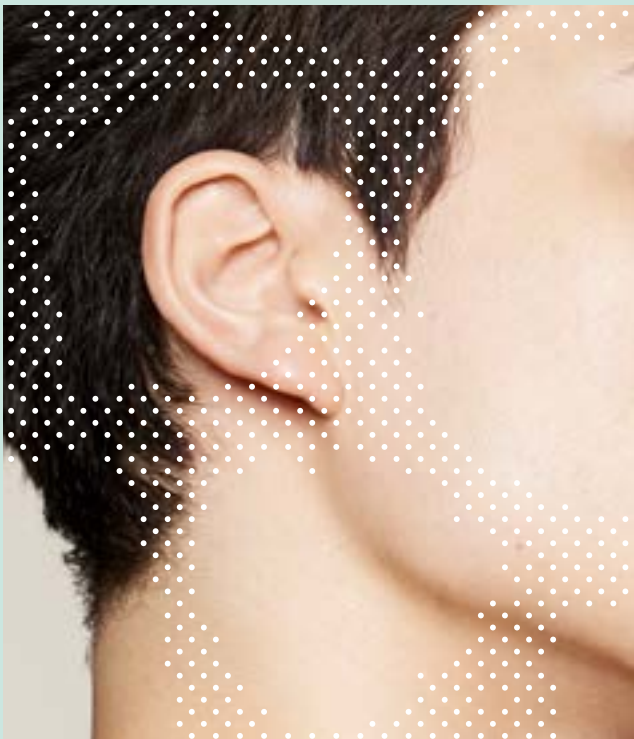


Mastoid Surgery



We are proud to deliver Smart Healing™ solutions for patients in need of mastoid reconstruction surgery. In this brochure we provide an overview on how to use Bonalive® granules for mastoid surgery.

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Through Smart Healing™ solutions we sustainably improve the anatomical and functional healing of mastoidectomy patients – restoring and sustaining their quality of life.

Smart Healing™

Antimicrobial resistance (AMR) is one of the greatest challenges facing healthcare today. In the face of growing resistance, we need solutions to an increasingly complex global problem. Solutions, that are smarter and more sustainable for patients worldwide.

Coming to life at the intersection of biology and technology, Smart Healing™ represents a new standard. A new era for patient care.

As Smart Healing™ enables increasingly antibiotic-free patient care, we provide the world with biomaterial technologies that restore body function through the patient's own biological processes.

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.



Inhibit bacterial growth with Bonalive® granules

Bonalive® granules is a smarter and more sustainable solution for medical professionals performing mastoid surgery.

The reconstruction of chronically infected and discharging mastoid cavities is made more effective by using the healing capabilities of Bonalive® granules. This allows new tissue to regenerate over a period of years, ensuring the patient's body is given enough time to facilitate regeneration.

The most notable feature of the granules is their ability to naturally inhibit bacterial growth, significantly decreasing the need to use antibiotics.

The clinical efficacy and performance of the granules has been proven over the past 20 years in orthopedic, trauma, septic surgery and mastoid surgery. Bonalive® granules is verified as safe for use in pediatric surgery and consists only of elements that are naturally present in the human body.

By supporting the reconstruction of anatomical structures in the human body, the biodegradable S53P4 bioactive glass is gradually resorbed and replaced by natural tissue over a period of years. Bonalive® granules radio-dense quality enables post-operative evaluation, allowing surgeons to monitor the healing of their patients.

INDICATIONS

- Mastoid cavity obliteration
- Bone cavity filling in cranio-maxillofacial area including the jaw
- Frontal sinus obliteration after severe chronic sinusitis or fractures in the frontal bone area

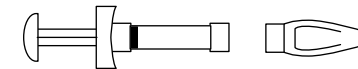
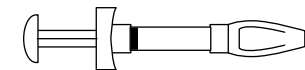
PROPERTIES

