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HEAD AND NECK

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

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Abstract

Purpose To evaluate the appearance of mastoid and epitympanic obliteration using S53P4 bioactive glass (BG) granules in high-resolution computed tomography (HRCT) and MRI.

Materials and methods Patients undergoing mastoid and epitympanic obliteration between May 2013 and December 2015 were prospectively included in an uncontrolled clinical study. All patients underwent a temporal HRCT scan 1 year after surgery, aimed at evaluating the attenuation, homogeneity, and osseointegration of the BG granules, as well as the ventilation of the middle ear and the volume of the obliterated paratympanic spaces. If a cholesteatoma was found during surgery, additional MRI, including at least pre- and post-contrast T1-weighted, T2-weighted, and axial non-echo-planar diffusion-weighted (DW) sequences, was performed 1 year after surgery, to study the normal signal of the BG granules and the presence of residual cholesteatoma and/or other temporal bone pathologies.

Results Seventy cases were included. On 1-year HRCT, the mean attenuation of the BG granules was 888.34 ± 166.10 HU. The obliteration was found to be mostly homogeneous with partial osseointegration. The appearance of the BG granules having a low-intensity signal in T2-weighted imaging and DW MRI was always different from the appearance of cholesteatoma. A longer follow-up has shown no attenuation or signal modification of the BG granules compared with the 1-year imaging.

Conclusion Radiological follow-up of patients operated on with mastoid and epitympanic obliteration using BG granules is effective using both HRCT and MRI. A cholesteatoma and/or other potential complications could easily be detected due to the specific radiological appearance of the BG granules.

Key Points

- *The appearance of mastoid and epitympanic obliteration by S53P4 bioactive glass (BG) granules on high-resolution computed tomography (HRCT) scans was homogeneous with an attenuation significantly higher than the attenuation of cholesteatoma and lower than mastoid bone attenuation.*
- *The granules have a low-intensity signal on non-echo-planar diffusion-weighted sequences and on T2-weighted images and present contrast enhancement allowing the differential diagnosis with cholesteatoma and effective for the detection of other underlying temporal bone pathologies.*
- *The volume and radiological appearance of the obliteration appear to be stable with time.*

Keywords Cholesteatoma · Middle ear · Mastoidectomy · Osseointegration

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Abbreviations

BG Bioactive glass
CWD Canal-wall-down
CWU Canal-wall-up
HRCT High-resolution computed tomography

Introduction

Cholesteatoma is the destructive and expanding growth of skin in the middle ear and/or mastoid commonly defined as "skin in the wrong place" [1]. Whether congenital or acquired, surgery is the sole therapeutic option for the management of middle ear cholesteatoma. Over the years, the otological debate has focused on the advantages/disadvantages of leaving or removing the posterior and superior canal walls of the external auditory canal, thus performing a canal-wall-up (CWU) or a canal-wall-down (CWD) tympanomastoidectomy.

Following the tympanomastoidectomy, obliteration of the paratympanic spaces has been described since the beginning of the twentieth century [2], and numerous materials have been used in mastoid and epitympanic obliteration including autologous materials such as muscular flap [3], bone [4], bone pâté [5], cartilage [6], fat [7], or biocompatible materials such as hydroxyapatite granules [8], hydroxyapatite cement [9], or biphasic ceramic granules [10, 11].

S53P4 bioactive glass (BG) is a bone-substitute material that allows restoration of bone stock by resorption and further apposition of new bone from differentiated tissue. It is a mixture of oxides (53% SiO_2, 23% Na_2O, 20% CaO, and 4% P_2O_5), and in its preparation for mastoid obliteration, it is composed of granules of 0.5/0.8 mm in size. BG has an attractive antibacterial action against germs in the chronically infected ear, as it locally increases the osmotic pressure and pH [12]. It has been widely used in orthopedic and craniofacial procedures [13].

In cholesteatoma surgery, very few clinical articles have been published [14–19], and none have studied the radiological appearance of BG in obliterated mastoid. Indeed, the major drawback of performing obliteration is the risk of leaving skin remnants inside or under the obliteration, undetectable on clinical examination; thus, imaging follow-up by high-resolution computed tomography (HRCT) and magnetic resonance imaging (MRI) is required. Currently, MRI with non-echo-planar (non-EP) diffusion-weighted (DW) sequences has become the gold standard for detecting residual cholesteatoma, dispensing with the need for "second-look" surgery [20, 21]. No previous studies have evaluated the radiological aspects of obliteration with BG.

