tissues before the reconstruction.



Filling of the frontal cavity with 25 cc BonAlive® granules and closing the bony gap towards the dura with a BonAlive® plate; an autograft bone plate can alternatively be used.



Courtesy of Dr. Janek Frantzén Turku University Hospital, Finland

Clinical outcome: At 2 months the patient had made an excellent recovery. The bacterial cultures were negative. At 5 months ENT doctors performed as planned a FESS procedure to widen the maxillary sinus ducts. At 32 months follow-up the patient was symptom free and had returned to work. No signs of infection was shown on the MRI.

INFECTED CERVICAL SPINE (CASE 2)

Patient: 72-year-old patient with cervical instability C3/C4 and radicular pain on both sides. Primary anterior intercorporal fusion (ACIF) using a titanium cage and autograft. Revision 18 months later due to malunion using cage, plate and autograft from iliac crest. Immediate revision due to a perforation of hypopharynx. Broadspectrum antibiotics for 3 months.

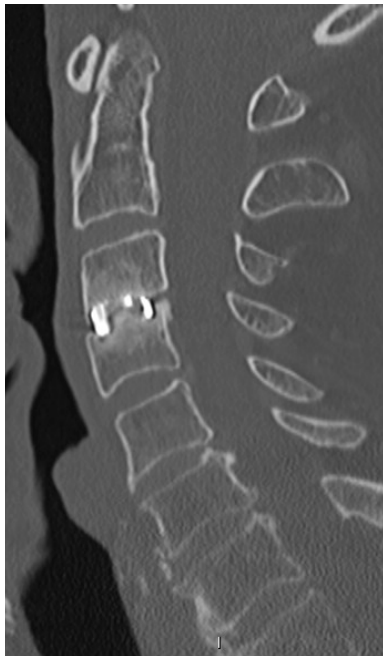
Operation: In the second revision all hardware was removed, debridement was performed, the defect was filled with 2.5 cc/ 0.5–0.8 mm (small) BonAlive® granules and covered with a TachoSil® fibrin sealant patch. Stifneck® cervical collar was applied for 3 months.

Bacterial culture: *Enterococcus faecium, Staphylococcus epidermidis, Stenotrophomonas maltophilia*

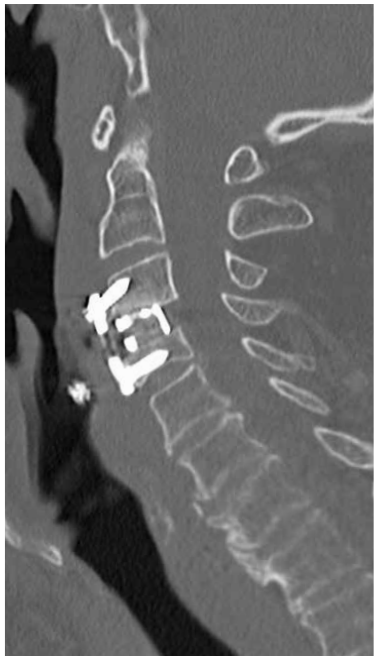
Observation (extract from instructions for use):

BonAlive® granules does not provide mechanical strength to support load bearing defects before hard tissue has formed. If a fracture requires load supporting fixation, standard internal or external stabilization techniques must be used to achieve rigid stabilization in all planes.

