Inhibition of bacterial growth

Bioactive bone bonding

Osteostimulation*

*non-osteoinduction
BonAlive® granules is a resorbable bioactive glass based biomaterial for bone regeneration. Composition: 53% SiO$_2$, 23% Na$_2$O, 20% CaO, 4% P$_2$O$_5$.

**Mechanism of action (after implantation)**

**Surface reaction cascade**

**1 hour**

Release of ions increases pH and osmotic pressure (Na, Ca, P, Si)

- Inhibits bacterial growth on granule surface

**1 day**

Silica gel layer forms on granule surface

- CaP precipitates on surface

**1 week**

CaP crystallizes to natural HA

- Bonds to bone and promotes osteointegration
**Bone formation** *(scanning electron microscopy images)*

Hydroxyapatite starts to form on BonAlive® granules surface

1 day

Hydroxyapatite covers BonAlive® granules surface

1 week

BonAlive® granules bonds to bone and stimulates new bone formation (osteostimulation*)

6-12 weeks

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**Basis for osteostimulation***

Osteostimulation* signifies that BonAlive® granules has the capacity to:

1) stimulate the recruitment and differentiation of osteoblasts
2) activate osteoblasts to produce new bone
3) activate specific osteoblast genes as a response to ion dissolution from the material

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

*(Virolainen et al. 1997)*

*non-osteoinduction*
Inhibition of bacterial growth

A total of 29 aerobic and 17 anaerobic clinically important bacterial species have been tested. Growth was inhibited in all tested species. Selected species are listed below:

### Aerobic bacteria

<table>
<thead>
<tr>
<th>Gram positive</th>
<th>Growth inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. epidermidis</em></td>
<td>Effective</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>Effective</td>
</tr>
<tr>
<td><em>S. aureus</em> (MRSA)</td>
<td>Effective</td>
</tr>
<tr>
<td><em>E. faecalis</em></td>
<td>Effective</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>Effective</td>
</tr>
</tbody>
</table>

### Anaerobic bacteria

<table>
<thead>
<tr>
<th>Growth inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. difficile</em></td>
</tr>
<tr>
<td><em>B. adolescentis</em></td>
</tr>
<tr>
<td><em>E. lentum</em></td>
</tr>
<tr>
<td><em>P. gingivalis</em></td>
</tr>
<tr>
<td><em>P. acnes</em></td>
</tr>
<tr>
<td><em>P. anaerobius</em></td>
</tr>
</tbody>
</table>

### Aerobic bacteria

<table>
<thead>
<tr>
<th>Gram negative</th>
<th>Growth inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. coli</em></td>
<td>Effective</td>
</tr>
<tr>
<td><em>P. aeruginosa</em></td>
<td>Effective</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>Effective</td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td>Effective</td>
</tr>
</tbody>
</table>

**Test with pigmented *P. gingivalis***

**Bacteria (adherence)**

**Bacteria (non-adherence)**

**Hydroxyapatite (HA)**

**BonAlive® granules**


Visual appearance of BonAlive® granules vs. CaP

**Patient:** A male with a comminuted calcaneus fracture.

**Operation:** The hardware was removed at 8 weeks post-op and CaP cement was applied to a bone defect. Infection and fistula formation to the bone was observed and radical debridement was performed. The bone cavity was filled with BonAlive® granules (3 months after hardware removal).

**Clinical outcome:** At 12 months post-op the healing was uneventful and clear osteointegration could be seen in the area of the BonAlive® granules.
**Aneurysmal bone cyst (ABC) in the proximal phalanx in a child**

**Patient:** A three year old child with a recurrent aneurysmal bone cyst of the proximal phalanx of the index finger.

**Operation:** The bone tumour was removed and the defect was grafted with 2 cc/0.5-0.8 mm BonAlive® granules and two 2-3 mm pieces of autogenous bone.

**Clinical outcome:** Follow-up was at 1, 3, 12 and 24 months post-op. At 24 months, no cavity was observed and the homogenous region resembled normal trabecular bone. The phalanx had grown in length and remodelled to almost normal shape. BonAlive® granules does not disturb the natural growth of bone in children.
Large aneurysmal bone cyst (ABC) in the proximal femur in a child

**Patient:** 16-year old male with a large aneurysmal bone cyst in the proximal femur.

**Operation:** In the 1st operation the cavity was filled with autograft and the 2nd time with a CaP based synthetic bone graft. In both cases the grafts had resorbed. In the 3rd operation 60 cc/2.0-3.15 mm BonAlive® granules was used for the grafting.

**Clinical outcome:** Healing could be observed due to the osteostimulative* and slow resorption properties of BonAlive® granules.

*non-osteoinductive
Large pelvic aneurysmal bone cyst (ABC)

Patient: 15-year old girl with a large pelvic aneurysmal bone cyst.