The aims of this study were to analyze the appearance of BG granules using HRCT and MRI 1 year after surgery, to assess the degree and kinetics of osseointegration of the BG granules as well as the imaging and clinical outcomes in patients, and to determine the normal and pathological imaging aspects of this material.

Materials and methods

Patients

This article was prepared following the STROBE guidelines for reporting observational studies [22]. This prospective study was authorized by the ethics committee and the local institutional review board (CPP Île-de-France VI). All patients provided written informed consent for the use of their clinical data. The inclusion criterion was all cases of tympanomastoidectomy with mastoid and epitympanic obliteration using BG granules in a tertiary referral center performed between May 2013 and December 2015 by two experienced surgeons using the same surgical technique [18].

Imaging follow-up procedure

All cases ($n = 70$) underwent HRCT 1 year after surgery. In addition, patients in whom a cholesteatoma was found during surgery ($n = 45$) underwent an MRI study 1 year after surgery.

HRCT acquisition

Temporal bone CT acquisition was performed using a Discovery 750HD CT scanner (GE Healthcare) using the following parameters: 120 kVp tube voltage, 80–220 mA auto modulation of tube current, 0.5 s tube rotation time, 0.625 mm slice thickness, with secondary high-resolution reconstruction resulting in an in-plane resolution of 0.2 × 0.2 × 0.2 mm.

MRI acquisition

The MRI studies were performed with a 3-T MR (HDxT, GE Healthcare) whole-body scanner with an eight-channel head coil. The MRI acquisition centered on the temporal bone and composed axial T1-weighted (T1-w) spin echo imaging (TR 381 ms, NEX 3, receiver bandwidth 15.63 kHz, FOV 20 cm, slice thickness 1.5 mm), high-resolution 3D T2-weighted (T2-w) imaging (flip angle (FA) 60°, NEX 1, receiver bandwidth 83.33 kHz, FOV 22 cm, slice thickness 0.4 mm), axial non-EP DW imaging (TR/TE/FA 75/6 ms/90°, receiver bandwidth 83.3 kHz, b value 1000, NEX 2, slice thickness 3 mm), and 3D spoiled gradient recalled (SPGR) T1-w fat-saturated sequence (TR/TE 9/2.9 ms, NEX 3, receiver bandwidth 19.2 kHz, FOV 24 cm, in-plane resolution 0.75 × 0.94 × 1.2 mm) acquired after gadolinium injection (0.2 mL/kg, Dotarem).

Imaging analysis

The HRCT images were reconstructed for each ear in the plane of the lateral semicircular canal (LSCC).

All of the image analysis was performed on an Advantage Workstation (AW 4.6, GE Healthcare) by two expert radiologists blinded to the patient's status for quantitative measurements, and by two experienced radiologists for qualitative analysis. For conflicting evaluations, the agreement between raters was reached.

The HRCT analysis (Table 1) aimed to determine:

- The attenuation and osseointegration of the BG granules: The quantitative analysis included bone attenuation measurements (in Hounsfield units, HU) in the circular region of interest (34 mm^2) of BG and of surrounding cortical bone and otic capsule using the otic capsule adjacent to the LSCC and the posterior fossa dural plate (DP) as described in previous studies [23] (Fig. 1). The osseointegration was assessed visually as the presence or absence of the clear limit between BG granule filling and the mastoid bone;
- The extent of the obliterated paratympanic spaces: the maximum diameter and surface area were measured (Fig. 1);
- The attenuation of BG granules, shape, osseointegration, and middle ear ventilation were evaluated qualitatively;
- Any suspicion of residual cholesteatoma was evaluated and confidence in the diagnosis was rated using a Likert scale from 1 (not at all) to 5 (completely confident). The

Table 1 One-year high-resolution CT results ($n = 70$)