- Inhibition of bacterial growth
- Osteoconductive
- Osteostimulative*

COMPOSITION

- 53% SiO₂
- 23% Na₂O
- 20% CaO
- 4% P₂O₅

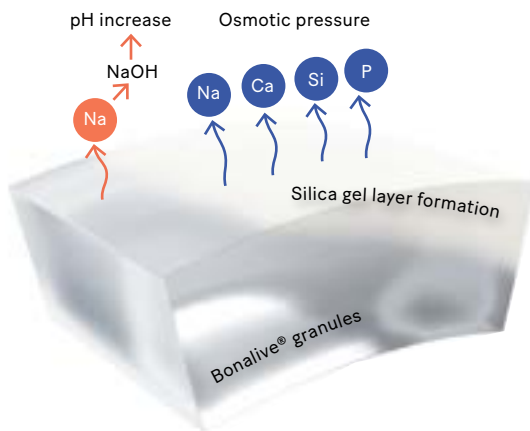
Unit size	Granule size	Ref. no.
2.5 cc prefilled applicator	0.5-0.8 mm	13120
5 cc prefilled applicator	0.5-0.8 mm	13130



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.

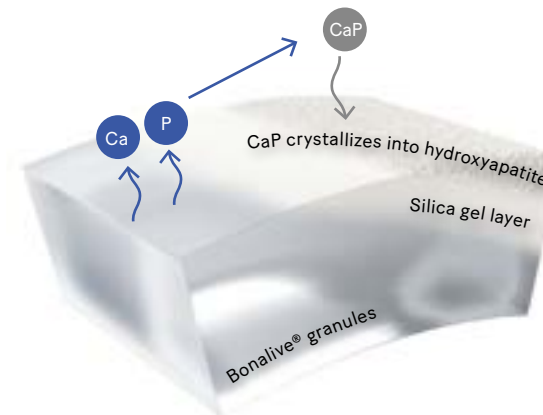


Mechanism of actions

1. Sodium (Na) is released from the surface of the bioactive glass and induces an **increase in pH** (alkaline environment), which is not favourable 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 salt concentration, i.e. an environment where bacteria cannot grow.

Bone regeneration and remodelling

Bonalive® S53P4 bioactive glass is osteoconductive and also osteoproduative in the promotion, migration, replication and differentiation of osteogenic cells and their matrix production.**



The release of ions and surface reactions developed 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*.



Courtesy of University of Milan, Italy

Gram positive bacteria

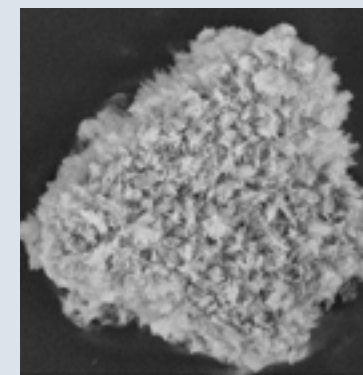
- *Bacillus cereus*
- *Bifidobacterium adolescentis*
- *Clostridium difficile*
- *Clostridium perfringens*
- *Clostridium septicum*
- *Corynebacterium ulcerans*
- *Enterococcus faecalis*
- *Enterococcus faecium*
- *Eubacterium lentum*
- *Listeria monocytogenes*
- *Micrococcus sp.*
- *Peptostreptococcus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

Methicillin-resistant bacteria

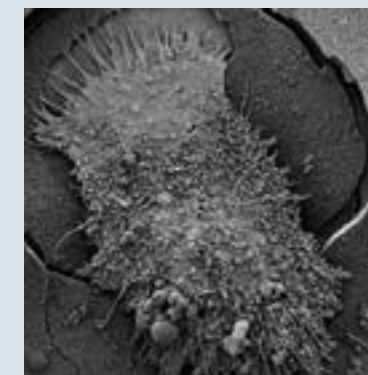
- *Pseudomonas aeruginosa*
- *Staphylococcus aureus* (MRSA)
- *Staphylococcus epidermidis* (MRSE)

Gram negative bacteria

- *Acinetobacter baumannii*
- *Bacteroides fragilis*
- *Bacteroides thetaiotaomicron*
- *Chryseobacterium 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*

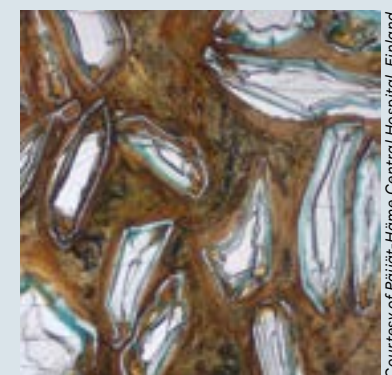


Natural hydroxyapatite layer formed on bioactive glass granule 72 hours after exposure to an aqueous solution.



