REVIEW
ANNUAL REPORT
DOI: 10.5152/B-ENT.2024.22947

Use of Biomaterials in Endoscopic Tympanic Repair

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Cite this article as: Vilain J, Hanot A, Fosseprez J, Doyen A. Place of the use of biomaterials in endoscopic tympanic repair. B-ENT. 2024;20(Suppl. 1):S38-S41.

ABSTRACT

Numerous materials have been used to reconstruct the tympanic membrane and restore its mechanical and vibratory properties with varying degrees of success. If endoscopic ear surgery is to be considered "minimally invasive," it must avoid any unnecessary incision or scarring. The biomaterials currently used in surgery, therefore, have their place in this recent approach to ear surgery.

Keywords: Endoscopic ear surgery, tympanic membrane repair, minimal invasive surgery, biomaterials, porcine small intestinal submucosa (SIS)

The optimal material would have the following qualities, biocompatible, etc, immunologically safe, easy to use, and flexible but resistant, with sufficient sustainability to allow total epithelialization before resorption, some translucency after healing, and limitless supply, and finally would be available at a reduced cost.

Autografts, such as temporalis facia, perichondrium, cartilage, adipose tissue, and skin, are most commonly used. In multiple revision surgeries, the native graft is sometimes insufficient or unavailable, and allograft (human donor) or xenograft (donor from another species) offers an interesting alternative, among them a few examples are dura mater, pig pericardium Tutopatch®, acellular human dermal matrix AlloDerm®, etc. Unlimited supply, avoiding donor-site complications, saving operating time, xenograft has been successful.

Graft intake assumes intimate contact between the graft and the covering epidermal flaps. It depends on a kinetic balance between the longevity of the support and the rate of host cell proliferation. By its biochemical and mechanical properties, small intestinal submucosa (SIS) promotes cell proliferation, differentiation, and migration.

Biomaterial and tissue engineering has led to a better understanding of the bioactive properties of xenografts, such as cell adhesion and migration, angiogenesis, and hemostasis, with the arrival on the market of products such as Gelfoam®, EpiDisc®, and so on

Acellular porcine SIS, Biodesign® (Bloomington, Indiana USA), has been used for some years now as a xenograft in abdominal, thoracic, plastic, vascular, and neurosurgery.[1,2]

One of the goals of endoscopic ear surgery is to avoid a sampling site or a retro-auricular scar, in respect of "the minimally invasive surgery"; SIS has, therefore, become a material of choice.

Structural and Biochemical Properties of Small Intestinal Submucosa

Porcine SIS is an acellular, biological extracellular matrix (ECM) that has been studied to significantly improve healing in chronic wounds in humans.[3]

Used as a scaffold to promote ingrowth of the native tympanic membrane, ECM has structural properties and biochemical composition that stimulates cellular development and differentiation.[4]

The basic components of SIS are protein (70%), primarily collagen type I (90%), elastin, and collagen types III, IV, and VI. Complete composition is reported in Table 1.

Fibronectin, integrin, and proteoglycans provide cell attachment and binding.[3,5,6]

The bioactivity of SIS includes the release of growth factors (fibroblast growth factor-2, transforming growth factor-beta 1, and vascular endothelial growth factor) and reduces the

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Received: March 7, 2022 **Revision Requested:** May 26, 2022 **Last Revision Received:** June 5, 2022 **Accepted:** August 25, 2022 **Publication Date:** December 5, 2022
Available online at www.b-ent.be