		Scale	Results
BG filling size	Maximum diameter	cm	2.51 ± 0.53
	Surface area	cm^2	2.05 ± 0.67
Attenuation	Mean BG granule attenuation	HU	888.34 ± 166.10
	Mean LSCC attenuation	HU	1844.93 ± 169.12
	Mean posterior fossa DP attenuation	HU	1241.41 ± 178.15
	BG/LSCC attenuation		0.49 ± 0.08
	BG/DP attenuation		0.72 ± 0.16
Qualitative analysis	Osseointegration	1: Low	1: 21.4% (15/70)
		4: Complete	2–3: 57.1% (40/70)
			4: 21.4% (15/70)
	Attenuation	1: Low attenuation	1: 11.4% (8/70)
		4: Close to bone attenuation	2–3: 75.7% (53/70)
			4: 12.9% (9/70)
	Homogeneity	1: Heterogeneous	1: 4.3% (3/70)
		2: Mostly homogeneous	2: 50% (35/70)
		3: Homogeneous	3: 45.7% (32/70)
	Mastoid cavity obliteration	1: < 25%	1: 1.4% (1/70)
		2: 25–50%	2: 11.4% (8/70)
		3: 50–75%	3: 15.7% (11/70)
		4: > 75%	4: 71.4% (50/70)
	Mastoid cavity obliteration shape	1: Sharp	1: 4.3% (3/70)
		2: Intermediate	2: 31.4% (22/70)
		3: Smooth limits	3: 64.3% (45/70)
	Middle ear aeration	0: Complete opacity	0: 25.7% (18/70)
		2: Complete aeration	1–2: 74.3% (52/70)
	Middle ear filling shape	0: None	0: 24.3% (17/70)
		1: Concave	1: 51.4% (36/70)
		2: Convex	2: 24.3% (17/70)
	Cholesteatoma recurrence	0: No	0: 75.7% (53/70)
		1: Possible	1: 24.3% (17/70)
		2: Yes	

BG, S53P4 bioactive glass; *LSCC*, lateral semicircular canal; *DP*, dural plate

Quantitative analysis: mean ± SD; qualitative analysis: number and percentage

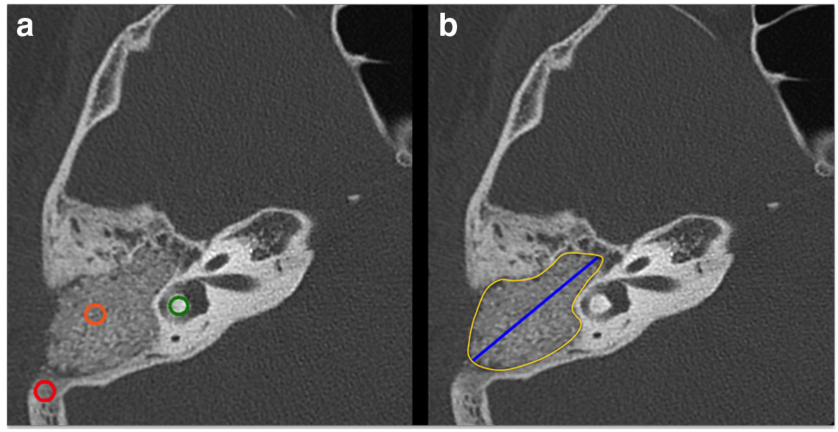

Fig. 1 Attenuation measurements for S53P4 bioactive glass (BG) granule filling. **a** Region of interest (ROI) placement in the lateral semicircular canal (green), BG granules (orange), and posterior dural plate (red). **b** BG granule filling measured at maximum cross section: diameter (blue) and area (yellow)

residual cholesteatoma was suspected while observing while finding convex or polypoid border of soft tissue opacity;

- Complications.

The MRI analysis aimed to determine:

- The normal MRI appearance of BG granules on the sequences detailed above;
- The presence of possible residual/recurrent cholesteatoma was evaluated and confidence in the diagnosis was rated using a Likert scale from 1 to 5;
- Complications.

Aside from the usual protocol, some patients underwent additional imaging studies earlier or later for different clinical reasons. On the HRCT scans, potential modifications of the attenuation (from resorption and/or osseointegration of the BG granules) and volume of the mastoid and epitympanic obliteration were assessed. Moreover, modifications of position of the granules compared with the ossicular replacement prosthesis and of ventilation of the middle ear were studied. On the MRI, the potential modification of the signal was analyzed.

From a clinical point of view, cases were divided into CWU or CWD procedures, primary/revision surgery, and presence/absence of cholesteatoma. Comparisons were made between these groups to see whether any significant differences were present in the imaging results.

Statistical analysis

Descriptive statistics were calculated for all variables. Data are presented as mean ± SD. The data was first tested for normality of distribution using a Kolmogorov-Smirnov test. The data followed normal distribution ($p > 0.05$) for the HRCT measurements at 1 year. Consequently, HRCT measurements at 1 year were compared using one-way analysis of variance (ANOVA). The Bonferroni posttest correction for multiple comparisons and Student's t test for paired observation were used. The p value < 0.05 was considered to be statistically significant. The subgroup analyses for the follow-up data and for the confidence analysis were performed using the Wilcoxon signed-rank test.