Primary surgery

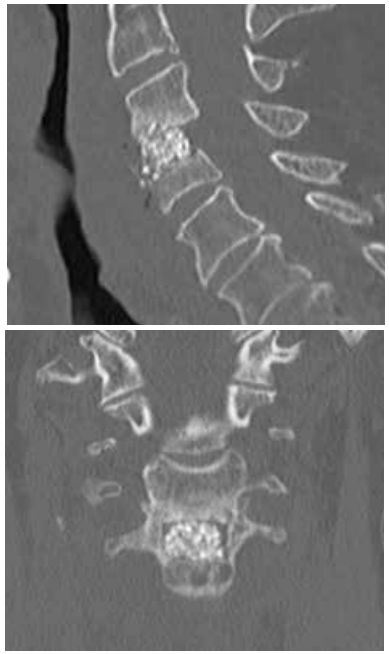


Revision surgery

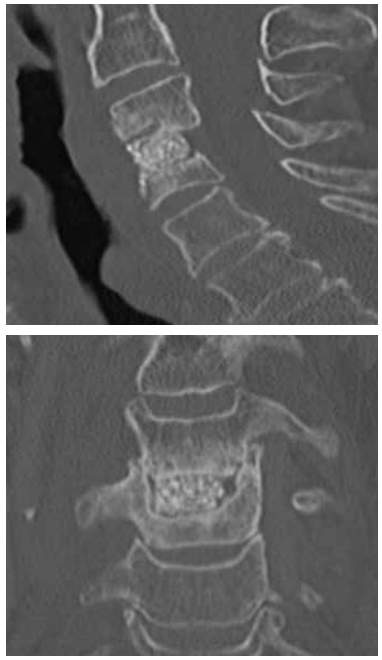


Second revision (using BonAlive® granules)

3-day post-op CT



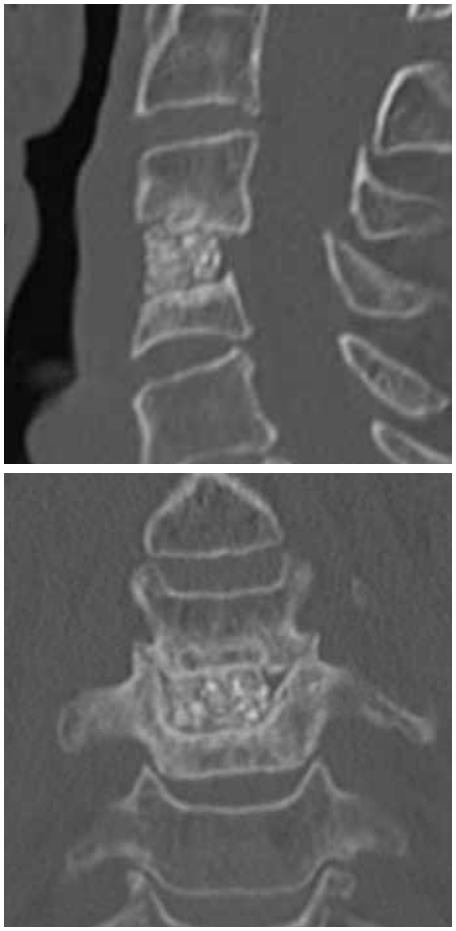
3-month post-op CT



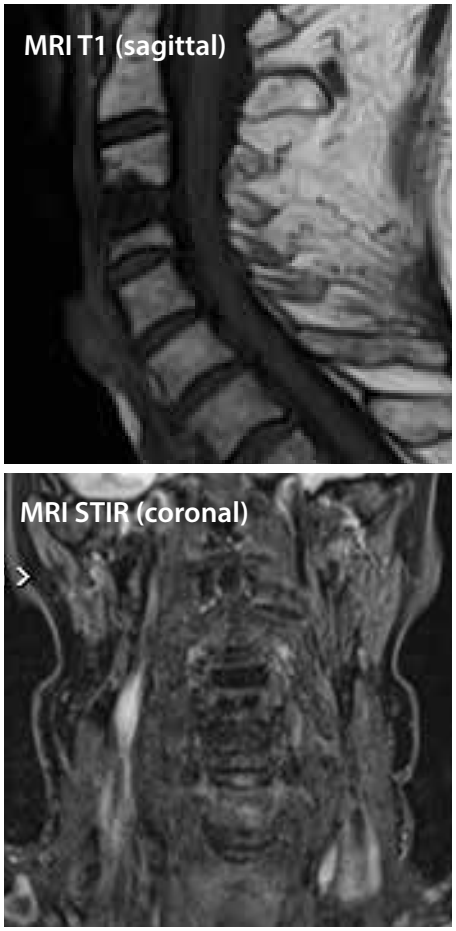
Clinical outcome: At eight months postoperatively the patient had made a good recovery. No feeding tube and fistula closed spontaneously. The patient experienced some swallowing difficulties, neckpain and radicular component to the shoulders.

No signs of infection on postoperative MRI could be observed and a fusion was clearly visible at flexion and extension X-rays images 28 months postoperatively.

