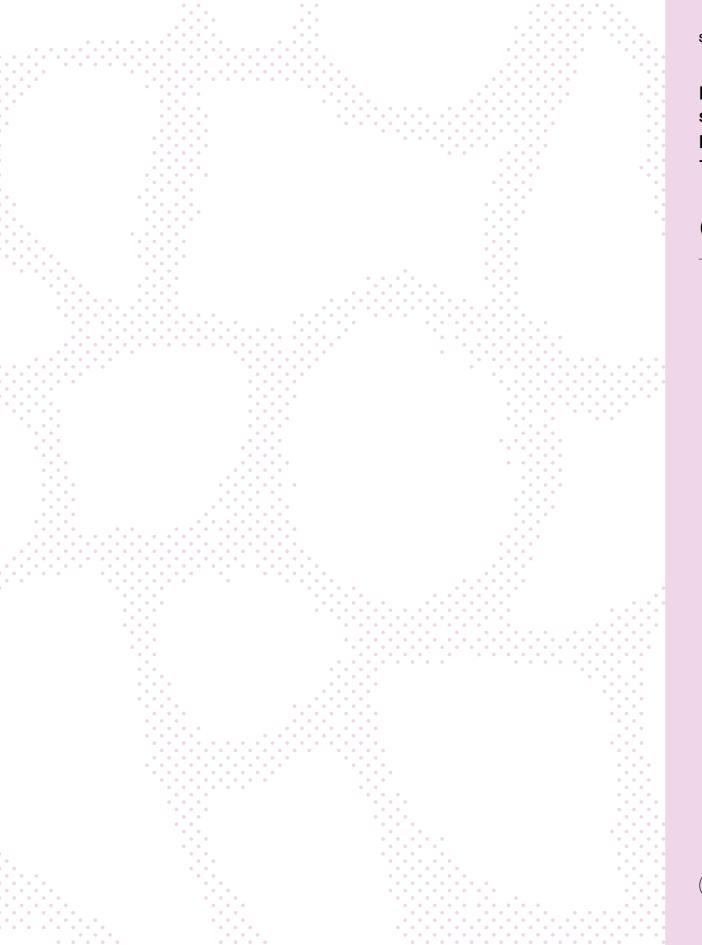
Benign Bone Tumor Surgery





Smart Healing[™]



Smart Healing™

Benign bone tumors and pediatric orthopedic surgery is our focus area. Together with medical professionals we create Smart Healing[™] – a smarter future for healthcare.

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Bonalive is an ISO 13485:2016 certified, Class III medical device company.

Q

Bonalive[®] granules and Bonalive[®] putty are CE marked medical devices.

Bonalive is committed to the promise of Smart Healing[™]. Through Smart Healing[™] we sustainably improve the anatomical and functional healing of benign bone tumor patients – supporting healthy bone formation also in a growing skeleton.

Smart Healing[™]

Coming to life at the intersection of biology and technology, Smart Healing[™] represents a new standard in healthcare. A new era for patients.

Pediatric patients require special attention since surgery on a growing skeleton can be challenging. We provide Smart Healing[™], which means we focus on solutions that restore the functions of the body through the patient's own biological processes.

The long-term use of our Bonalive® products has proven their clinical safety and effectiveness without disturbing the normal growth of bone in children. The world needs solutions that are smarter and more sustainable for all patients worldwide.

About us Bonalive is a smart biomaterials company, transforming healthcare at the intersection of biology and technology. With over 20 years of clinical history, and one of the most evidence-based technologies in the industry, we are re-imagining a smarter future for healthcare. Bonalive is a medical device Class III certified company.



Smart Healing[™]

Bonalive® putty

A unique bone regeneration technology that naturally stimulates bone formation and inhibits bacterial growth.

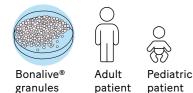
PROPERTIES

Inhibition of

bacterial growth

Bonalive[®]

granules



INDICATIONS

- Bone cavity filling
- Bone cavity filling in the treatment of chronic Osteoconductive osteomyelitis Osteostimulative*

COMPOSITION

- 53% SiO,
- 23% Na Ô
- 20% CaO
- 4% P₂O₅

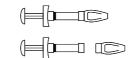
The clinical efficacy and performance of the granules has been proven over the past 20 years. Bonalive® granules is verified as safe for use in both adult and pediatric patients and consists solely of elements that are naturally present in the human body.

