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An Exploratory Study on the Efficacy of Gelfoam and Medical Cyanoacrylate Glue Combination for Passive Reduction of Vascular Pulsatile Tinnitus

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Studies on the materials that can be used in sigmoid sinus wall reconstruction have been lacking. To treat pulsatile tinnitus (PT) using autologous/exogenous materials by passively insulating the vascular noise, it is necessary for surgeons to reconstruct the sigmoid sinus wall using repairing materials with sufficient volume density. In this study, we investigated the optimal moisturization of a specific reparative material made of a combination of gelatin sponge (GS) and N-butyl cyanoacrylate (NbCG) (GS-NbCG), and its potential to preclude sound transmission. An impedance tube and acoustic sensors were used to differentiate five distinct states of moisturization of GS-NbCG. Additionally, Doppler ultrasound was used to visualize the outcome of GS-NbCG application. The results showed that GS-NbCG saturated with 1 g of 0.9% saline solution (sodium chloride) showed the highest level of soundproofing at frequencies below 1 kHz compared with those having other degrees of moisturization. A moderate level of moisture is desired to optimize the polymerization reaction and produce a dense, strong final product. In conclusion, the optimal material density and total areal density required for PT suppression can be achieved by regulating the moisturization level of the GS strip/pieces, thereby avoiding excessive or insufficient moisturization.

1. Introduction

Vascular pulsatile tinnitus (PT), also known as pulse-synchronous tinnitus, is a type of objective tinnitus that manifests as an abnormal perception of blood flow sounds.(1) Among the sound production mechanisms underlying this type of tinnitus, dehiscence of the temporal bone near the inner ear has been identified as a causative factor in some cases of vascular PT.(2) In

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cases where dehiscence is implicated, the venous flow sounds are the primary sound source that can be readily identified, along with their transmission pathway.(1,3) Moreover, various anatomical variants, such as sigmoid sinus diverticulum and transverse sinus stenosis, contribute to the complex flow patterns and states that result in venous PT.(4,5)

In otologic surgery, transtemporal sigmoid sinus wall reconstruction or repair has become a standard procedure for reducing venous PT. The primary objective of this surgery is to passively dampen the flow-borne vascular sound by reshaping and increasing the thickness of the dehiscent sigmoid plate.(2,3) According to systematic reviews and surgical case studies, the success rate of the transtemporal method ranges from 70 to 90% and can involve the use of various repairing techniques and materials.(6)

Notwithstanding the numerous options for repairing materials, ensuring the sigmoid sinus wall has adequate thickness for sound insulation is of utmost importance. This goal is usually achieved by layering multiple materials at the dehiscent area. Autologous materials, such as temporalis muscle/fascia and auricular cartilage, boast higher density than exogenous biomaterials.(7) Meanwhile, synthetic materials, despite their lower density, offer the advantages of being pliable, easily stackable, low in cost, and readily available in abundance.(7)

Gelfoam or gelatin sponge (GS) is a complex 3D network of cross-linked gelatin molecules, used in surgical procedures for hemostasis and clot promotion. It is a porous, spongy material made from gelatin, a protein derived from collagen, and is highly absorbent.(8) This synthetic biomaterial has a wide range of surgical applications, including orthopedic, spinal, and neurosurgical procedures. In skull base and ear surgeries, GS is frequently employed for hemostasis and as a physical barrier or to secure applied materials. There are also studies advocating the use of GS saturated with aural and encephalic glue to prevent cerebrospinal fluid leakage in the case of frontal sinus perforation.(9)

In the medical field, various surgical adhesives are used for specific purposes. Some of the most widely used include fibrin glues, endothelial cell (EC) glues, collagen-based glues, and cyanoacrylate glues. Cyanoacrylate, commonly referred to as superglue, is prized for its quick and strong bonding properties, although it can also be brittle and challenging to remove. 2-octyl cyanoacrylate and N-butyl cyanoacrylate (NbCG), with low toxicity and irritancy, are the preferred formulations for medical use.(10) The latter type forms a strong bond that is resistant to water and bodily fluids and has proven successful in fixing layers of repairing materials during sigmoid sinus wall reconstruction.(3)

Despite the widespread use of autologous materials for sinus wall reconstruction, achieving ample thickness can prove difficult as they tend to be thinly layered because of limited availability. The sound insulation capabilities of the repairing materials for sigmoid sinus dehiscence have received limited attention. Furthermore, otologists have diverse predilections and modus operandi for reconstructing the walls of the sigmoid sinus. To address these gaps in knowledge, this study represents an initial investigation into the optimal moisturization of the GS-NbCG combination for mitigating the transmission of vascular sound. Understanding the optimal application of these exogenous materials can ensure successful surgery and minimize surgical incisions.