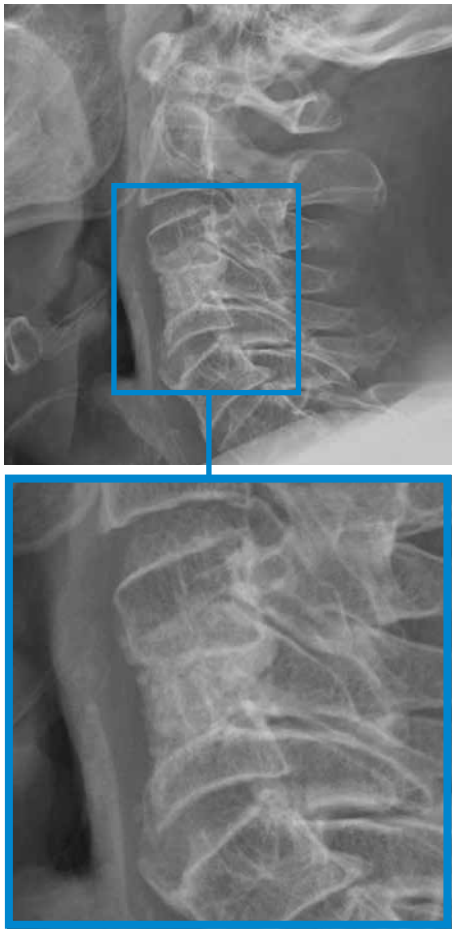
8-month post-op CT



28-month post-op MRI



28-month post-op X-ray (lateral)



Courtesy of Dr. Janek Frantzén Turku University Hospital, Finland

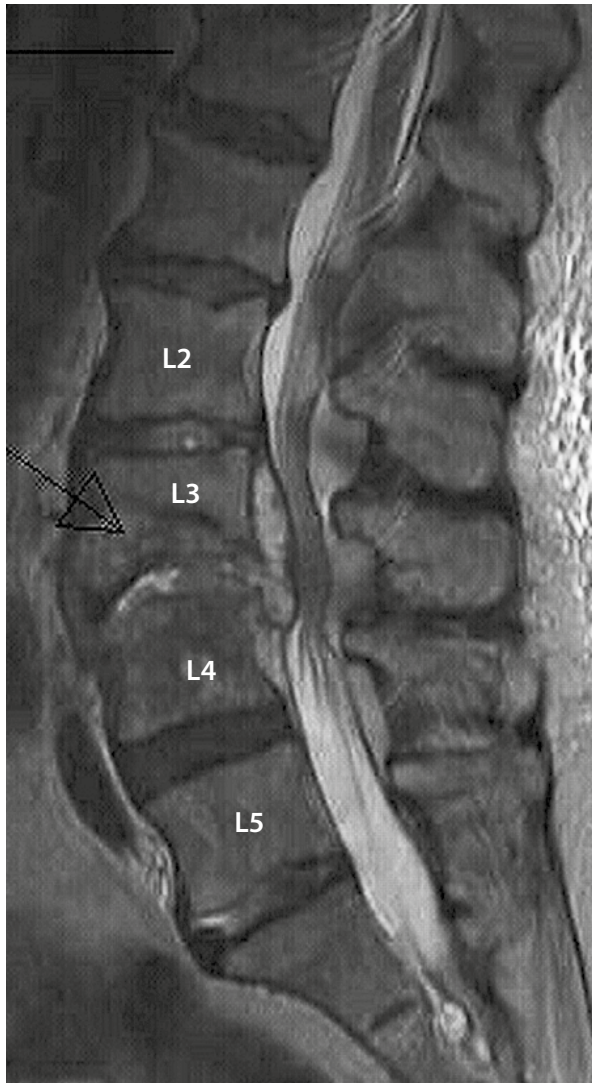
CHRONIC OSTEOMYELITIS IN THE SPINE (CASE 3)

Patient: 75-year-old patient, abscess formation in the spine.