Bioactive glass does not disturb the normal growth of bone in children: its performance has been proven in a prospective randomized study that involved follow-up of up to 14 years.

Bonalive[®] granules is intended for larger defects. For small and medium size defects of up to 20 cc Bonalive[®] putty can be used.

Patient cases on page 12, 14, 16, 18, 20, 22 and 24.

Unit size	Granule size	Ref. no.
5 cc prefilled applicator	1.0-2.0 mm	13330
10 cc prefilled applicator	1.0-2.0 mm	13340



A highly moldable, easy-to-apply bone regeneration technology that naturally stimulates bone formation.



INDICATIONS FOR USE

Bony voids and gaps

• Filling, reconstruction

and regeneration

of bone defects

INTENDED USE

Osteoconductive Osteostimulative*

PROPERTIES

COMPOSITION

- 53% SiO
- 23% Na₂Ò
- 20% CaO
- 4% P₂O₂
- Polyethylene glycols (PEGs) and glycerol

Bonalive® putty is an optimized bone graft substitute for orthopedic and trauma surgery. The putty is a sterile ready-to-use paste that can be delivered directly to the bone defect without mixing or preparation.

Bonalive[®] putty is intended for use in small and medium size bone defects up to 20 cc in size.

Patient cases on page 18 and 23.

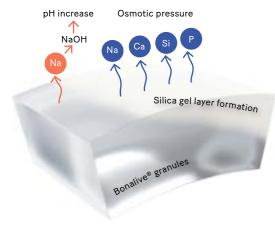
Unit size	Ref. no.
1 cc prefilled applicator	16110
2.5 cc prefilled applicator	16120
5 cc prefilled applicator	16130
10 cc prefilled applicator	16140



Our technology

Inhibition of bacterial growth

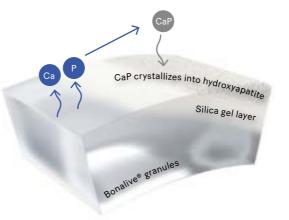
The bacterial growth inhibiting feature of Bonalive[®] granules consist of two simultaneous chemical and physical processes occurring once the bioactive glass reacts with body fluids.



Mechanism of actions

1. Sodium (Na) is released from the surface of the bioactive glass and induces an increase in pH (alkaline environment), which is not favorable for the bacteria, thus inhibiting their growth.

2. The released Na, Ca, Si and P ions give rise to an increase in osmotic pressure due to an elevation in the salt concentration, i.e. an environment where bacteria cannot grow.



Bone regeneration and remodeling

Bonalive® S53P4 bioactive glass is osteoconductive and also

osteoproductive in the promotion, migration, replication and

differentiation of osteogenic cells and their matrix production.**

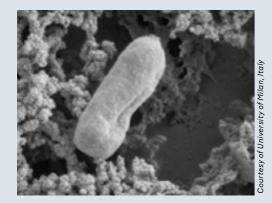
The release of ions and surface reactions develope a silica gel layer on the bioactive glass that attracts CaP to crystallize into natural hydroxyapatite.

Once the hydroxyapatite layer is formed the bioactive glass interacts with biological entities, i.e. blood proteins and growth factors. Following this interactive, osteoconductive and osteostimulative process, new bone grows onto and between the bioactive glass structures.

Efficacy

Bonalive® granules effectively inhibit the bacterial growth of up to 50 clinically relevant bacteria including MRSA, MRSE*.

The following image illustrates the impact of S53P4 on Klebsiella pneumoniae.