The SEM (scanning electronic microscopy) image shows the osteoclast activity on the surface of the Bioactive glass.

Courtesy of Maastricht UMC+, The Netherlands



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

Courtesy of Päijät-Häme Central Hospital, Finland

* Leppäranta et al. 2008; Munukka et al. 2008. Drago et al. 2014, Drago et al. 2015.

** Virolainen et al. 1997

Visualization of the healing process

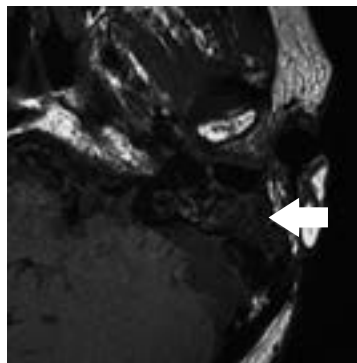
The radio-opaque feature of the Bonalive® granules enables significant benefits, both for patients and medical professionals.

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

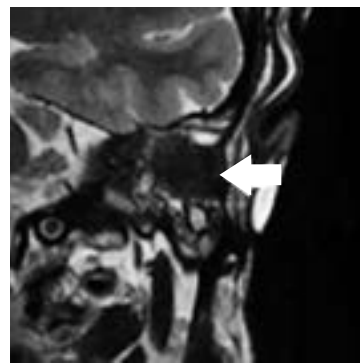
The following imaging was produced after mastoid obliteration. Residual cholesteatoma, for example, can easily be detected in all CT scans and MRI sequences since the appearance of the granules is completely different from cholesteatoma. The white arrows point to where Bonalive® granules have been applied.



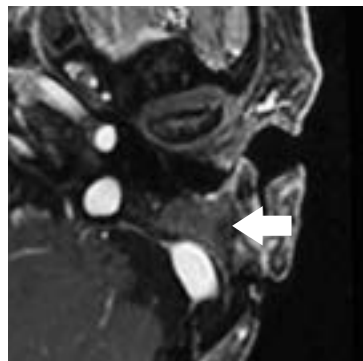
CT-scan



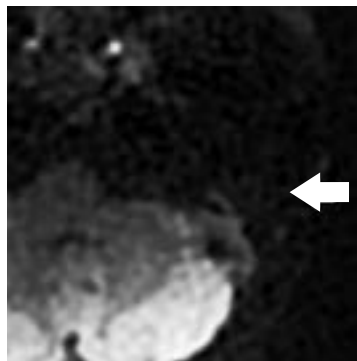
T1-WI



T2-WI



Post-contrast T1-WI



1-year post-op non-EPI-DW MRI

Reference: Bernardeschi D. et al. Bioactive glass granules for mastoid and epitympanic surgical obliteration: CT and MRI appearance. *Eur Radiol.* 2019 Mar 19. doi: 10.1007/s00330-019-06120-z.

Areas of use

Several long-term studies have shown that mastoid cavities that suffer from continuous infections and cleaning problems can be obliterated with Bonalive® granules. With more than 15 years, in both adult and pediatric patients, Bonalive® granules has achieved success in mastoid reconstruction surgery.

Cholesteatoma

Creating a safe and dry ear is of importance in the surgical management of cholesteatoma. There are two surgical techniques associated with cholesteatoma surgery, Canal Wall Down (CWD) and Canal Wall Up (CWU). Recurrence rate of 5–17% for CWD compared to 9–70% for CWU has been demonstrated. By using mastoid obliteration to combine the advantages of both surgical treatments, patients have less cholesteatoma recidivism and less problems associated with their changed middle ear anatomy.