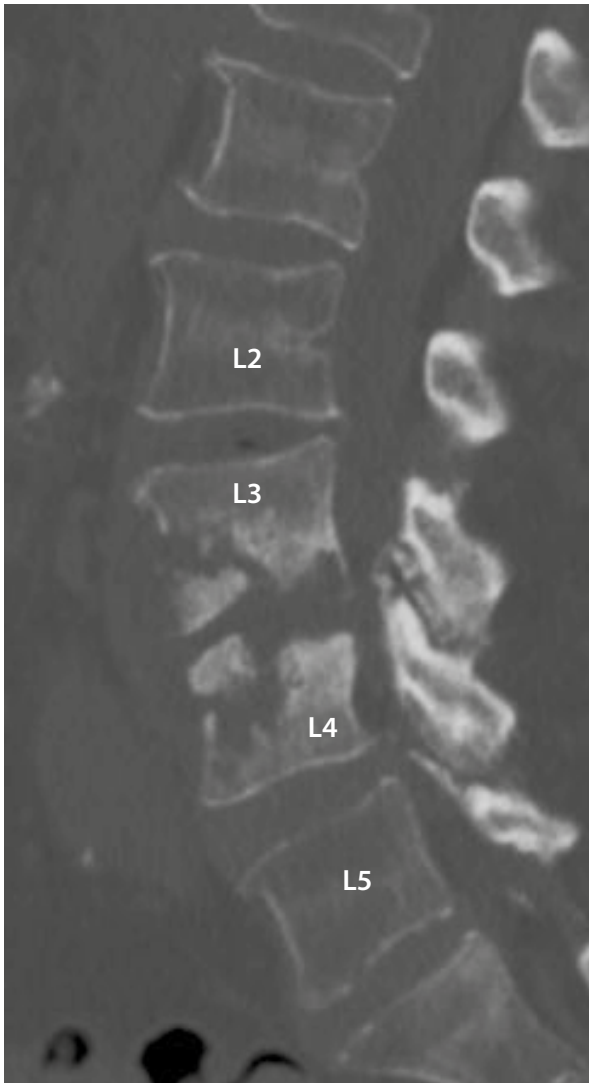
Bacterial culture: *Mycobacterium tuberculosis*

Operation: Posterior decompression L2/L3 and L3/L4, posterolateral spondylodesis L2–L5 with autogenous bone, lumbotomy, canalization of paravertebral abscess, resection of L3/L4, anterior decompression and reconstruction using an expandable spinal implant covered with 32 cc of BonAlive® granules.