Gram positive bacteria

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

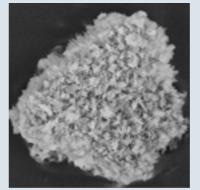
Methicillin-resistant bacteria

- Pseudomonas aeruginosa
- Staphylococcus aureus (MRSA)
- Staphylococcus

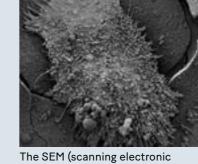
epidermidis (MRSE)

- Gram negative bacteria
- Acinetobacter baumannii
- Bacteroides fragilis
- Bacteroides thetaiotaomicron
- Chryseobacterium (former Flavobacterium) meningosepticum
- Enterobacter aerogenes
- Enterobacter amniaenus
- 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
 - Shiqella sonnei

 - Veillonella parvula
 - Yersinia enterocolitica



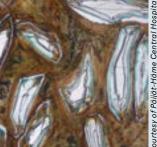
Natural hydroxyapatite layer formed on bioactive glass granule 72 hours after exposure to an aquous solution.



microscopy) image shows the osteoclast activity on the surface of the Bioactive glass.

- * Leppäranta et al. 2008. Antibacterial effect of bioactive glasses on clinically important anaerobic bacteria in vitro. / Munukka et al. 2008. Bactericidal effects of bioactive glasses on clinically important aerobic bacteria. / Drago et al. 2015. Antimicrobial activity and resistance selection of different bioglass S53P4 formulations against multidrug resistant strains. / Drago et al. 2014. In vitro antibiofilm activity of bioactive glass S53P4
- ** Virolainen et al. 1997. Histomorphometric and molecular biologic comparison of bioactive glass granules and autogenous bone grafts in augmentation of bone defect healing.





Histological 20µm-thick section from the mastoid area at 3 months after Bonalive[®] granules implantation (human biopsy).

Visualization of the healing process

Areas of use

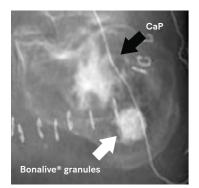
The radio-opaque feature of the Bonalive[®] granules and Bonalive[®] putty enables significant benefits, both for patients and medical professionals.

Bonalive[®] granules and Bonalive[®] putty can be visualized perioperatively and postoperatively, allowing for the post-operative evaluation of the healing process without the need for further surgical intervention.

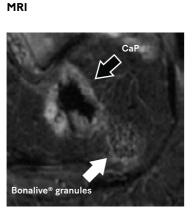
The white arrows indicate the application of Bonalive® granules. For comparison, the dark arrows point to the calsium phosphate (CaP).

Clinical experience has been gained from several extensive studies where pediatric and adult patients with benign bone tumors have been treated. By effectively sustaining the bone cavity volume long term, Bonalive® granules can be used even in the most demanding large cavities.

X-ray

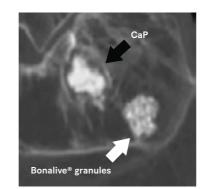


Bonalive® granules 2 months post-op, CaP cement 5 months post-op



Bonalive[®] granules 2 months post-op, CaP cement 5 months post-op





Bonalive® granules 12 months post-op, CaP cement 15 months post-op

Aneurysmal bone cyst (ABC)

Aneurysmal bone cyst (ABC) is a benign reactive and hyperplastic lesion characterized by cystic cavities lined by mesenchymal tissue and filled with flowing blood. ABCs usually appear in the first two decades of life.

Enchondroma

Enchondroma is a type of benign bone tumor that originates from cartilage. The bones most often involved with this benign tumor are upper and lower extremities.

Simple bone cyst (UBC)

Simple bone cyst (unicameral bone cyst) is a primary solitary fluid-filled cystic lesion. They nearly always occur during the first decades of life.

Nonossifying fibroma (NOF)

Nonossifying fibroma consist of collagen rich connective tissue, fibroblasts, histiocytes and osteoclasts. They originate from the growth plate and are located in adjacent parts of the metaphysis and diaphysis of long bones, more often in the lower extremities.

Reference: Lindfors NC. et al. A prospective randomized 14-year follow- up study of bioactive glass and autogenous bone as bone graft substitutes in benign bone tumours. J Biomed Mater Res. 2010;94B(1):157-64.

Bonalive® bioactive glass should not be used in malignant tumor surgery or in patients that have

Pictures: Courtesy of Helsinki University Central Hospital, Finland received or are about to receive chemotherapy or radiation therapy at or near the implant site.