Reference: de Veij mestdagh P. et al. Mastoid obliteration with S53P4 bioactive glass in cholesteatoma surgery. *Acta Oto-Laryngologica* 2017;137(7):690-94.

Old radical cavities

The disadvantages of radical cavities are associated with the need for frequent cleaning of the cavity due to debris accumulation or infections, vertigo, imbalance and difficulties in using hearing aids. Revision surgery can be performed to decrease or eliminate the mastoid cavity with the aim of eradicating the infection and rebuilding a new external auditory canal as an alternative.

Reference: Bernardeschi D. et al. Anatomical, functional and quality-of-life results for mastoid and epitympanic obliteration with bioactive glass S53P4: a prospective clinical study. *Clin Otolaryngol.* 2017;42(2):387-96.

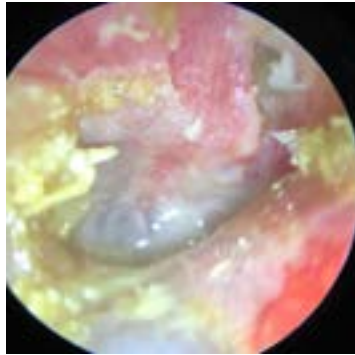
Chronic otitis media

The treatment of chronic middle ear infection (chronic otitis media) includes surgery after failing of conservative therapy. The obliteration of the mastoid cavity using Bonalive® granules significantly improves the achievement of a dry and safe ear when compared to the use of mastoidectomy on its own.

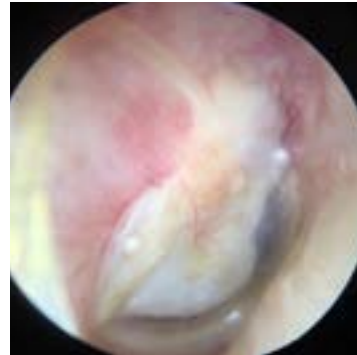
Reference: Vos J et al. Bioactive glass obliteration of the mastoid significantly improves surgical outcome in non-cholesteatomatous chronic otitis media patients. *Eur Arch Otorhino-laryngol* 2017; 274(12):4121-26.

Cholesteatoma

Canal wall up mastoidectomy in adult patient.

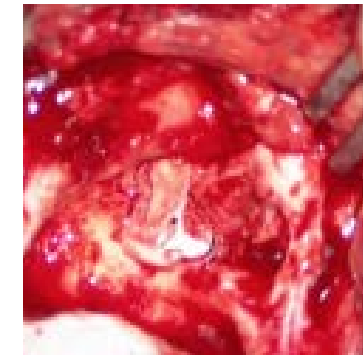


Pre-op

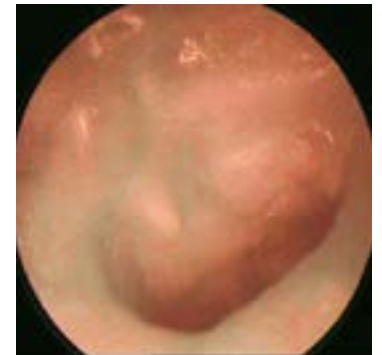


7 months post-op

Canal wall down mastoidectomy in pediatric patient.



Intraoperative



7 months post-op

PATIENT BACKGROUND

A 44-year old female with otorrhea evolving for 1.5 years in the right ear. Clinical examination showed an attic retraction pocket with profuse otorrhea. CT and MRI supported extensive cholesteatoma.

Bacterial culture: *Staphylococcus aureus*

OPERATION

Type 2 Tympanoplasty with transcanal atticotomy and canal wall up mastoidectomy.

The operation started with an endoscopic transcanal approach. After the atticotomy, the control of the posterior extension of the cholesteatoma was not possible by means of the endoscopic approach alone; a canal wall up mastoidectomy with retro auricular incision was performed to control the mastoid extension of the cholesteatoma. The eptympanic and mastoid spaces were obliterated with Bonalive® granules.