Results

Patients

Seventy cases (69 patients, one patient operated bilaterally, 31 women (31/69; 45%)) were included. Mean age was 47 ± 16.6 years (range 16–79 years). There were 42 right-side and 28 left-side cases. Of these 70 cases, 60 were revision surgery and only 10 were primary surgery. Surgery consisted of CWD mastoidectomy in 57 cases (57/70; 81.4%) and CWU in 13 cases (13/70; 19%). Cholesteatoma was found in 45 cases (45/70; 64.3%). In 6 cases (6/70; 8.6%) where an intact ossicular chain was found, ossicular chain reconstruction was not performed. When the ossicular chain was interrupted, a fully titanium prosthesis was always used; a partial ossicular chain replacement prosthesis was needed in 31 cases (31/70; 44.3%) and a total prosthesis was used in 33 cases (33/70; 47.1%). Fibrous tissue and thinned concha cartilage were used to reconstruct the tympanic drum.

HRCT results at 1 year ($n = 70$)

The HRCT data are summarized in Table 1. The mean largest obliteration surface was 2.05 ± 0.67 cm^2 (range 1.3 to 3.5 cm^2). The mean BG attenuation was 888.34 ± 166.10 HU. BG attenuation was significantly lower than in the bone surrounding the LSCC ($p < 0.0001$) and in the bone surrounding the DP ($p < 0.0001$). The attenuation ratio was 0.49 ± 0.08 for BG/LSCC and 0.72 ± 0.16 for BG/DP (Fig. 2).

There were no statistically significant differences for any of imaging parameters between patients undergoing CWD or CWD mastoidectomy, primary or revision surgery, and presence or absence of cholesteatoma.

For qualitative evaluation, the attenuation was evaluated as being low for 11.4% of patients whereas it was close to bone attenuation for 12.9%, and for the remaining 75.7%, it was considered to be intermediate attenuation. Osseointegration was partial in 78.6% of cases, with most of the defects being anterior to and internal to the obliteration. The obliteration was mostly or completely homogeneous in 95.7% of the cases and heterogeneous in 4.3% of the cases. Middle ear aeration was complete in 40% of cases and partial in 33% of cases. In most of the cases, the borders of the middle ear filling were concave and not suspected of cholesteatoma recurrence, while they were convex in 24% of cases raising the suspicion of cholesteatoma recurrence. The diagnostic confidence was 3.83 ± 1.06.

MRI results at 1 year (*n* = 43)

One patient had a pacemaker which prevented MRI from being performed and one patient refused MRI because of claustrophobia.

The global appearance of mastoid and epitympanic obliteration with BG on MRI (Fig. 2) was homogeneous (25/43, 58.1%) or mostly homogenous (18/43, 41.9%).

Analysis of T1-w images The obliteration presented mostly as a low-intensity T1-w signal (18/43, 41.9%) or isointense to the surrounding tissue (18/43, 41.9%), while it was intermediately high in the remaining 16.3% (7/43) of cases. In some cases (8/43, 18.6%), a high-intensity T1-w signal could be seen peripherally, possibly corresponding to trapped fluid.

Post-contrast T1-w imaging After contrast administration, a moderate enhancement was observed. No obliteration exhibited a low-intensity T1-w signal after contrast injection. The enhancement was homogenous in 60.5% (26/43) of cases while it was predominantly peripheral in 39.5% (17/43) of cases. The central part presented an isointense signal in 44.2% (19/43) and a high-intensity T1-w signal in 55.8% (24/43) and the periphery always presented a high-intensity T1-w signal apart from 7% (3/43) of cases which presented an isointense T1-w signal.

T2-w imaging The obliteration mainly exhibited a low-intensity T2 signal (41/43, 95.3%) while it was isointense in 4.7% (2/43). No obliteration presented a high-intensity T2 signal. In some cases (8/43, 18.6%), a high-intensity T2 signal could be noted peripherally, outside the obliteration, corresponding to some trapped fluid.

Non-EP DW imaging For all of the patients, the DW sequences were of good quality with no artifacts related to the material. All obliterations apart from one presented a low-intensity DW signal. In the latter case, a high-intensity DW signal indicated cholesteatoma recurrence (Fig. 3).

Global outcome The suspicion of recurrent cholesteatoma was confirmed by the revision surgery. No complication such as infection was found on imaging or clinically.