Operation: The large bone cyst was evacuated, the defect was fenolized and filled with 60 cc/2.0-3.15 mm BonAlive® granules.

Clinical outcome: At 9 months post-op the patient had fully healed and was free of any symptoms and signs of recurrence of the ABC.
Depressed tibial plateau fracture

**Patient:** 57-year old male with a depressed lateral tibial plateau fracture.

**Operation:** 15 cc/1.0-2.0 mm of BonAlive® granules was used to fill the defect.

**Clinical outcome:** No complications, current status is excellent. BonAlive® granules is a slowly resorbing biomaterial, but has completely remodelled to bone during the 11-year follow-up.

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Patient included in the following study: Bioactive glass S53P4 and autograft bone in treatment of depressed tibial plateau fractures. A prospective randomized 11-year follow-up.  

Ulnar fracture with post-op chronic infection

**Patient:** 45-year old male with an ulnar fracture.

**Bacterial species:** *Staphylococcus epidermis.*

**Operation:** The fracture was stabilised and CaP cement was applied to the bone defect. At 2 months post-op, fistula formation to CaP with *Staphylococcus epidermis* infection was observed. A two-stage revision was performed using antibiotic beads, radical debridement and grafting with BonAlive® granules (1.0-2.0 mm).

**Clinical outcome:** At 7 months after revision surgery the patient had healed well and the clinical outcome was considered to be good.
Chronic osteomyelitis in the distal tibia

Patient: 36-year old male with a chronic osteomyelitis in the distal tibia. After surgical debridement the defect size was 100 cc.

Operation: The patient received a pilon fracture in a car crash and the fracture was stabilised with an anterior plate in the distal tibia. The patient was diagnosed with severe chronic osteomyelitis with extensive pus formation in the distal tibia. The anterior fixation plate was removed and the area was surgically cleaned through radical debridement. The defect was filled with BonAlive® granules 48 cc/2.0-3.15 mm mixed with an equal amount of autologous bone.

Clinical outcome: The soft tissue healed well. Although a significant part of the anterior cortex of the distal tibia was removed, new cortical bone was formed. At 2.5 years post-op the fusion was stable and the patient outcome continued to be successful.
Chronically infected non-union of the distal tibia

Patient: 32-year old female, type A host, was in a car crash and received an exposed pilon fracture that was stabilized with an external fixator.

Bacterial species: *Staphylococcus aureus*.

Surgeon: Prof. Carlo Romanó, Istituto Ortopedico Galeazzi, Milan, Italy.

Operation: The patient was diagnosed with septic non-union 9 months after trauma. The patient refused new external fixation. The external fixator was removed and, after 15 days, an osteotomy of the fibula, debridement of the non-union septic focus, local application of BonAlive granules (20 cc/1.0-2.0 mm granules) and intramedullary nailing were performed.
Clinical outcome: Bone healing was achieved in 6 months from implantation. The soft tissue healed well, with no clinical or laboratory signs of infection recurrence. Dynamisation of the nail was performed 14 months post-op and the nail was removed 24 months post-op.
Chronic osteomyelitis in the spine

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

**Bacterial species:** *Mycobacterium tuberculosis.*

**Operation:** Posterior decompression L2-L3 and L3-L4, spondylodesis L2-L5, lumbotomy, canalisation of paravertebral abscess, resection of L3-L4, anterior decompression and reconstruction. Posterolateral fusion and application of BonAlive® granules and autograft bone (50/50) around the anterior cage.

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

<table>
<thead>
<tr>
<th>Lateral view</th>
<th>Anteroposterior view</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate post-op X-ray</td>
<td>Post-op X-ray</td>
</tr>
<tr>
<td>2-year post-op CT</td>
<td>2-year post-op CT</td>
</tr>
</tbody>
</table>

**Images:**
- BonAlive® granules
- New bone formation

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Mechanism of action (osteostimulation*)

Osteoblast response to continuous phase macroporous scaffolds under static and dynamic culture conditions.

Molecular basis for action of bioactive glasses as bone graft substitute.

Intact surface of bioactive glass S53P4 is resistant to osteoclastic activity.

Granule size and composition of bioactive glasses affect osteoconduction in rabbit.

Osteoblast differentiation of bone marrow stromal cells cultured on silica gel and sol-gel-derived titania.

Histomorphometric and molecular biologic comparison of bioactive glass granules and autogenous bone grafts in augmentation of bone defect healing.

Reference

The reputation of BonAlive® is built on solid clinical evidence
• Over 20 peer-reviewed published clinical articles
• More than a decade of human prospective randomized clinical data

Inhibition of bacterial growth

Antibacterial effects and dissolution behavior of six bioactive glasses.

Bactericidal effects of bioactive glasses on clinically important aerobic bacteria.

Antibacterial effect of bioactive glasses on clinically important anaerobic bacteria in vitro.