OUTCOME

The external ear canal (meatus) was treated with ear drops for 2 weeks. Otoscopy at 7 months showed a well-healed tympanic drum and attical reconstruction. The patient was satisfied with the outcome and the increased quality of life including the possibility to participate in watersports.

Courtesy of Dr. Bernardeschi and Prof. Sterkers Pitié-Salpêtrière Hospital, France

PATIENT BACKGROUND

A 12-year-old girl who was operated on for a recurrent cholesteatoma of the right ear. The patient had undergone a primary surgery for cholesteatoma 3 years earlier. The recurrent cholesteatoma was located in the tympanic sinus and epitympanic space and on the facial nerve.

OPERATION

Canal wall down mastoidectomy with the removal of the malleus and incus. The reconstruction of the ossicular chain with passive middle ear prosthesis and the reconstruction of the ear drum with cartilage. The posterior canal wall was reconstructed with cartilage and the mastoid and epitympanum was obliterated with Bonalive® granules.

OUTCOME

Postoperative healing was achieved without complications and a dry ear was obtained after four weeks. After healing of the reconstructed posterior wall and ear drum was good and the ear was dry.

Courtesy of Diaconessenhuis Hospital Utrecht, the Netherlands

Old radical cavity



Pre-op



5 months post-op



14 months post-op

Chronic ear with effusion and caloric stimulus in adult patient.

PATIENT BACKGROUND

A 46-year-old male with a radical cavity in the left ear. The patient was operated on two years previously, which resulted in a chronic ear with recurrent effusion, incomplete cleaning and caloric stimulus.

OPERATION

A massive cholesteatoma epithelium was removed from the terminal cell. The dura middle fossa cranii was visible. The mastoid and middle ear area was thoroughly cleaned of scar tissue.

A partial prosthesis was implanted with a thin plate of cartilage underneath the tympanic membrane. The visible dura was covered with perichondrium. The obliteration of the mastoid was performed with 5 cc Bonalive® granules, covered by pieces of cartilage. The attic was filled with cartilage. No postoperative treatment with antibiotics was given.

OUTCOME

At five months postoperatively, the skin of the external ear canal (meatus) was slightly reddish and swollen. At 14 months the meatus had healed well presenting a normal anatomy. At a 3.5-year check-up the patient was fully healed and presented a normal ear.

Courtesy of Dr. Goesta Schimanski
Zentrums für Mittelohrchirurgie in Lünen,
Germany

The unique bacterial growth inhibiting feature and slow resorption profile of Bonalive® granules give distinct advantages when used in both the primary and revision surgery of canal wall down and canal wall up procedures.

Techniques

Canal Wall Down (CWD) technique without obliteration

PROS

- Lower residual and recurrence rate of Cholesteatoma.

CONS

- Higher morbidity
- Need for frequent clinic visits due to the cleaning of the radical cavity.
- The risk of infection and water intolerance.
- Difficulties with wearing a hearing aid.

The advantage of obliteration for CWD patients is that it restores the normal anatomy and relieves most of the above-mentioned negative quality of life effects.

Canal Wall Up (CWU) technique without obliteration

PROS

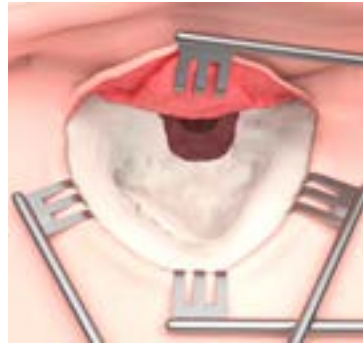
- Better functionality for the patient.
- Fewer changes of the middle ear anatomy

CONS

- Higher residual and recurrence rate of Cholesteatoma compared to CWD.

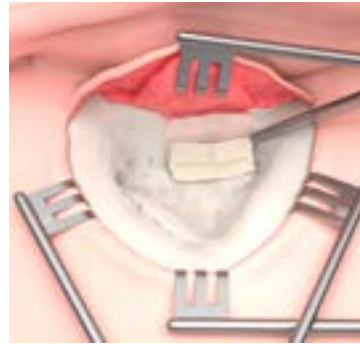
Obliteration for a CWU patient reduces the chances of a recurrence of the cholesteatoma.