2. Materials and Methods

2.1 Preparation of GS specimen

The thickness of GS (Jinling Pharmaceutical Company Ltd., Nanjing, China) was kept consistent during all acoustic assessments. Moisturization was carried out by evenly dripping and spreading 0.9% saline on the top surface of the GS strip using a syringe. The syringe was then capped with an end cap and used to smooth the saline drops on the surface of the GS strip. After the moisturization process, each category of moisturized GS (measuring 60 mm × 20 mm × 10 mm) was then cut into circular pieces of 15 mm diameter using a circular knife. An equal amount of 0.5 ml *N*-butyl cyanoacrylate glue was applied to the surface of each circular GS piece. Finally, five different levels of moisturization of GS-NbCG were grouped: a) 0.3 g of saline solution (GS-NbCG-$SS_{0.3g}$), b) 0.5 g of saline solution (GS-NbCG-$SS_{0.5g}$), c) 1 g of saline solution (GS-NbCG-SS_{1g}), d) 2 g of saline solution (GS-NbCG-SS_{2g}), and e) 3 g of saline solution (GS-NbCG-SS_{3g}). The preparation process of GS specimens is shown in Fig. 1. To avoid shrinkage of the GS-NbCG circular piece during polymerization, NbCG was added prior to separating the GS pieces from the internal edge of the circular knife.

Fig. 1. (Color online) (a) Moisturization of the gelatin sponge (GS) strip using the end cap of a syringe to smooth the saline drops on the surface of GS strip. (b) A 15-mm-diameter circular knife was used to cut the GS strip into circular pieces. (c) Polymerization of GS-NbCG. (d) GS-NbCG specimens.

2.2 Impedance tube testing

After the GS-NbCG circular pieces were polymerized, they were removed from the circular knife. The circumference of the GS-NbCG pieces was coated with clay to match the size of the impedance tube. The aluminum alloy tube used had a diameter of 20 mm, and impedance tube testing was set up following a previous method. The setup is shown in Fig. 2.(7) The test objects were positioned between four free-field microphones (Type 4939, Bruel & Kjær, Denmark), with two microphones on either side. The microphones had a sensitivity of 10 mV/Pa, and the planar wave sound source was a speaker (JBL). The sound impedance transmission loss and estimated density of the GS specimens were studied by utilizing the following transmission loss formula, which considers the density of air (ρ), the speed of sound (c), and the cross-sectional areas of the impedance tube inlet and outlet (Si and So, respectively):

$$TL = 20\log_{10}\left\{\frac{1}{2}\left|A_{12} + \frac{B_{23}}{\rho c} + \rho c \cdot C_{23} + D_{23}\right|\right\} + 10\log_{10}\left(\frac{S_i}{S_o}\right). \tag{1}$$

The size of all GS-NbCG specimens was standardized and each was tested three times adhering to the GB/Z 27764-2011 standard protocol. The final results were then presented as the average of these three tests.