In situ pH within particle beds of bioactive glasses.

Factors controlling antibacterial properties of bioactive glasses.

Comparison of antibacterial effect on three bioactive glasses.

Interactions between the bioactive glass S53P4 and the atrophic rhinitis-associated microorganism Klebsiella ozaeae.

Antibacterial effects of a bioactive glass paste on oral micro-organisms.

Interactions between the frontal sinusitis-associated pathogen Hemophilus Influenzae and the bioactive glass S53P4.
Chronic osteomyelitis

Through the looking glass; bioactive glass S53P4 (BonAlive®) in the treatment of chronic osteomyelitis.

Lindfors NC. J Biotechnol Biomaterial. 2011;1(5). (An open access journal.)

Bioactive glass S53P4 as bone graft substitute in treatment of osteomyelitis.

Preclinical publications

Bioactive glass as bone-graft substitute for posterior spinal fusion in rabbit.

Tissue response to bioactive glass and autogenous bone in the rabbit spine.

Bioactive glass and calcium carbonate granules as filler material around titanium and bioactive glass implants in the medullar space of the rabbit tibia.

Long term behaviour of bioactive glass cone and granules in rabbit bone.

Protein adsorption properties of bioactive glasses compared to their behaviour in rabbit tibia.

Bone formation in rabbit cancellous bone defects filled with bioactive glass granules.
BonAlive® granules

Products

BonAlive® granules in small applicator

<table>
<thead>
<tr>
<th>Ref. no</th>
<th>Granule size</th>
<th>Unit size</th>
</tr>
</thead>
<tbody>
<tr>
<td>13110</td>
<td>0.5-0.8 mm (small)</td>
<td>1 cc</td>
</tr>
<tr>
<td>13120</td>
<td>0.5-0.8 mm (small)</td>
<td>2.5 cc</td>
</tr>
</tbody>
</table>

BonAlive® granules in large applicator

<table>
<thead>
<tr>
<th>Ref. no</th>
<th>Granule size</th>
<th>Unit size</th>
</tr>
</thead>
<tbody>
<tr>
<td>13130</td>
<td>0.5-0.8 mm (small)</td>
<td>5 cc</td>
</tr>
<tr>
<td>13140</td>
<td>0.5-0.8 mm (small)</td>
<td>10 cc</td>
</tr>
<tr>
<td>13330</td>
<td>1.0-2.0 mm (medium)</td>
<td>5 cc</td>
</tr>
<tr>
<td>13340</td>
<td>1.0-2.0 mm (medium)</td>
<td>10 cc</td>
</tr>
<tr>
<td>13430</td>
<td>2.0-3.15 mm (large)</td>
<td>5 cc</td>
</tr>
<tr>
<td>13440</td>
<td>2.0-3.15 mm (large)</td>
<td>10 cc</td>
</tr>
</tbody>
</table>
BonAlive® granules

Instructions for use

Figure 1
Peel open the pouch and aseptically remove the sterile tray.

Figure 2
Moisten the granules by injecting sterile physiological saline slowly through the cap membrane.

Figure 3
Screw tightly the shovel onto the applicator body, 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.

For complete instructions for use, see package insert.
Contact details

Headquarters

BonAlive Biomaterials Ltd
Tel. +358 (0)401 77 44 00
Fax +358 (0)421 91 77 44 00
orders@bonalive.com
Biolinija 12
20750 Turku, Finland
www.bonalive.com

BonAlive Biomaterials Ltd
Tel. +358 (0)401 77 44 00
orders@bonalive.com
Biolinija 12
20750 Turku, Finland
www.bonalive.com

Distributors

EUROPE

AUSTRIA
Olympus Biotech Österreich GmbH
Tel. 0800 204 643
orders@bonalive.com
Fax +358 (0)421 91 77 44 00
Biolinija 12
20750 Turku, Finland
www.bonalive.com

GERMANY
Olympus Biotech Deutschland GMBH
Tel. +49 211 690 1319
orders@bonalive.com
Neuer Wall 50,
20354 Hamburg, Germany
www.olympusbiotech.com

IRELAND
Olympus Biotech International
Tel. +353 62 585 100
orders@bonalive.com
Raheen Business Park
Limerick, Ireland
www.olympusbiotech.com

ITALY
Mediplast Srl
Tel. +39 011 5185259
orders@bonalive.com
Via Roma n. 101
10123 Torino, Italy
www.mediplusitalia.it

NORWAY
Mediplast AS
Tel. +45 4444 4000
info.dk@mediplast.com
Valhus Allé 176-176
2610 Værløse, Denmark
www.mediplast.com

DENMARK
Mediplast AB
Tel. +46 40 671 23 00
orders@bonalive.com
24, Nicolea Roui Street
District 3, 03110 Bucharest, Romania
www.gotosolution.com