Obliteration technique for the Canal Wall Down procedure



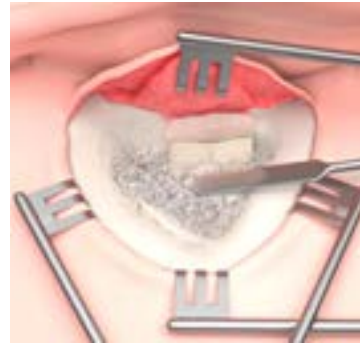
STEP 1

Retroauricular incision 1 cm from the ear base. All ridges are removed and the cavity is cleaned with a diamond burr.



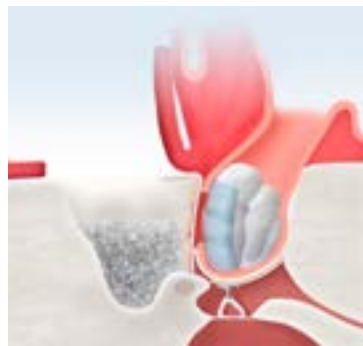
STEP 2

Pieces of cartilage are placed in the bottom of the cavity to reconstruct the new ear canal wall. Cartilage will also prevent Bonalive® granules from migrating into the ear canal. A layer of fascia can be placed between the ear canal and the cartilage to provide additional support for the new canal wall.



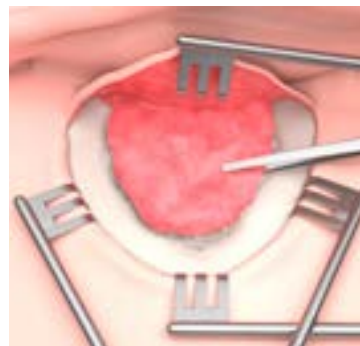
STEP 3

The cavity is partially obliterated with moistened Bonalive® granules during this stage. The external auditory canal is shaped and tamponed before the mastoid is filled completely.



STEP 4

The posterior ear canal wall is shaped from the external ear canal according to the desired anatomy. Silicon sheets are inserted along the external ear canal and the tampons are placed to give support to the ear canal wall.



STEP 5

The mastoid is filled with moistened Bonalive® granules to the level of the cortical bone. If suitable cartilage pieces are available, they can be placed on top of the granules. The musculoperiosteal flap will be placed to cover the granules and the incision is sutured.



STEP 6

According to clinical experiences, edematous swelling can be reduced and excess fluid can be evacuated by applying a vacuum drain into the area that has been obliterated with Bonalive® granules. The drain can be removed within a few days postoperatively; the vacuum is maintained for 8-12 hours.

Canal Wall Down patient case

Canal Wall Down (CWD) procedure with obliteration of a mastoid in order to sustainably improve patient quality of life.



Pre-op



1-year post-op

PATIENT BACKGROUND

A 79-year-old female, who had suffered chronic otitis in her right ear since childhood. The epitympanic cholesteatoma in her right ear extended into a very sclerotic mastoid with low middle cranial fossa.

PROCEDURE

Primary canal wall down tympano mastoidectomy was performed on the right ear of the patient. The epitympanic and mastoid was obliterated with Bonalive® granules. There were no postoperative complications.

OUTCOME

An otoscopy after one year showed a healthy, healed tympanic drum and an external auditory canal wall with no sign of recurring cholesteatoma.

Courtesy of Dr. Bernardeschi and Prof. Sterkers Pitié-Salpêtrière Hospital, France

Obliteration technique for the Canal Wall Up procedure



STEP 1

Retroauricular incision 1 cm from the ear base. Careful removal of the infected mastoid air cells and pathology. Important to identify the facial nerve to avoid injury. The back wall of the ear canal is left in place separating the ear canal from the hollowed out mastoid bone.