Bonalive®

granules

Pediatric

patient

Aneurysmal bone cyst in the finger



Pre-op

PATIENT

3-year-old child with a recurrent aneurysmal bone cyst of the proximal phalanx of the index finger.

OPERATION

1 month post-op

The bone tumour was removed and the defect was grafted with 2 cc Bonalive[®] granules and two 2-3 mm pieces of autogenous bone.

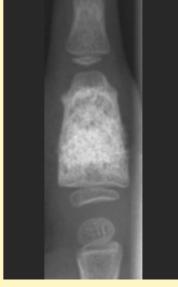


3 months post-op

CLINICAL OUTCOME

At 24 months, no cavity was observed and the homogenous region resembled normal trabecular bone.

The phalanx had grown in length and remodeled to



12 months post-op

almost normal shape. Bonalive® granules does not disturb the normal remodeling process of bone even when implanted in the

close vicinity of the growth plate.



24 months post-op

Courtesy of Helsinki University Hospital, Finland

Large pelvic aneurysmal bone cyst



Pre-op



Bonalive[®] Pediatric granules patient



Immediate post-op

PATIENT

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



9 months post-op

OPERATION

The large bone cyst was evacuated, the defect was fenolized and filled with 60 cc Bonalive® granules.



24 months post-op

CLINICAL OUTCOME

At 24 months post-op the patient had fully healed and was free of any symptoms.

3 months post-op

after 2nd surgery

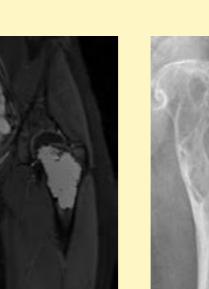
2nd surgery

OPERATION

1st surgery (another hospital)

Fixation was performed with an elastic stable intramedullary nailing (ESIN).

Aneurysmal bone cyst in the proximal femur



Pre-op MRI

Pre-op MRI

Bonalive[®]

granules

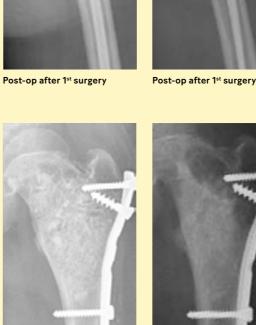
Pediatric

patient



PATIENT

10-year-old girl had pain in the left proximal femur and an aneurysmal bone cyst was encountered. The left thigh had a +0.5 cm (left) rotation error after first operation.



after 2nd surgery

2 years after the 1st surgery a reintervention was

Curettage and careful debridement of the bone

was filled with 60 cc Bonalive® granules mixed

necessary, because the ABC was increasing.

walls was performed. The remaining cavity

with autogenous bone harvested from the

distal femur. The mixing ratio was 80 / 20.







18 months post-op after 3rd surgery

CLINICAL OUTCOME

Two operations were necessary to fill the ABC cavity because of the location and enormous size of the ABC. At 18 months follow-up a full consolidation can be observed without any evidence of recurrence of the ABC. The patient continues to be painless and the bone is stable.

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Courtesy of Cnopfschen Kinderklinik
Germany
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Pre-op

Aneurysmal bone cyst in the distal femur



Pre-op X-ray

Pre-op X-ray

Pre-op MRI



Bonalive® Pediatric granules patient

PATIENT

Pre-op MRI

14-year-old girl injured her leg while jumping. A large bone cyst (ABC/ UBC) was discovered in the distal femur.

The MRI showed an aneurysmal bone cyst, which was confirmed by biopsy.

OPERATION

A cortical window was made on the medial aspect of the femur and the cyst was intralesionally cauterized carefully.

Thereupon removal of the cystic bone tumor was performed at the distal femur medially, including curettage and milling. The cavity was filled







2 years post-op



9 months post-op

2 years post-op

CLINICAL OUTCOME

Knee range of motion is normal and there has been no sign of obvious muscle atrophy. The patient is free of pain.

with autologous corticospongious and cancellous bone chips mixed with Bonalive® granules. Additionally bridging osteosynthesis was performed at the distal/medial femur with an 8-hole semi-tubular plate.

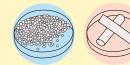
2 months post-op

The plate was removed 9 months post-op.