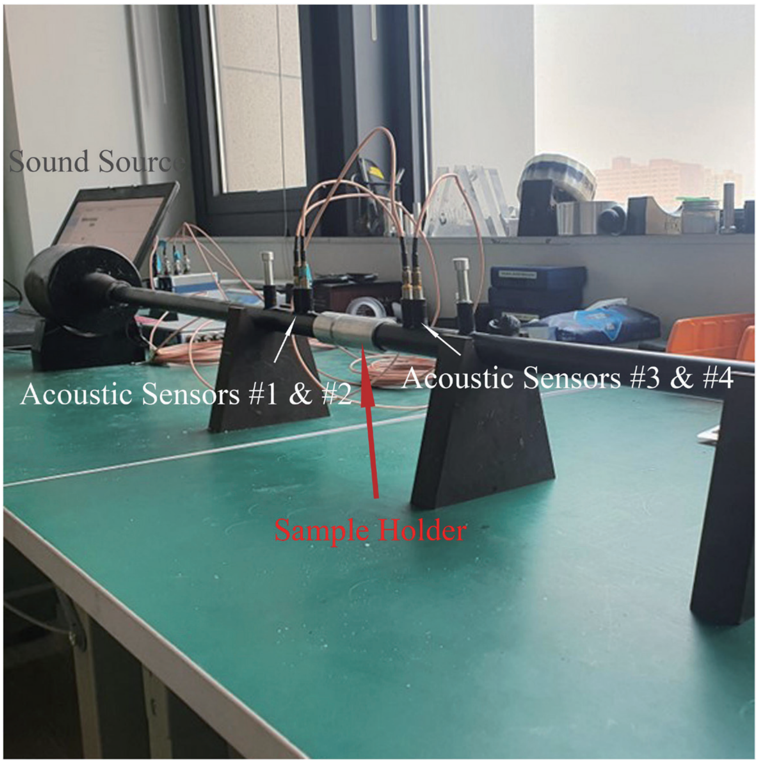

Fig. 2. (Color online) Setup of the impedance tube test.

2.3 Doppler ultrasonographic and radiologic examination

We employed the Arietta 60 medical ultrasound system (Hitachi Aloka Medical Ltd., Japan) with the L441 (12-2 MHz) transducer to perform a postoperative retroauricular ultrasound and elastosonographic examination on a 37-year-old male patient who had undergone transtemporal surgery to treat left-sided PT associated with sigmoid sinus diverticulum. The surgical procedure involved complete reduction of the diverticulum and reconstruction of the dehiscent plate using adequate GS-NbCG. The transducer was positioned at the patient's surgical area nearly one year after the surgery. B-mode, color-mode, and transient elastrography were used to view the operative area. The retroauricular technique used in the study was similar to the method used in our previous research.(5)

Imaging modalities, including contrast-enhanced CT and MR imaging (performed using equipment manufactured by Siemens, Germany), were utilized to examine both the surgical area and the GS-NbCG combination. These imaging techniques have been described in detail in our previous study.(11)

The participant provided written informed consent to participate in this study. Data collections for engineering studies were conducted in accordance with the Declaration of Helsinki.

3. Results

According to the results of impedance tube testing (Fig. 3), GS-NbCG-SS_{1g} with a moisturization of 1 g of saline solution showed the highest level of soundproofing at frequencies

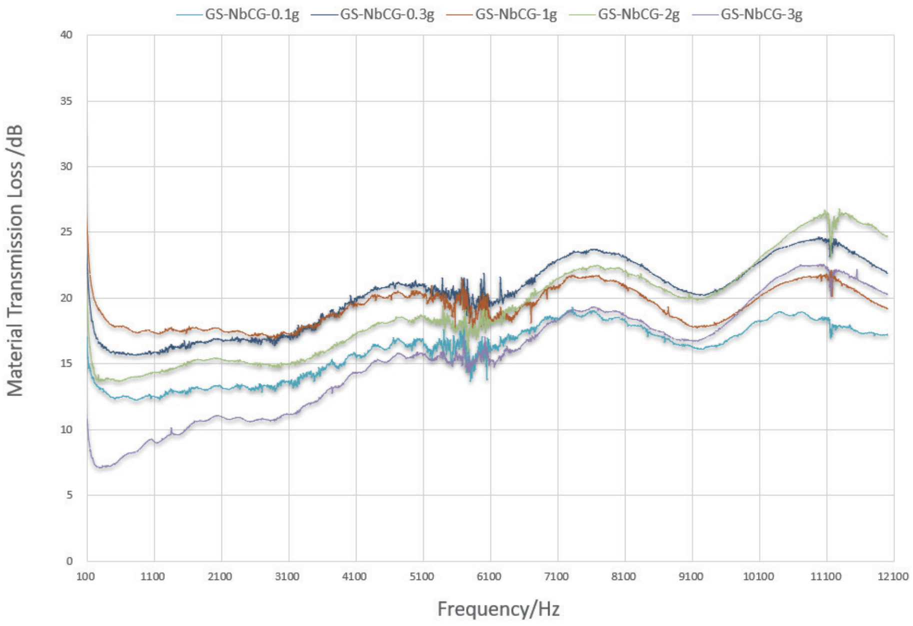

Fig. 3. (Color online) Results of impedance tube test.

below 1 kHz compared with other levels of moisterization. The second highest sound insulation capability was demonstrated by GS-NbCG$_{0.3g}$, which was higher than that of GS-NbCG$_{0.1g}$ and GS-NbCG$_{2g}$. Surprisingly, GS-NbCG$_{2g}$ was more effective in blocking sound than GS-NbCG$_{0.1g}$. This was probably due to the fact that the higher volume and weight of the saline solution led to a higher transmission loss of the acoustic stimuli. In contrast, GS-NbCG$_{3g}$ was the least effective group in blocking the sound besides the control, likely because of the overly rapid and excessive polymerization reaction caused by excessive moisturization, leading to a porous and less dense final product.