STEP 2

Access and better overview to the mesotympanum can be done by removing the bone of the canal wall within the facial recess. The entire attic space (anterior and posterior) is obliterated with moistened Bonalive® granules. Cartilage is used to cover the granules towards the external auditory canal.



STEP 3

Then the mastoid cavity is then obliterated with the moistened Bonalive® granules and filled up to the level of the cortical bone. If suitable cartilage pieces are available, they can be placed on top of the granules. The musculoperiosteal flap will be placed to cover the granules and the incision is sutured.

According to clinical experiences, edematous swelling can be reduced, and excess fluid can be evacuated by applying a vacume drain into the area that has been obliterated with Bonalive® granules. The drain can be removed within a few days postoperatively, when the vacuum maintains for 8–12 hours.

Pictures: Courtesy of Dr. Bernardeschi and Prof. Sterkers Pitié-Salpêtrière Hospital, France

Canal Wall Up patient case

Canal Wall Up (CWU) procedure with obliteration of the mastoid to accomplish less residual and recurrent disease and the preservation of good hearing.



Pre-op



1-year post-op

PATIENT BACKGROUND

A 25-year-old male with chronic otitis since childhood. Right epitympanic cholesteatoma extending to a well-pneumatized mastoid.

PROCEDURE

Canal Wall Up (CWU) tympanomastoidectomy was performed on the right ear of the patient. The epitympanic and mastoid was obliterated with Bonalive® granules. No post-operative complications.

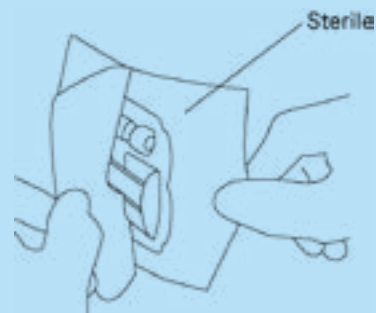
OUTCOME

Otoscopy at two years shows a well-healed tympanic drum and attical reconstruction. There was no sign of a recurring cholesteatoma.

Courtesy of Dr. Bernardeschi and Prof. Sterkers Pitié-Salpêtrière Hospital, France

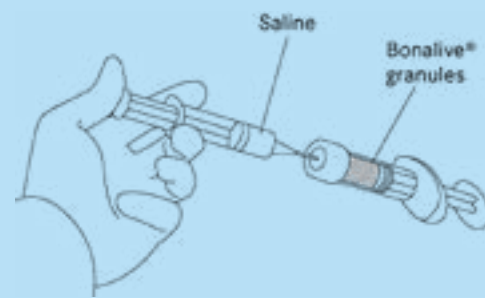
Handling the applicator

1



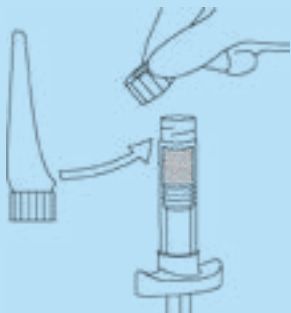
- Peel open the pouch (start from the corners) and aseptically remove the sterile tray.
- Detach the applicator from the tray.
- Note that the pouch provides a sterile barrier for the device.

2



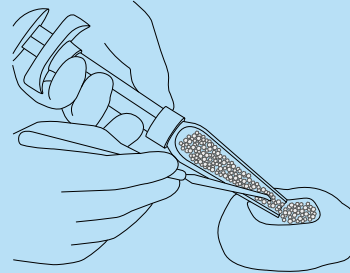
- Moisten the granules by injecting sterile physiological saline slowly through the cap membrane.
- Make sure the granules are evenly moistened. The applicator can be turned upside down or tapped to allow the saline to moisten all granules.
- Note: saline injection can cause an increase in pressure inside the applicator unless the excess pressure is released, e.g. with an injection needle.

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 the shovel tightly onto the applicator body.

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.
- 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.

References

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

IN VITRO

Bioactive glass granules inhibit mature bacterial biofilms on the surfaces of cochlear implants.