Table 1. Structural Properties and Biochemical Composition of Porcine SIS

Property	Description
Thickness	0.05-0.22 mm
Ultrastructure	Pores varying from 20 to 30 μm
Mechanical strength	First layer: 20.6 MPa (dry) and 7.2 MPa (wet)
	Second layer: 24.7 MPa (dry) and 18.8 MPa (wet)
	Third layer: 31.2 MPa (dry) and 22.0 MPa (wet)
	Fourth layer: 36.7 MPa (dry) and 22.4 MPa (wet)
Suture retention	First layer: 0.5 N (dry) and 0.7 N (wet)
	Second layer: 1.3 N (dry) and 2.6 N (wet)
	Third layer: 2.1 N (dry) and 4.1 N (wet)
	Fourth layer: 2.8 N (dry) and 5.2 N (wet)
Oxygen diffusion coefficient	7×10^{-6}-2×10^{-5} cm²/s
Fiber structure	Single, continuous preferred fiber direction, parallel to the long axis of the intestine
Biochemical composition	Collagen
	Elastin
	Fibronectin
	Laminin
	Glycosaminoglycans and proteoglycans
	Fibroblast growth factor-2
	Transforming growth factor-beta1
	Vascular endothelial growth factor

Source: Shi and Ronfard.[3]

destructive activity of matrix metalloproteinases, which contribute to the degradation of the ECM (Figure 1). This bioactivity is of great importance in the race for epithelialization.[5-7]

The mechanical properties are based on its multilayer structure, which gives it elasticity, durability, and resistance.[5]

Shi and Ronfard[3] report a study on pigs in which wound biopsies taken 17 days after the incorporation of the biomaterial showed better epithelialization on the multilayer version even though it was still incomplete.[3]

Main Points

- Endoscopic ear surgery is a minimally invasive surgery.
- Biomaterials are attractive and safe alternatives to autografts and do not require scarring.
- The long-term results of using porcine small intestinal submucosa as a tympanic membrane reconstruction material in terms of tympanic closure are comparable to those of using temporal fascia or cartilage.

Small intestinal submucosa is the subject of much work in biological engineering (Figure 2); it can be surfaced modified in various ways to adjust the mechanical or biological properties until a powder, sponge, or hydrogel form is obtained. These different textures of SIS can be of interest in middle ear surgery. Furthermore, the combination of SIS and bioceramic hydroxyapatite results in a new pore scaffold similar to that trabecular bone which could be of interest as material in the "bone obliteration technique."[7]

Clinical Study of the Use of Small Intestinal Submucosa as Tympanic Membrane Perforation Repair: A Literature Review

Several studies report the use of SIS as a tympanic graft both endoscopically and microscopically in children.

The largest of these involved 432 children aged 3-15 years, over 11 years. Dry tympanic perforations over the past 3 months were secondary to trauma in 5.8% and acute otitis media in 94.2%.[8]

Follow-up is done for 2-11 years. All procedures were performed by a single surgeon under general anesthesia and retro-auricularly under the microscope. In 215 cases, the graft used was an autologous temporal fascia, and in the remaining 217 cases, a xenograft (SIS) was used. Postoperative otoscopic controls performed under the microscope and endoscope were carried out by an Ear Nose and Throat (ENT) examiner who was blind to the surgical technique.

After 2 years, a stable and closed tympanic membrane is observed in 89.2% of temporal fascia grafts and 91.2% in SIS. After 11 years, the healing rate is recorded in 94.8% of temporal fascia grafts and 96.3% of SIS. No statistical difference of pure tone audiometry is observed between the 2 groups.

Basonbul and Cohen[2] detail the surgical techniques for using SIS in different types of tympanic perforation without presenting a series. They underline that the use of xenograft brings a time saving of 7.7 minutes and a gain in safety concerning the potential transmission of viral or prion infections linked to human allografts.

In a retrospective 250 pediatric cases (mean age 12.7 years), James[9] compares different grafts used in endoscopic or microscopic surgery. He recorded an equivalent tympanic closure rate with temporal fascia or SIS regardless of the technique used. He notes a significant reduction in the length of stay, 13 hours shorter for TEES with SIS than the postauricular approach.