There was no sign of any fractures at 9 months post-op,

and growth was undisturbed.

Distal femur bone cyst (ABC/UBC)



Bonalive[®] putty patient

PATIENT

Bonalive®

granules

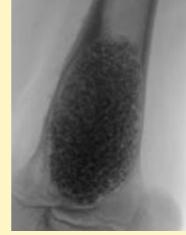
11-year-old girl injured her leg while jumping. Large bone cyst (UBC/ABC) finding in the distal femur during the examination.

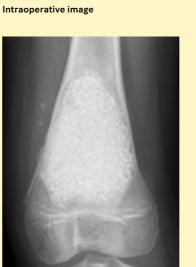


Pre-op



Pre-op





2 months post-op



8 months post-op

8 months post-op

14 months post-op



14 months post-op

OPERATION

A cortical window was made on the medial aspect of the femur and the cyst was intralesionally cauterized carefully. The removal was completed with 75% phenol treatment. The cortical bone around the cyst was very thin.

The cavity was filled with 50 cc Bonalive[®] granules and 5 cc Bonalive[®] putty. The cavity was closed with a cortical bone lid and the periosteum was sutured. Postoperatively, a plaster splint was applied and it was used for one week. Thereafter, a hinged

orthosis with a range of 0-60 degrees was applied for eight weeks. Partial weight bearing (5-10kg) was allowed immediately.

Full weight bearing was allowed at two months and unlimited physical education was started within six months.

CLINICAL OUTCOME

In radiographic follow-up, Bonalive[®] granules and Bonalive[®] putty seemed to work well and the femur was growing normally. The patient is free of pain and the growth is undisturbed. There was no sign of any fractures at 2 months post-op.

A small stress fracture was observed in radiographs on the lateral side at 8 month post-op. The fracture healed without any symptoms.

At 14 months post-op the patient was allowed to return to doing sports. The distal end of the femur has grown 12 mm since the operation. The cortical bone has increased around the cavity. In clinical examination the range of knee movement was full with no obvious muscle atrophy.

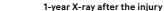
Courtesy of Helsinki University Hospital, Finland

20

Simple bone cyst in the proximal humerus

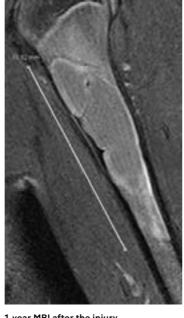






PATIENT

right proximal humerus.



1-year MRI after the injury



Post-op after Bonalive® implantation



1.5 years post-op



4 years post-op

Bonalive[®] Pediatric granules patient

9-year-old boy. A simple bone cyst with a pathological fracture of the

The fracture healed under conservative treatment but X-rays and MRI showed an expanding residual lesion one year later.

OPERATION

The recurrent simple bone cyst was opened through a 12 x 6 mm cortical window, the cyst membrane and fluid were evacuated, and the space was filled with Bonalive[®] granules.

CLINICAL OUTCOME

The specimen for pathology confirmed the diagnosis. The lesion healed uneventfully.

Aneurysmal bone cyst in the humerus

Chondroblastoma in the humerus







PATIENT

10-year-old boy with a proximal humerus ABC. Two pathological fractures. The first one had healed conservatively.

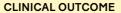


Bonalive[®] Pediatric

granules patient

OPERATION

After the second fracture a large bone cyst was evacuated with a high-speed drill. The defect was filled with Bonalive® granules.



24 months post-op

At 1-year post-op the patient had fully healed and was free of any symptoms. At 2 years the Bonalive[®] granules have continued to remodel into bone.

Courtesy of Turku University Hospital, Finland



PATIENT

18-year-old male with chondroblastoma of the right proximal humerus.



Bonalive® Adult putty patient



OPERATION

The tumor was evacuated by curettage and the cavity was filled with 7 cc Bonalive® putty.

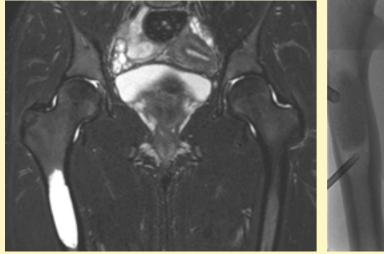
CLINICAL OUTCOME

At 9 months post-op the patient was free of symptoms, and had full range of motion in shoulder. The progress of the osteointegration is proceeding well.