Pre-op MRI

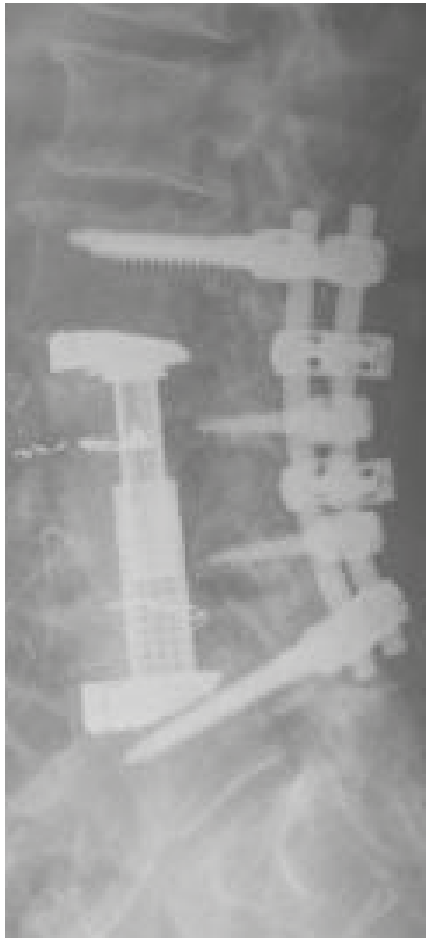


Pre-op CT

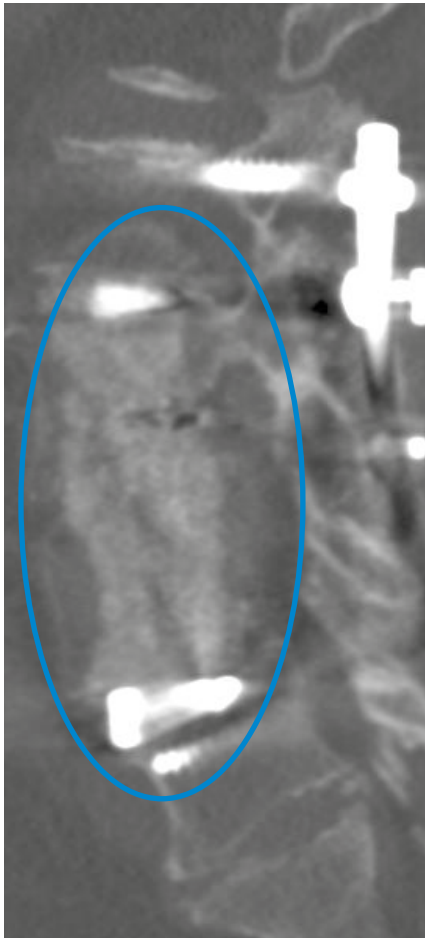


Clinical outcome: Complete fusion at 2 years post-op. The patient was fully healed.

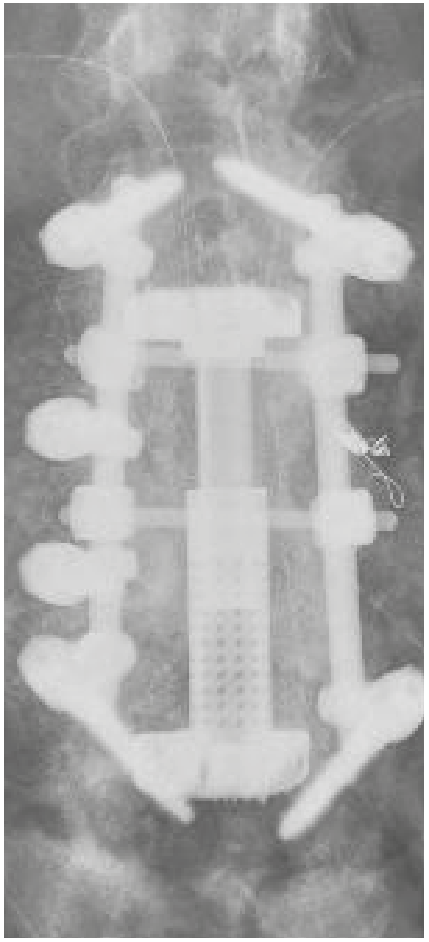
Immediate post-op X-ray



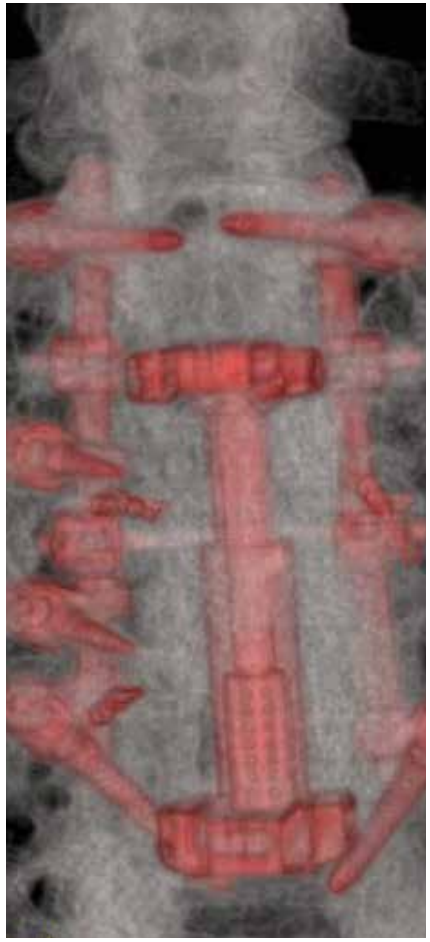
2-year post-op CT



Immediate post-op X-ray



2-year post-op CT



Courtesy of Helsinki University Central Hospital

BonAlive®
putty

1 cc | 2.5 cc | 5 cc | 10 cc

Small applicator

Ref. No.	Unit size
16110	1 cc
16120	2.5 cc

Large applicator

Ref. No.	Unit size
16130	5 cc
16140	10 cc

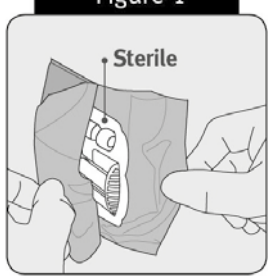
Instructions for Use

Step 1.