The polymerized α-cyanoacrylate physically intermingles with the GS and increases its strength and durability. The polymerization reaction between α-cyanoacrylate and moisture can be described as

$$C_5H_5NO_2 + H_2O \rightarrow (C_5H_5NO_2)_n + H_2O, \tag{2}$$

where $C_5H_5NO_2$ represents the monomeric form of α-cyanoacrylate, and $(C_5H_5NO_2)_n$ represents the polymerized form of α-cyanoacrylate. The test outcome indicates that a moderate level of moisture is desired to optimize the polymerization reaction and produce a dense, strong final product.

The Doppler ultrasonographic examination revealed the presence of multiple clumps of GS-NbCG in the mastoid surgical site (Fig. 4), indicating proper application of the GS-NbCG combination to cover the sigmoid sinus. The blood flow signal in the sigmoid sinus was not detected during the examination, as evidenced by the absence of coloration in the color mode. Imaging techniques, including contrast-enhanced computed tomography (CT) and magnetic resonance (MR) imaging, confirmed the absence of any retained fluids in the mastoid cavity. The radiopacity of GS-NbCG was found to be similar to that of soft tissue. Additionally, T2-MR imaging excluded the presence of any fluid remaining inside GS-NbCG.

4. Discussion

This study constitutes an initial exploration into the optimal moisturization of the GS-NbCG combination to prevent the transmission of vascular sound. While prior research has established the efficacy of the GS-NbCG combination in resolving PT, the preferred materials for reconstructing the sigmoid sinus wall remain autologous.(6) It is essential to note that reducing low-frequency vascular noise necessitates an adequate mass, which can be achieved by stacking and aggregating exogenous biomaterials in thick layers, as well as applying bone wax and/or bone cement on top of the GS-NbCG combination to increase its areal density.(7) In addition, clinical research has advocated the use of both autologous and exogenous materials to attain maximum material density and insulate vascular noise.(2,12,13)

It is a common misconception that an autologous bone dust/plate has the same density as innate mastoid bone. This is not the case, as bone dust is a powdery material that still contains voids even after being gathered and consolidated with glue. Our previous study showed that bone dust and GS-NbCG have similar noise reduction capacities, although the moisturization of