Courtesy of Rambam Medical Center, Israel



Symptomatic simplex cyst of the femur



Pre-op MRI

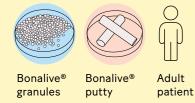


Intra operative X-ray





6 months post-op



PATIENT

18-year-old female and professional athlete. She experienced pain in the right femur.

MRI shows a big cyst on the proximal diaphysis of the of the femur.

OPERATION

The defect was subjected to careful mechanical cleaning followed by lavage with saline solution. No denaturation agents were used.

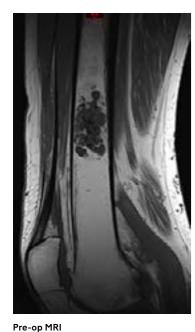
Percutaneous radiological filling was carried out with 20 cc Bonalive® granules using a 6 mm metal cannula to channel the granules into the defect. The cortical window was closed with 2.5 cc Bonalive® putty using a 4 mm metal cannula.

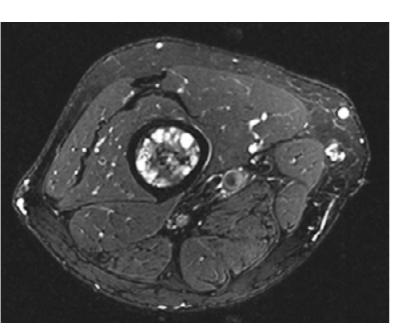
CLINICAL OUTCOME

In the two months control the patient was pain free and permitted to resume athletics.

At the six months control the patient was pain free and able to participate in sports at a competitive level.

Enchondroma in the distal femur





Pre-op MRI





2.5 years post-op



2.5 years post-op



patient

granules

PATIENT

64-year-old female with a symptomatic intramedullary cartilage tumor of the distal femur.

A CT-guided biopsy confirmed the diagnosis of benign enchondroma with a maximum length of 5.5 cm (MRI images).

OPERATION

CLINICAL OUTCOME

The bone healed uneventfully.

evacuated through a 3 cm cortical bone window and the space was filled with Bonalive® granules.

The site was stabilized with a 6 screw plate.

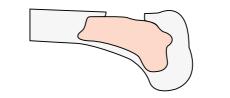
The lesion was exposed using a

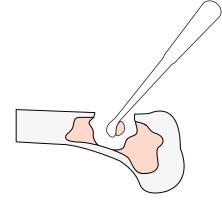
lateral approach. The tumor was



One-stage surgical technique

The majority of the operations have been performed in a one-stage, even in large benign bone tumor surgeries.





Surgical technique

Pediatric patients require special attention and surgery in a growing skeleton can be challenging. Bone replacement strategies differ between children and adults as allograft and autograft from the iliac crest are not always the preferred option for children.

Our Smart Healing[™] solutions enable one-stage surgery even in cases with significant bone defects. This enables a faster recovery time, fewer surgeries and a higher quality of life for the patient.

1. Access is opened to the cyst cavity avoiding disturbance of epiphyseal blood supply.

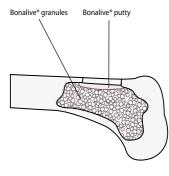
3. The cavity is either filled with Bonalive[®] granules or with Bonalive[®] putty, depending on the defect size.

Cyst volume can be measured by injecting saline into the defect until it is completely filled (ml/cc).

If the cyst is larger than 20 cc, the defect is filled with Bonalive® granules. In case of smaller defects Bonalive® putty can be used.

2. The tumor is carefully evacuated by curettage, and the inner wall of the bone is refreshed.

A mechanical curettage with the use of a curette and high-speed drilling is used to inspect the whole cavity. The tumor is resected as thoroughly as possible. After curettage an adjuvant treatment may be performed depending on the tumor type and the local clinical practice.



4. Closure with sufficient soft tissue.

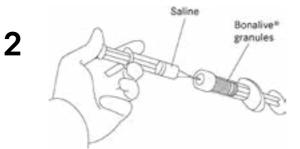
The filled cavity requires sufficient soft tissue coverage.