- Peel open the pouch and aseptically remove the sterile tray (see Figure 1).
- Detach the applicator from the tray.

Note that the pouch provides a sterile barrier to the device.

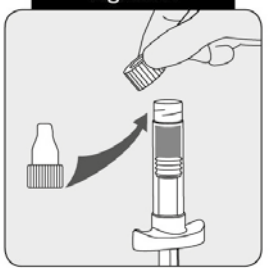
Figure 1



Step 2.

- Unscrew the cap (remove the stopper).
- Screw tightly the nozzle onto the applicator body (see Figure 2).
- Alternatively, without the nozzle, push the plunger rod to force the putty to a sterile cup and subsequently perform the implantation with a sterile instrument.

Figure 2



Step 3.

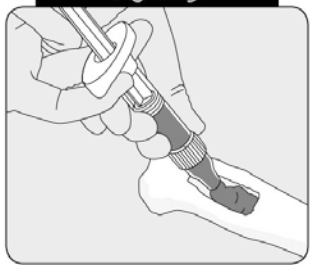
- Push the plunger rod to force the putty into the nozzle.
- Move the applicator to the defect site.
- Push the plunger rod to gently fill the defect with the putty
- (see Figure 3).

A sterile instrument (e.g. spatula) can be used as an aid if needed.

While extruding BonAlive® putty through the nozzle, a small amount of the product remains in the nozzle. If needed, use a sterile instrument to scrape out all the remaining BonAlive® putty from the nozzle.

Avoid spilling putty outside the bone defect. Misplaced putty must be removed.

Figure 3



For complete instructions for use, see package insert.

BonAlive®
granules

1 cc | 2.5 cc | 5 cc | 10 cc

Small applicator

Ref. No.	Granule size	Unit size
13110	0.5-0.8 mm (small)	1 cc
13120	0.5-0.8 mm (small)	2.5 cc

Large applicator

Ref. No.	Granule size	Unit size
13130	0.5-0.8 mm (small)	5 cc
13140	0.5-0.8 mm (small)	10 cc
13330	1.0-2.0 mm (medium)	5 cc
13340	1.0-2.0 mm (medium)	10 cc
13430	2.0-3.15 mm (large)	5 cc
13440	2.0-3.15 mm (large)	10 cc

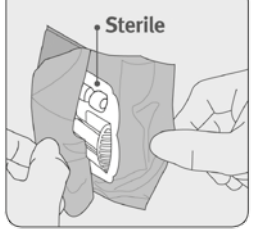
Instructions for Use

Step 1.

- Peel open the pouch (start from the corners) and aseptically remove the sterile tray (see Figure 1).
- Detach the applicator from the tray.

Note that the pouch provides a sterile barrier to the device.

Figure 1

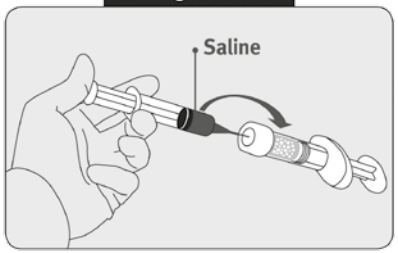


Step 2.

- Moisten the granules by injecting sterile physiological saline slowly through the cap membrane (see Figure 2).
- Make sure the granules are evenly moistened. The applicator can be turned upside down or tapped to allow the saline to moisten all granules.

Note that saline injection can cause increase in pressure inside the applicator unless the excess pressure is released e.g. with the injection needle.

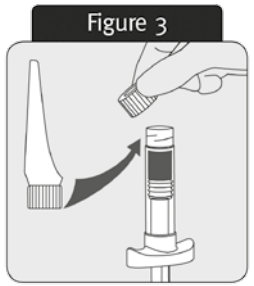
Figure 2



Step 3.

- In order to prevent spilling of the moistened granules from the applicator keep the cap facing upwards.
- Unscrew the cap (remove the stopper) and screw the shovel tightly onto the applicator body (see Figure 3).

Figure 3



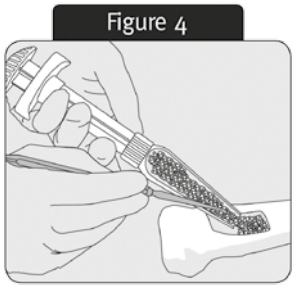
Step 4.