Höing B, Kirchoff L, Arnolds J, Hussain T, Buer J, Lang S, et al. *Otology & Neurotology*. 2018;Oct 16. [Epub ahead of print]

Antimicrobial activity and resistance selection of different bioglass S53P4 formulations against multidrug resistant strains.

Drago L, De Vecchi E, Bortolin M, Toscano M, Mattina R and Romano CL. *Future Microbiol*. 2015;10(8):1293-9.

In vitro antibiofilm activity of bioactive glass S53P4.

Drago L, Vassena C, Fenu S, De Vecchi E, Signori V, De Francesco R, Romano CL. *Future Microbiol*. 2014;9(5):593-601.

Bactericidal effects of bioactive glasses on clinically important aerobic bacteria.

Munukka E, Leppäranta O, Korkeamäki M, Vaahtio M, Peltola T, Zhang D. et al. *J Mater Sci: Mater Med*. 2008;19:27-32.

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

Leppäranta O, Vaahtio M, Peltola T, Zhang D, Hupa L, Ylänen H, et al. *J Mater Sci: Mater Med*. 2008;19:547-51.

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

Virolainen P, Heikkilä J, Yli-Urpo A, Vuorio E, Aro HT. *J Biomed Mater Res*. 1997;35A(1):9-17.

CLINICAL

Bioactive glass granules for mastoid and epitympanic surgical obliteration: CT and MRI appearance.

Bernardeschi D, Law-ye B, Bielle F, Hochet B, Sterkers O, Dormont D, Pyatigorskaya N. *Eur Radiol*. 2019 Mar 19. doi: 10.1007/s00330-019-06120-z.

Mastoid obliteration with S53P4 bioactive glass in cholesteatoma surgery.

de Veij mestdagh P, Colnot D, Borggreven P, Orelio C, Quak J. *Acta Oto-Laryngologica* 2017;137(7):690-4.

Anatomical, functional and quality-of-life results for mastoid and epitympanic obliteration with bioactive glass S53P4: a prospective clinical study.

Bernardeschi D, Pyatigorskaya N, Russo FY, De Seta D, Corallo G, Ferrary E, Nguyen Y, Sterkers O. *Clin Otolaryngol*. 2017;42(2):387-96.

Bioactive glass obliteration of the mastoid significantly improves surgical outcome in non-cholesteatomatous chronic otitis media patients.

Vos J, de Vey Mestdagh P, Colnot D, Borggreven P, Orelio C, Quak J. *Eur Arch Otorhinolaryngol* 2017; 274(12):4121-6.

Mastoid cavity obliteration with bioactive glass granules.

Schimanski G, Schimanski E. In: Lalwani A, Pfister M. *Recent Advances in Otolaryngology – Head and Neck Surgery*. Lalwani A, Pfister M. 2016;5:249-81.

Cutaneous and labyrinthine tolerance of bioactive glass S53P4 in mastoid and epitympanic obliteration surgery: prospective clinical study.

Bernardeschi D, Nguyen Y, Mosnier I, Smail M, Sterkers O. *BioMed Research International*. 2015:1-6.

Obliteration von Mastoidhöhlen. 30 Jahre Erfahrung mit Empfehlungen zur Operationsstrategie.

Schimanski G, Schimanski E. *HNO* 2015;63(8):538-45.

Bioactive glass S53P4 in mastoid obliteration surgery for chronic otitis media and cerebrospinal fluid leakage.

Sarin J, Grénman R, Aitasalo K, Pulkkinen J. *Annals of Otolaryngology, Rhinology & Laryngology*. 2012;121:563-9.

Mastoidectomy cavity obliteration with bioactive glass: a pilot study.

Silvola JT. *Otolaryngol Head Neck Surg*. 2012;147(1):119-26.

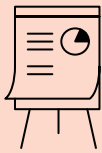
Bioactive glass S53P4 in the filling of cavities in the mastoid cell area in surgery for chronic otitis media.

Stoor P, Pulkkinen J, Grénman R. *Annals of Otolaryngology, Rhinology & Laryngology*. 2010;119(6):377-82.

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