SWEDEN
Mediplast AB
Tel. +46 40 671 23 00
orders@bonalive.com
Kantnexplan 29
SE-23376 Malmo, Sweden
www.mediplusitalia.it

PORTUGAL
Atos Medical Spain SL.Sucursal em Portugal
Tel. +351 96 4927781
info.pt@atosmedical.com
Avenida da Liberdade, Nº78 - 1º-B
2855 - 385 Corroios
Portugal
www.atosmedical.se

ROMANIA
GTS Solution SRL
Tel. +40 (21) 256 0095
office@gotosolution.com
24, Nicolae Roui Street
District 3, 03110 Bucharest, Romania
www.gotosolution.com

SPAIN
Bemad Productos Y Distribuciones, S.L.
Tel. +34 94 674 0774
Bemad.co@gmail.com
Lausaxeta Olekari, 46 C - 1º B
48100 Mungia, Spain

SWITZERLAND
Medico-CH Sarl
Tel. +41 22 307 01 70
orders@bonalive.com
No. 73, II Floor, Lal Bagathur Colony, Pearamedu
641004 Coimbatore, Tamilnadu, India
www.mediplusitalia.it

AUSTRIA
Olympus Biotech Austria
Tel. +43 222 429 551
customers@device.com.au
8/25 Frenchs Forest Road
Frenchs Forest, NSW 2086, Australia
www.device.com.au

INDIA
Shreyas Medical Technologies Pvt Ltd
Tel. +91 800 429 551
orders@bonalive.com
73, II Floor, Lal Bagathur Colony, Pearamedu
641004 Coimbatore, Tamilnadu, India
www.mediplusitalia.it

MALAYSIA
Malex Medical Asia (M) Sdn Bhd
Tel. +603 7880 0192
sales@malexmedical.com
No.10-1, Block E1, Jalan PJU 1/42
Dataran Prima, 47301 Petaling Jaya
Selangor, Malaysia
www.malexmedical.com

UNITED KINGDOM
Olympus Biotech UK Limited
Tel. +44 1923 853 426
orders@bonalive.com
Seven Gables House
30 Lenhammore Road
Radlett, Herts, WD7 8HT, U
www.mediplusitalia.it

MIDDLE EAST/ASIA-PACIFIC
AUSTRALIA
Device Technologies Australia Pty Ltd
Tel. +61 800 429 551
customers@device.com.au
8/25 Frenchs Forest Road
Frenchs Forest, NSW 2086, Australia
www.device.com.au

NEW ZEALAND
Device Technologies New Zealand
Tel. +64 9 913 2000
sales@device.co.nz
47 Arrenway, Albany
Auckland, New Zealand
www.device.com.au

UNITED ARAB EMIRATES
Bayan Medical Co.
Tel. +97143468772
sales@bayanmed.com
Office 302, Emarat Atrium Bldg.
Sheikh Zayed Road
Dubai, United Arab Emirates
www.bayanmed.com

BRAZIL
Osis Medical
Tel. +55 11 4301-3714
sales@osismed.com
Office 302, Emarat Atrium Bldg.
Sheikh Zayed Road
Dubai, United Arab Emirates
www.bayanmed.com

ISRAEL
D-Med Ltd.
Tel. +972 9 954 3616
sales@d-med.co.il
19 Beiri Street
46560 Herzliya, Israel
www.d-med.co.il

KINGDOM OF SAUDI-ARABIA
Husn Al Emirat Est
Tel. +966 1 453 6171
www.fiksmed.com.tr

ANKARA, TURKEY
www.fiksmed.com.tr

TAIWAN
Chi Fu Trading Co. Ltd.
Tel. +886 2 2790 0799
info@chifupharma.com
69, Lane 77, Xin Ai Road
7th Floor, Neihu District
Taipei 11494, Taiwan
www.chifupharma.com

AFRICA
SOUTH-AFRICA
Stratmed
Tel. +27 21 68 55 146
di@stratmed.co.za
7 Thicket road, Rosebank
7705, Cape Town, South-Africa
www.stratmed.co.za

CENTRAL AMERICA AND CARIBBEAN
Kaisermed SA de CV
Tel. +52 55 112 3978
info@kaisermed-cz.net

OTHER REGION

AFRICA
SOUTH-AFRICA
Stratmed
Tel. +27 21 68 55 146
di@stratmed.co.za
7 Thicket road, Rosebank
7705, Cape Town, South-Africa
www.stratmed.co.za

AMERICAS
BRAZIL
Osis Medical
Tel. +55 11 4301-3714
sales@osismed.com
Office 302, Emarat Atrium Bldg.
Sheikh Zayed Road
Dubai, United Arab Emirates
www.bayanmed.com

CENTRAL AMERICA AND CARIBBEAN
Kaisermed SA de CV
Tel. +52 55 112 3978
info@kaisermed-cz.net

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