The confidence in the presence or absence of cholesteatoma was high (4.95 ± 0.21). This confidence

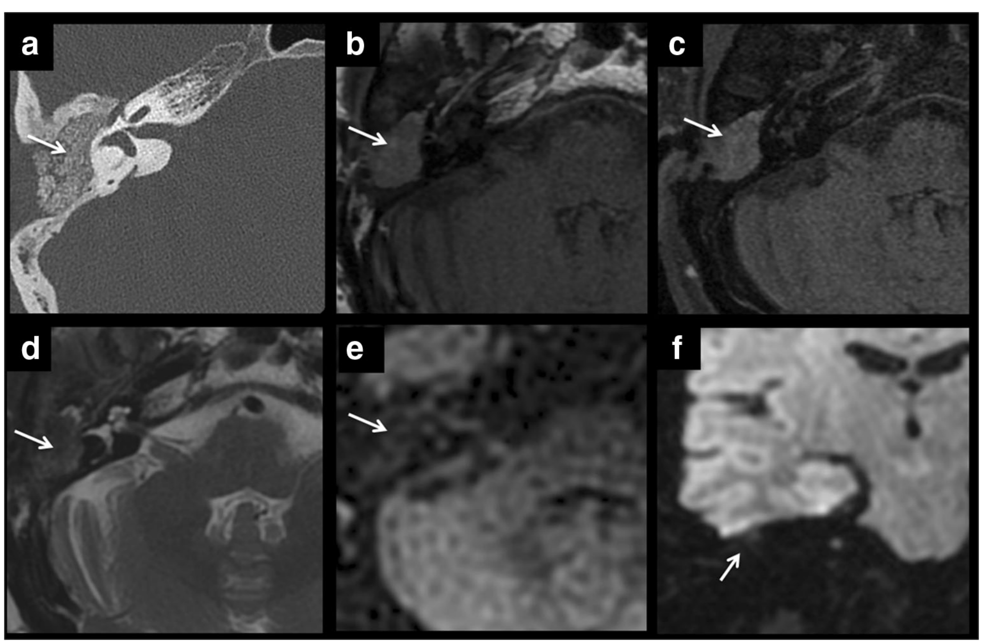

Fig. 2 Example of S53P4 bioactive glass (BG) granule filling at 1 year after surgery. Axial CT imaging (**a**) shows homogenous BG granule filling (arrow), appearing less hyperdense than surrounding bone. Axial T1 contrast-free T1-weighted image (**b**) shows the BG with isointense signal, and with moderate homogenous contrast enhancement on T1-weighted fat-saturated post-contrast image (**c**). The filling has a low-intensity T2-weighted signal (**d**) as well as a low-intensity diffusion-weighted signal on axial (**e**) and coronal (**f**) diffusion-weighted imaging

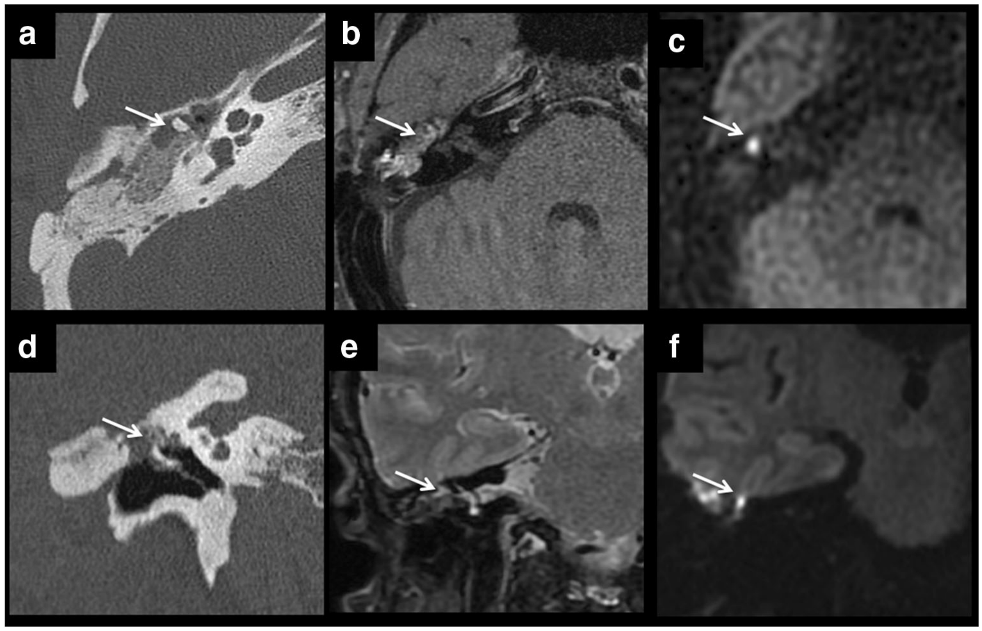

Fig. 3 Cholesteatoma recurrence at 1 year after surgery. Axial CT imaging (**a**) shows a hypodense soft tissue mass in contact with bioactive glass (BG) granule filling. The post-contrast T1-weighted image (**b**) shows a hypointense soft tissue nodule in contact with BG filling which has a high-intensity T1-weighted signal. Axial non-echo-planar diffusion-weighted imaging (non-EP DWI) (**c**) shows a nodule with high-intensity signal related to recurrent cholesteatoma. Coronal CT (**d**) showing a hypodense nodular mass. The coronal T2-weighted image shows a formation with a high-intensity signal (**e**), also appearing as a high-intensity signal on coronal DWI (**f**), corresponding to recurrent cholesteatoma (arrow)

increased statistically significantly from HRCT to MRI ($p < 0.0001$).