Granules can also be covered with Bonalive® putty or cortical bone lid or both. Bone stabilization is considered when needed.

Bonalive® granules



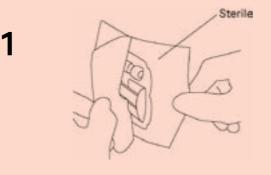
- Peel open the pouch (start from the corners) and aseptically remove the sterile tray.
 Detach the applicator from the tray.
- Detach the applicator from the tray.
 Note that the pouch provides a sterile barrier for the device.



Moisten the granules by injecting sterile physiological saline slowly through the cap membrane.
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: saline injection can cause an increase in pressure inside the applicator unless the excess

pressure is released, e.g. with an injection needle.

Bonalive® putty



• Peel open the pouch and aseptically remove the sterile tray. Detach the applicator from the tray.



 Unscrew the cap. Screw tightly the nozzle onto the applicator body. 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.

3

- In order to prevent the spillage of the moistened granules from the applicator, keep the cap facing upwards.
 Unscrew the cap (remove the stopper) and screw
- Unscrew the cap (remove the stopper) and scree the shovel tightly 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.
- 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.

- Push the plunger rod to force the putty into the nozzle.
- Move the applicator to the defect site.

3

• Push the plunger rod to gently fill the defect with the putty.

Supporting services

A prospective randomized

14-year follow- up study

bone graft substitutes in

Treatment of a recurrent

aneurysmal bone cyst

with bioactive glass in a

remodeling and growth.

2009;45:398-400.

Lindfors NC, Aho A. Bone.

child allows for good bone

of bioactive glass and

benign bone tumours.

Lindfors NC. Aho A.

J Biomed Mater Res.

2010;94B(1):157-64.

autogenous bone as

References

An overview of our most significant references. Our reference list is continuously updated. As new studies emerge regularly, the upto-date reference list can be accessed by request.



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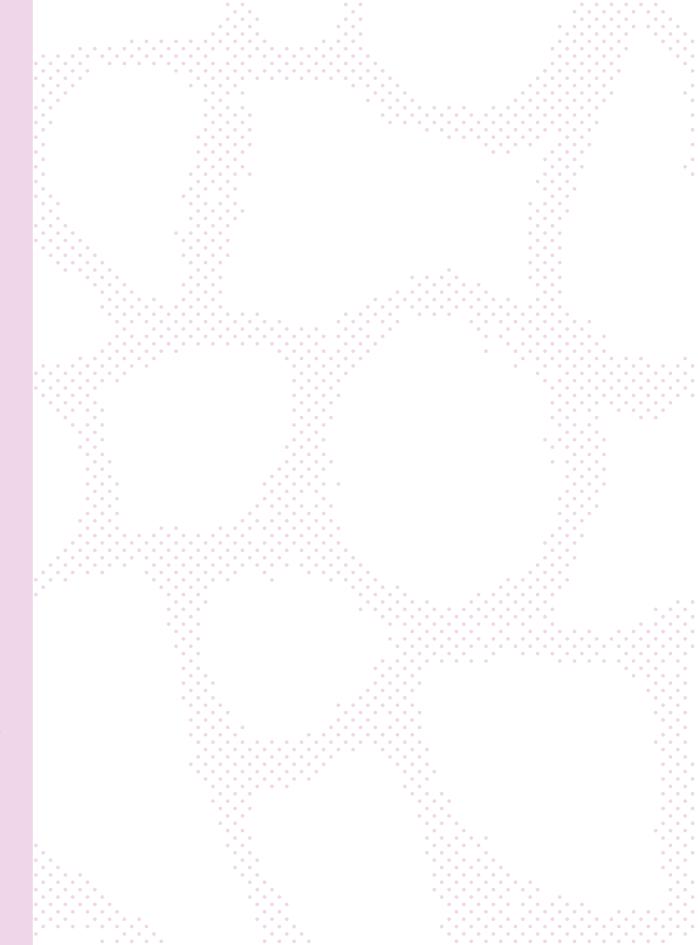
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