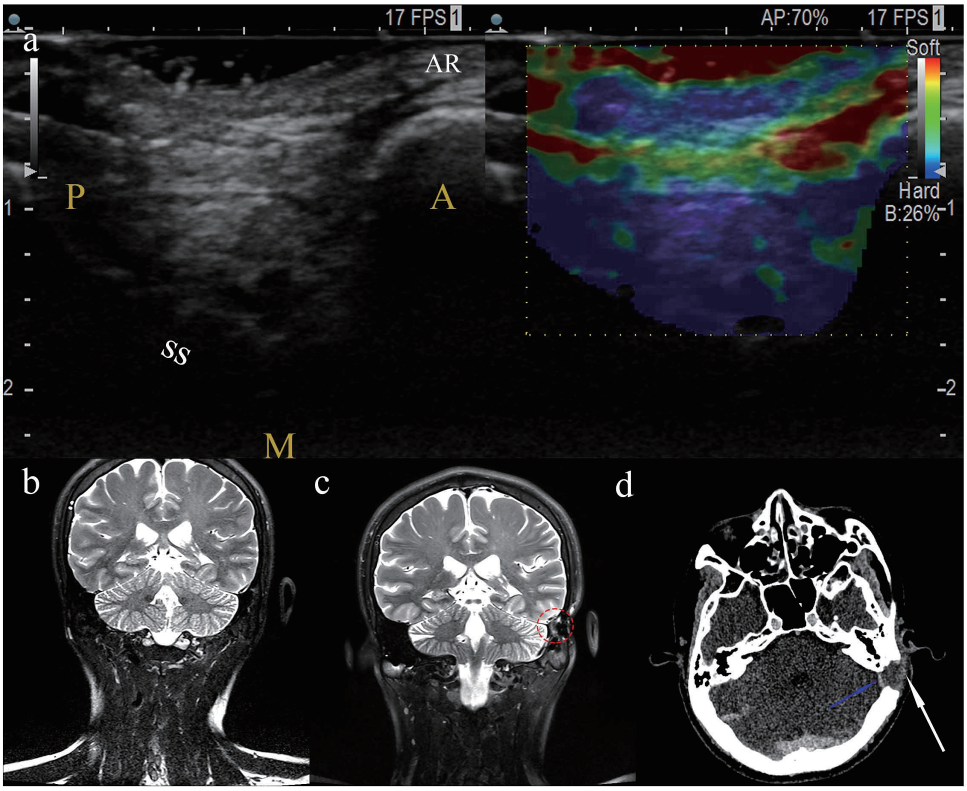

Fig. 4. (Color online) (a) (left panel) Ultrasonographic B-mode view of postoperative retromastoid region with multiple clumps of gelatin sponge (GS) and N-butyl cyanoacrylate (GS-NbCG) combinations. A, anterior; P, posterior; M, medial; SS, sigmoid sinus; AR, the root of auricle. (Right panel) Elastrographical view of the operative region. Note that this is solely an exploration, and a standardized technique to detect tissues and materials at this region has been lacking. (b) Preoperative and (c) postoperative T2-coronal magnetic resonance imaging exhibiting the operative application of GS-NbCG at the surgical site (red dotted circle). (d) Postoperative contrast-enhanced CT demonstrating the compression of the sigmoid sinus diverticulum (blue arrow) using multiple blocks of GS-NbCG (white arrow).

GS-NbCG was not considered. It is possible that GS-NbCG with optimal moisturization provides higher transmission loss than bone dust, given its additional advantages in terms of pliability and feasibility for reconstructing the sigmoid plate and filling dead spaces.

Exogenous materials offer the advantage of being malleable, replenishable, and able to form a dense, wall-like structure without leaving spaces for sound permeation and transmission. GS-NbCG can be shredded into pieces to barricade the antrum and wadded into small air cells to block vascular noise transmission. Additionally, the use of GS-NbCG can prevent the migration of other repairing materials post-surgery. For instance, bone wax may migrate if not properly applied although it is flexible enough to cover the irregular osseous and vascular surfaces.(7) As such, a combination of bone wax and GS-NbCG is encouraged to achieve high material density and maintain robust structural integrity of the fillers.

In the context of a surgical procedure, the degree to which GS may be absorbed following the addition of NbCG and saline solution is contingent upon the unique characteristics of the adhesive and solution, as well as the specific circumstances and mode of employment. While the incorporation of NbCG into GS can reinforce its hemostatic properties and provide supplementary stabilization to the surgical site, the glue itself is not inherently absorbable, necessitating its removal or eventual sloughing.(10) Therefore, it is incumbent upon the surgeon to consider judiciously the attributes of all materials implemented during the surgical process, and to identify the optimal products for the particular circumstances at hand. In our systematic monitoring of individuals who have undergone postoperative CT/MR imaging several years after their surgical procedures, we have not detected any occurrences of the absorption of the GS-NbCG combination. Notably, the most extensive duration investigated in our study spans a period of five years.

This study has several major limitations, including the unavailability of the absolute value of transmission loss and material density owing to the application of clay onto the edge of the specimens, which eliminates morphological changes owing to chemical reactions and heat release. At present, we cannot guarantee the morphologic unity of the clay applied to specimens, which may affect the outcome of material transmission loss, despite the fact that the current results conformed to the actual intraoperative application and outcomes. Additionally, the components of GS and NbCG products may vary among manufacturers, and this study only reveals a trend in terms of the soundproofing capacity and insight for the method of applying GS-NbCG. Furthermore, it is not possible to estimate the saturation and distribution of liquid weight/volume (saline solution and NbCG) in GS, hindering a precise understanding of how these materials impact the final product density. Nevertheless, moderate moisturization of GS is controllable using a syringe, and NbCG can be applied in sufficient amounts. Further clinical and experimental studies are required to verify the correlation between PT transmission loss and the method used to optimize the creation of the GS-NbCG combination.

5. Conclusions

GS, as an exogenous hemostatic stuffing material, offers desirable properties such as compressibility, packability, cost effectiveness, and robustness after NbCG application and polymerization. It is important, however, for surgeons to control the degree of moisture in the GS prior to NbCG application, as it can impact the density of the final product. To maximize soundproofing effectiveness, avoiding excessive or insufficient moisturization of GS-NbCG is recommended to achieve optimal volumetric mass density for PT suppression.

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