No complications were detected on 1-year image analysis.

Follow-up results

Early imaging (Table 2) Six patients had early imaging (between 2 and 10 days after surgery; six patients had an HRCT scan and one patient an MRI study).

On HRCT, there was a trend toward a decrease in attenuation of the obliteration over time; however, that difference was not statistically significant ($p = 0.11$). There was no statistically significant difference for any of the other parameters. For the patient who underwent early MRI, no difference in signal between the early and 1-year study in any of the sequences performed was observed.

Late follow-up (Table 3) Fifteen patients had imaging between 2 and 4 years after surgery: 14 HRCT and 12 MRI. There was no statistically significant difference for any of the HRCT parameters, namely, there were no modifications in the attenuation of the obliteration or its homogeneity. No reduction in the volume of the obliterated spaces was noted. In addition, for seven patients of these patients who had MRI scans at both 1-year and 3-year follow-ups, we observed no significant signal differences on any of the sequences performed, apart from one patient who developed a residual cholesteatoma 3 years after the primary surgery. No other complications were detected in the late follow-up studies. There was no bony erosion in contact with the granules.

Discussion

In this study, we observed that BG granules had a distinctive appearance on HRCT and MRI and are clearly differentiable from the surrounding temporal bone 1 year after surgery. Moreover, their attenuation and signal clearly differ from those for cholesteatoma recurrence, allowing straightforward imaging follow-up. Finally, we observed no change in aspect

Table 2 Comparison between early high-resolution CT and 1-year follow-up ($n = 6$)

	1-year follow-up (mean ± SD)	Early follow-up (mean ± SD)	*p* value (Wilcoxon test)
Maximum diameter (cm)	2.44 ± 0.54	2.54 ± 0.57	0.95
Surface area (cm^2)	2.58 ± 0.72	2.34 ± 0.72	0.34
Mean BG attenuation (HU)	886.17 ± 207.46	1197.4 ± 155.77	0.10
Mean LSCC attenuation (HU)	1867.00 ± 248.16	1757.2 ± 303.84	0.54
Mean posterior fossa DP attenuation (HU)	1151.00 ± 136.63	1241.00 ± 289.11	0.84
BG/DP attenuation	0.78 ± 0.21	0.99 ± 0.19	0.55
BG/LSCC attenuation	0.47 ± 0.08	0.71 ± 0.21	0.06

BG, S53P4 bioactive glass; *LSCC*, lateral semicircular canal; *DP*, dural plate

Table 3 Comparison between delayed (2- to 4-year) high-resolution CT and 1-year follow-up ($n = 14$)

	1-year follow-up (mean ± SD)	3-year follow-up (mean ± SD)	p value (Wilcoxon test)
Maximum diameter (cm)	2.16 ± 0.51	2.16 ± 0.48	0.85
Surface area (cm^2)	1.59 ± 0.53	1.58 ± 0.54	1
Mean BG attenuation (HU)	809.17 ± 131.67	874.17 ± 152.99	0.07
Mean LSCC attenuation (HU)	1839.00 ± 192.28	1886.25 ± 132.02	0.75
Mean posterior fossa DP attenuation (HU)	1281.00 ± 154.11	1394.33 ± 182.25	0.08
BG/DP attenuation	0.63 ± 0.10	0.63 ± 0.10	0.70
BG/LSCC attenuation	0.44 ± 0.06	0.46 ± 0.06	0.26

BG, S53P4 bioactive glass; *LSCC*, lateral semicircular canal; *DP*, dural plate

of the BG granules over time, both on HRCT and MRI, and no increasing osseointegration.

On HRCT, osseointegration of the BG granules was not complete. This trend has already been noted in other fields, such as treatment of chronic osteomyelitis and benign bone tumors where BG granules have been used [24, 25], and seen radiologically up to 14 years after surgery. Similarly, radiological evidence of BG granules 2 years after filling of upper and lower jaw cavities was found [26]. However, in these regions, the osseointegration appeared to be more prominent than in our study, which might be explained by the stronger osteoblastic/osteoclastic activity in former regions. In the spine [27], the radiological presence of the granules has been demonstrated 10 years after surgery. In frontal sinus surgery, an environment more similar to the mastoid cavity, the late osseointegration of the BG granules appearing 10 years after surgery was observed [28, 29], with the volume of the obliterated frontal sinus remaining stable over time.