This material is used in endoscopic office myringoplasty in selected adults under local anesthesia limited to small dry perforations whose margins are fully visible under microscopic examination. Two discs of SIS are placed in a "sandwich-type scaffold"[10] in a bilayer graft.[11]

Personal Experience

In a preliminary retrospective study, 143 endoscopic middle ear surgeries were performed by the same surgeon (senior author

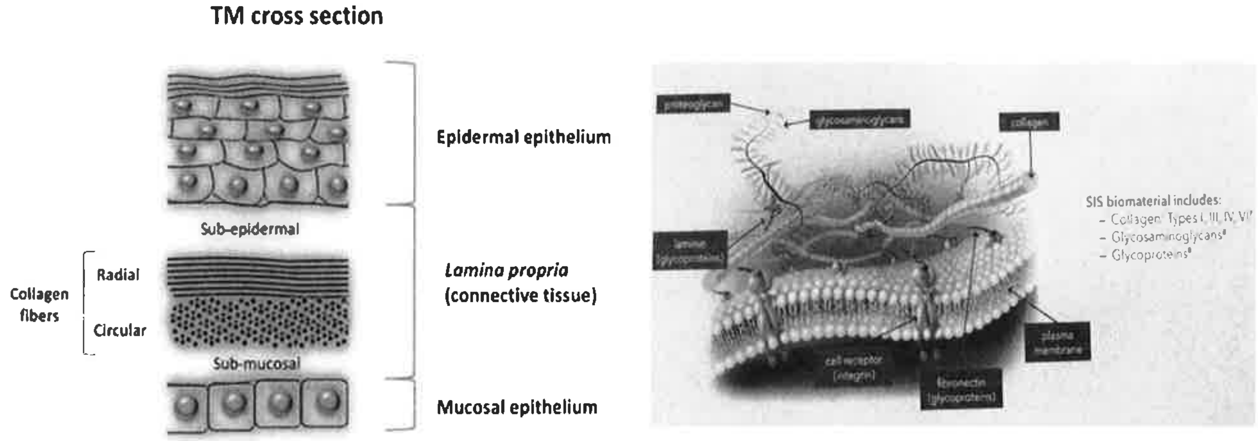

Figure 1. Comparison of natural tympanic membrane structure and porcine small intestinal submucosa. Source: Teh et al.[4]

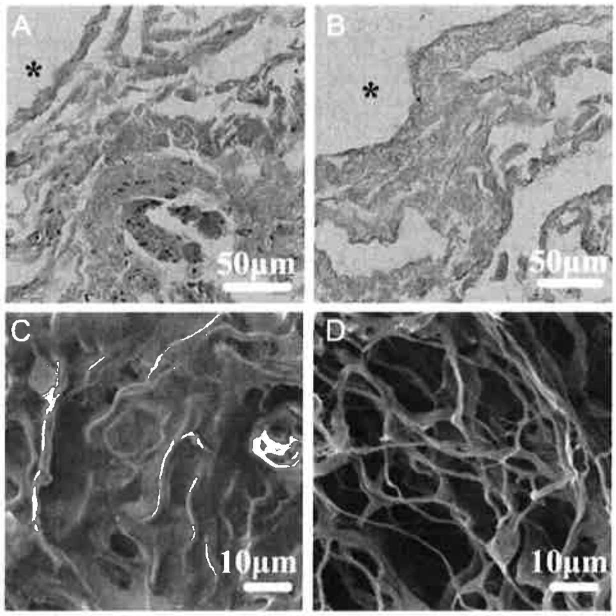

Figure 2. (A) Hematoxylin–eosin staining (HE) image of small intestinal submucosa (SIS) without decellularization, showing many blue nuclei; (B) HE image of decellularized SIS, almost no nuclear signs; (C) Scanning electron microscopy (SEM) image of undecellularized SIS showed coarse, dense, and nonporous structure; (D) SEM image of decellularized SIS shows loose 3D network structure. Source: Zhao et al.[7]

JV) over 3 years for tympanic perforation, retraction pockets, limited cholesteatomas, and ossiculoplasties with tympanic reinforcement. Excluded from the study are extensive cholesteatomas requiring a retro-auricular approach, interventions combining the use of the microscope and the endoscope, the combined use of Biodesign® and cartilage, and a narrow auditory canal. One hundred twenty-one patients were included in the comparative study of outcomes between SIS and tragal cartilage as graft material with a follow-up of 24 months. Tympanic closure is achieved in 84,3% of cases in the SIS group (n = 71) and 80,0% of cases in the cartilage group (n = 50). Epidermal pearl occurred in 15.5% with SIS for 6% with cartilage. Functional results are similar in both groups in terms of Air Bone Gap (ABG) and Speech Reception Threshold (SRT).