- Turn the applicator to a horizontal position, and push the plunger rod to slide the moistened granules onto the shovel. Move the applicator to the defect site and implant the moistened granules from the shovel into the defect with the aid of a sterile instrument (see Figure 4).

(Alternatively, if the shovel is not used, turn the applicator over a sterile cup, push the plunger rod to slide the moistened granules into the cup and subsequently perform the implantation with a sterile instrument.)

Avoid dropping the granules outside the bone defect. Misplaced granules must be removed.

Figure 4



For complete instructions for use, see package insert.

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**non-osteoinductive*

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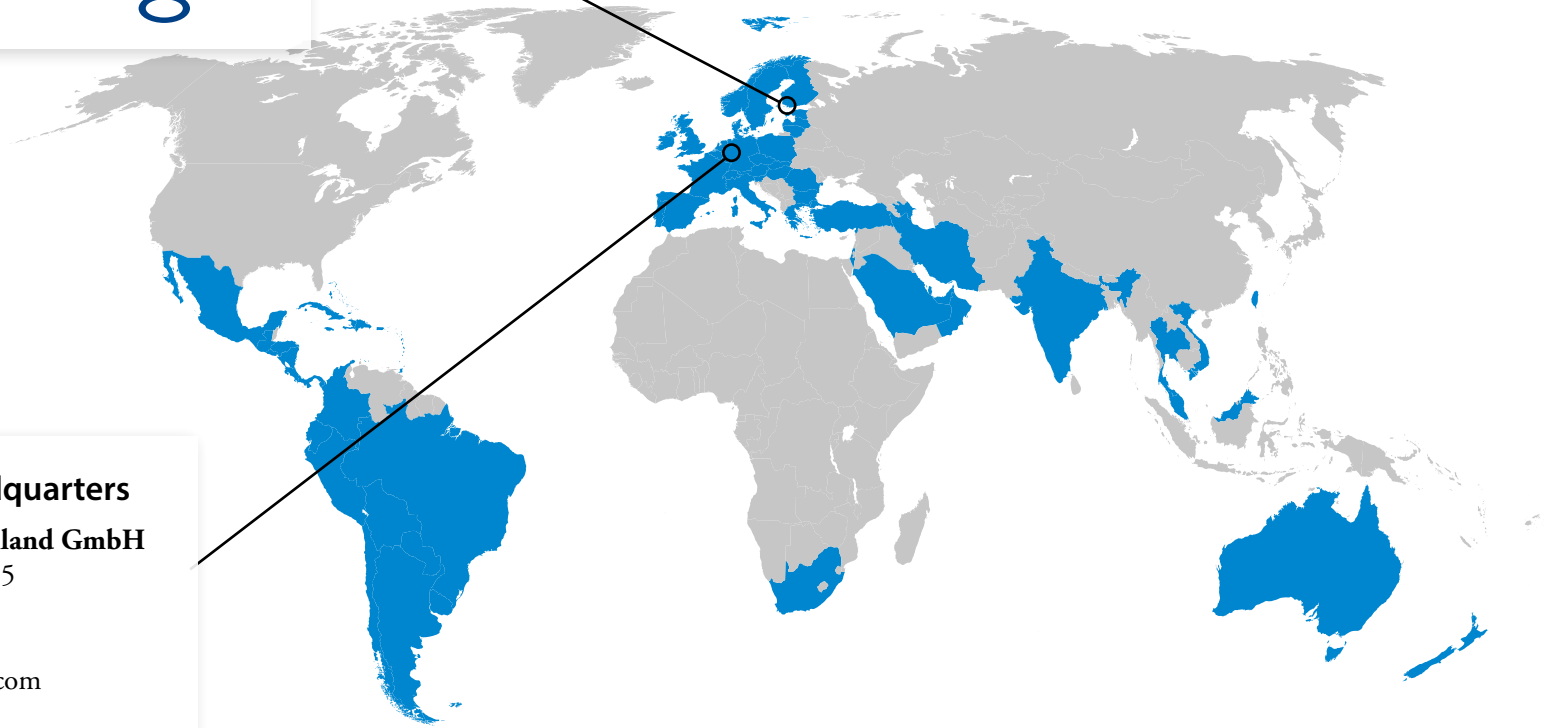

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