The attenuation of the BG granules was found to be significantly different from both normal bone and cholesteatoma. The mean attenuation observed in our study (888.3 ± 166.1 HU) is similar to the one found in frontal sinus obliteration (969.6 ± 65 HU) [29]. Moreover, BG granules appear to be mostly homogeneous, without hypodense intrusions, which could facilitate the follow-up of obliterated ears even in the absence of MRI, since the average attenuation of the cholesteatoma is low [30]. It should be noted that, in our population, no cholesteatoma was detected within the BG filling, and the only case of cholesteatoma was found outside the filling. This is in line with previous studies [31] on other fillings and with an animal study which suggested that bony obliteration interfered with trophic conditions for cholesteatoma recurrence [32].

We have observed that the attenuation of the BG granules differs significantly from the surrounding bone and that ossification of the implanted material remains incomplete, even after 3 years. This finding is clinically rather advantageous than disadvantageous because, unlike long bones, the mastoid bone is not a load-bearing one and the resistance provided by the new bone is not required. Moreover, in the case of revision surgery, the difference in appearance between normal bone of the otic capsule and obliteration is of paramount importance so as not to damage important structures such as the semicircular canal and/or the fallopian canal. In addition, it is important for mastoid obliteration to maintain a stable volume over time. This obliteration was usually greater that 75% of the mastoid cavity and stability was observed in our study up to 3 years after surgery.

On MRI, mastoid and epitympanic obliteration with BG appeared as a low- or intermediate-intensity T1-w signal, a low-intensity T2-w signal, and a low-intensity non-EP DW imaging signal with mild post-contrast enhancement. This association appears to allow the obliteration to be easily differentiated from residual cholesteatoma, characteristically exhibiting a high-intensity signal on both T2-w and non-EP DW imaging with no contrast enhancement.

The characteristic signal of BG granules is also different from other pathologies, allowing easy diagnosis of recurrent cholesteatoma recrudescence or post-surgical complications (Table 4). Even though BG granules have a bacterial growth-inhibiting effect [33], it is also important to detect a post-surgical infection. Granuloma and chronic retention are distinguishable from BG as they are usually hyperintense on T2-w images. However, BG granules can have a similar appearance to fibrosis on MRI; fibrosis can present as a low-intensity T2-w signal with mild enhancement. This observation can be related to partial fibrosis transformation of BG that has also been observed on pathology sections (Fig. 4) from revision surgery.

We also aimed to evaluate the possible influence of different surgical procedures on the filling outcome. The CWU procedure was hypothesized to favor better osseointegration due to the higher amount of bone surrounding the granules (the posterior and superior canal walls of the external auditory canal) and primary surgery was thought to provide a higher rate of osseointegration as the mastoid bone had never been drilled. However, there was no influence of these different techniques on the appearance of BG, signal, or attenuation, showing a clear stable behavior of the BG granules in different clinical scenarios.

The appearance of BG differs from previous ear fillings. For instance, biphasic ceramic granules and fibrin sealant

Table 4 MRI typical aspect of S53P4 bioactive glass (BG) granules compared with the most common post-surgical pathologies/findings for temporal bone

	T1-weighted signal	T2-weighted signal	Post-gadolinium enhancement	Non-EP DWI
BG granules	Hypo/isointense	Hypointense	Moderate	Hypointense
Cholesteatoma	Hypo/isointense	Hyperintense	None	Hyperintense
Granuloma/retention	Hyperintense	Hyperintense	None	Variable
Infection	Hypo/isointense	Hyperintense	Strong	Variable
Fibrosis	Hypo/isointense	Variable	Moderate/late	Hypointense

BG, S53P4 bioactive glass; *non-EP DWI*, non-echo-planar diffusion-weighted imaging

composite [34] are more dense with a mean attenuation of 975.6 HU on CT scans, similar to bone. It also presents a higher rate of osseointegration that can make revision surgery more challenging.

Another material commonly used for mastoid obliteration is "bone pâté," consisting of bone dust harvested from autologous cranial bone [23]. Two studies [23, 35] found a rather low attenuation of bone pâté, of 572 and 536 HU, respectively. It has also been observed that the filling was heterogeneous in 25.5% of cases appearing as non-specific soft tissue opacity that could not be differentiated from cholesteatoma on HRCT [31]. By appearing more dense and more homogeneous on HRCT, BG granules could be helpful in raising the suspicion of cholesteatoma recurrence, as already demonstrated with other biomaterials such as hydroxyapatite granules [30].