Conclusion

Transcanal endoscopic tympanic perforation repair is widely accepted as minimally invasive, more cosmetic, painless, and saving time. Porcine SIS has been widely used as a reconstructive material in abdominal, urologic, plastic, and neurosurgery around the world. Based on numerous studies and hindsight, it is currently accepted that tympanic membrane repair can extend this list.

Its ease of use, availability, and safety make SIS a suitable alternative to autografts in minimally invasive endoscopic ear surgery.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – J.V.; Design – A.H., J.F.; Supervision – J.V.; Anaïs Hanot; Materials – J.V., A.D.; Data; Collection and/or Processing – J.V., A.H., J.F.; Analysis and/or Interpretation – J.F., J.V., A.D., A.H.; Literature Review – J.V., A.H., J.F., A.D.; Writing – J.V., A.H., J.F.; Critical Review – A.D., J.V., A.H., J.F., A.D.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

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Morphologie 105 (2021) S1–S5

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CP AM.1

Ostéogenèse imparfaite : anomalies craniofaciales chez la souris oim

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Introduction Outre une grande fragilité osseuse, les patients atteints de la forme sévère (type III) d'ostéogenèse imparfaite présentent un facies triangulaire, une protubérance fronto-pariétale, un prognathisme relatif et de fréquents os wormiens [1]. La souris oim est un modèle validé des manifestations squelettiques de la maladie humaine, mais peu de données existent à propos des anomalies craniofaciales. Nous rapportons ici des observations densitométriques et céphalométriques chez la souris oim.

Matériel et méthodes Après euthanasie à 13 semaines, les têtes de souris oim ($n = 13$) et Wild type ($n = 12$) ont subi des analyses densitométrique (pQCT), céphalométrique et histomorphométrique.

Résultats Chez les souris oim, la densité minérale osseuse et la surface totale de l'os pariétal et du ramus mandibulaire sont significativement inférieures à celles des souris Wild type. À l'analyse histomorphométrique, l'épaisseur de l'os pariétal des souris oim est significativement inférieure à celle des Wild type. Ces résultats attestent la fragilité de ces os et corroborent des observations de fractures du crâne chez des patients atteints de l'ostéogenèse imparfaite de type III.

Sur les coupes frontales utilisées pour la densitométrie, la hauteur frontale supérieure, correspondant à la hauteur de la partie antérieure de la cavité crânienne, et la largeur interpariétale sont supérieures chez les souris oim par comparaison avec les Wild type, tandis que la largeur inter-temporale n'est pas modifiée. Ces données céphalométriques reflètent celles rapportées à propos du phénotype craniofacial de patient souffrant de l'ostéogenèse imparfaite de type III.

Conclusion Ces résultats permettent d'envisager la souris oim comme un modèle complet de l'ostéogenèse imparfaite humaine de type III, incluant le squelette craniofacial. Des analyses complémentaires, notamment par microCTscan et reconstruction tridimensionnelle, permettront d'obtenir des données supplémentaires à propos de la base du crâne et de la présence d'os wormiens.

Mots clés Ostéogenèse imparfaite ; Squelette craniofacial

Déclaration de liens d'intérêts Les auteurs déclarent ne pas avoir de liens d'intérêts.

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https://doi.org/10.1016/j.morpho.2021.05.005

CP AM.2

Reconstruction 3D du fœtus humain entre 7 et 14 semaines d'aménorrhée dans le cadre du projet FETTAL : optimisation du contraste en micro-TDM

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