Our study has several limitations. First, it was a short-term study, while the evolution of BG over time might be slow. However, in the cases of a 3-year follow-up, no signal or attenuation changes were observed. Second, an early CT scanning and a 3-year follow-up analysis were not performed with the same patients. Consequently, we could not perform a longitudinal attenuation analysis with several time points. Future longitudinal analyses can be interesting in this context. Third, we did not perform a randomized control study, but this is not advisable nor ethic in cholesteatoma surgery: obliteration has proven to give better results in terms of residual/recurrence

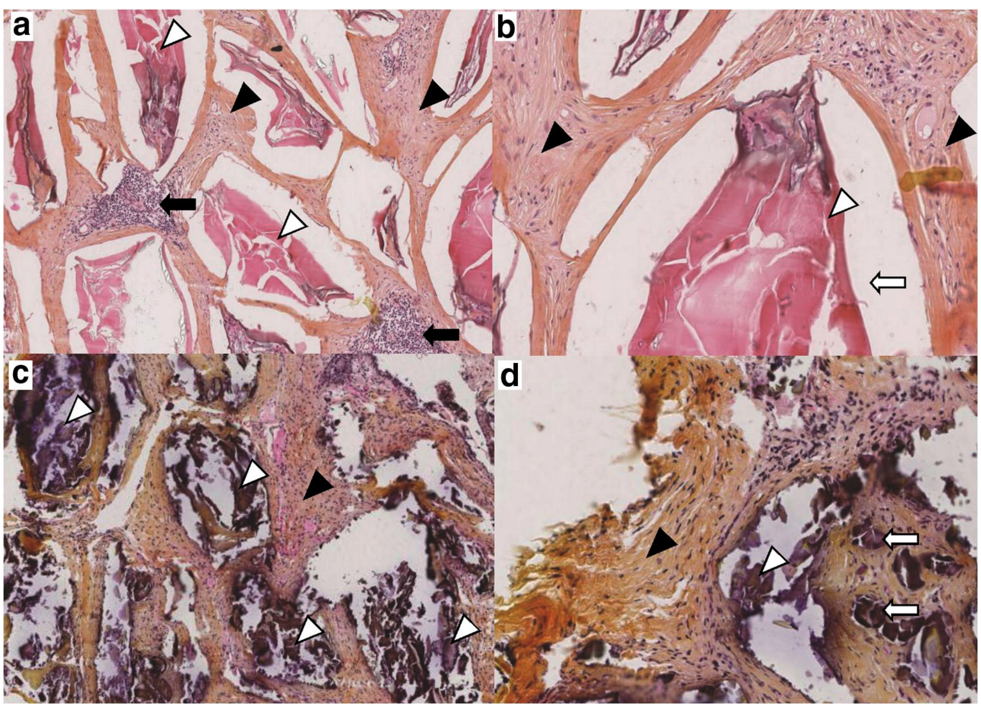

Fig. 4 Histopathological aspects of the bone substitute. Hematoxylin-eosin-safran (HES) staining at low (**a**) and high (**b**) magnification of a surgical sample of S53P4 bioactive glass (BG) granules harvested during revision surgery performed 1 year after primary surgery. The BG granules (white arrowheads in **a**, **b**) are surrounded by a collagen-rich fibrous tissue (black arrowheads in **a**, **b**) containing lymphoid nodules (black arrows in **a**). The hollow space (white arrow in **b**) between the granules and the fibrous tissue is probably an artifact caused by the histological processing. HES staining at low (**c**) and high (**d**) magnification of a surgical sample of BG granules harvested during revision surgery performed 3 years after primary surgery. The BG granules (white arrowheads in **c**, **d**) are surrounded by a collagen-rich fibrous tissue (black arrowheads in **c**, **d**) without lymphoid nodules. They had a more blueish aspect in comparison with the panels **a** and **b** suggesting that they underwent a mineralization. They are sometimes split into smaller parts (white arrows in **d**)

rate compared with non-obliterative techniques, so the decision of randomly perform obliteration was not acceptable from a clinical point of view. Finally, our results applied only to adult patients, since only adults can be treated in our institution. Thus, complementary studies might be useful in children, as osseointegration could be different from that in adults.

In summary, our study showed that the appearance of BG granules in mastoid epitympanic obliteration is characteristic on both MRI and HRCT scans and stable over time, allowing easy and effective detection of cholesteatoma recurrence and other complications.

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Compliance with ethical standards

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Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology
• prospective
• cross-sectional study
• performed at one institution

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