SHORT SCIENTIFIC COMMUNICATION

What is new in tympanoplasty?

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ABSTRACT

Medicine is in an era of technical development and innovation. Creating a tympanic membrane by using a 3D printer can exceed the disadvantages that classic graft materials have. The field of otolaryngology can be experiencing a paradigm shift towards the use of 3D-printer.

KEYWORDS: 3D-printer, tympanoplasty, scaffold

INTRODUCTION

The tympanic membrane is composed of collagen fibers that are exactly aligned to enable sound waves to be transmitted to the ear ossicles. Mechanical movement is afterward transmitted by the ossicles to the inner ear where motion of the perilymph results in stimulation of the hair cells, which convert mechanical energy into neuronal impulses. Tympanic perforations, regardless of the cause (infectious, traumatic, iatrogenic), result in hearing loss due to ineffective sound transmission¹.

Surgical management of tympanic perforations is still a controversial topic. Currently, no surgical technique has 100% success rate. A successful tympanoplasty builds a barrier between the canal and the middle ear and also re-establishes sound transmission to the ossicular chain. Graft materials that are used in tympanoplasty (e.g. perichondrium, cartilage or fascia temporalis) do not possess similar structural arrangements as the native tympanic membrane and may have intrinsic defects. There are several potential healing problems after tympanoplasty as: lateralization of the graft, anterior blunting, epithelial cysts and reperforation. Revision surgery rates are 10-30%². Research in the field has become increasingly focused to reproduce the tympanic membrane. Technologies that exist in the clinic today can design and fabricate a biomimetic eardrum graft with the goal of reproducing specific structural features of the human tympanic membrane.

NEW TRENDS IN TYMPANOPLASTY

New possibilities are on the horizon. Modern 3D printing should be able to produce grafts that have the stiffness to reduce retractions, material properties to promote normal functionality of the tympanic membrane and biological properties that encourage graft acceptance.

The number of studies is growing rapidly: at the recent 10th International Conference on Cholesteatoma and Ear Surgery (5-8 June), Edinburgh, UK, a new study was reported by John J. Rosowski. The research group of Wyss Institute, Harvard University and Massachusetts Eye and Ear Infirmary has been able to make significant progress using 3D printing graft scaffolds. The constructed scaffolds can be printed using biocompatible or biological materials (fibrin and/or collagen biogels). Radial and circumferential fibrous arrangements of two separate filament counts (8 circumferential [C] x 8 radial [R] or 16 C x 16 R) were chosen for evaluation. As for materials, resorbable polycaprolactone (PCL) and nonresorbable polydimethylsiloxane (PDMS), that were studied to optimize 3D printed fiber configurations, were used³.

The study has shown that higher fiber counts (>8C/8R) improve fibroblast confluence on tympanic membrane grafts. Extremely high fiber counts (16 C/16R) limit the available hydrogel space between fibers, preventing fibroblast ingrowth. Deposition of collagen I in samples with fibrin-only hydrogel infill was confirmed by immunofluorescence; addition of colla-

gen I to the hydrogel infill improved cell proliferation. The scaffold can give strength and mechanical properties similar to those of real tympanic membranes, while infills of biological materials (including growth factors as basic fibroblast growth factor bFGF) can encourage growth acceptance³.

To study the mechanical properties of scaffolds, researchers used laser Doppler vibrometry (the laser directly measures the velocity of a single point near the umbo as opposed to some average motion of the entire tympanic membrane) and stroboscopic holography (quantifies mechanical oscillations)^{4,5}.

Another recent study was led by Lorenzo Moroni and the team from MERLN Institute for Technology-Inspired Regenerative Medicine at Maastricht University reported on 3D printed scaffolds with design features similar to the human tympanic membrane. The team has also been able to recreate, using the 3D printer, scaffolds using polymer-based materials that interfere with stem cells. Stem cells stimulate the proliferation of connective tissue and fibers in the lamina propria, possibly mediated by secreted substances, although the stiffness properties do not seem to be altered^{6,7}.

CLINICAL APPLICATION

An autologous graft may be associated with lack of graft material in revision cases and longer operative time. It is known the fact that the use of allografts can increase the potential risk of infection transmission.

A 3D printed eardrum may approximately reproduce the human tympanic membrane characteristics and should also promote wound healing as well as restoring the native trilaminar structure, which is decisive in maintaining the tympanic membrane vibroacoustic properties. The 3D graft would be advantageous in revision cases which translate to substantial economic benefits. An artificial tympanic membrane that is transparent is also highly desirable, as it allows direct visualization on the middle ear⁸. A graft available in various thicknesses and sizes can be tailored specifically for perforations of different sizes and for underlying pathology, such as middle ear inflammation and Eustachian tube dysfunction.

Furthermore, a 3D printer offers an easy and quick way to obtain tympanic grafts. Another advantage is that they will be available in unlimited quantities. An important fact, especially for women, is that artificial grafts cause no cosmetic changes in the ear.

Limitations of the 3D printed graft are that the attachment of the tympanic membrane to the malleus is purposefully not included in designs as the utility of such a structure in a biomimetic graft is as yet unclear. Surgical placement of 3D printed eardrum grafts will require consideration of graft orientation to allow for

a reliable connection to the ossicular chain⁹. Finally, the testing performed during this investigation was done *in vitro*. It will be difficult to foresee whether these results would be equivalent if the grafts were incorporated into living tissue.

The 349 model can be made quickly and inexpensively enough to have 350 potential applications for educational training.

CONCLUSIONS

These are exciting times in otology. Moving from the laboratory to clinical application is always a challenge. Although, of course, it is important to be pragmatic about what will really help patients. Perhaps we can all hope for a future in which 3D printing of the tympanic membrane is feasible.

Conflicts of interests: None

Contribution of authors: All authors have equally contributed to this work.

REFERENCES

1. Strens D., Knerer G., Van Vlaenderen I., Dhooge I. - A pilot cost-of-illness study on long-term complications/sequelae of AOM. *B-ENT* 8, 2012;8(3):153-165.
2. Rizer F.M. - Overlay versus underlay tympanoplasty. Part II: the study. *Laryngoscope*, 1997;107(12 Pt 2):26-36.
3. Kozin E.D., Black N.L., Chenq J.T., Cotler M.J., McKenna M.J., Lee D.J., Lewis J.A., Rosowski J.J., Remenschneider A.K. - Design, fabrication, and *in vitro* testing of novel three-dimensionally printed tympanic membrane grafts. *Hear Res.*, 2016. pii: S0378-5955(15)30281-1. doi: 10.1016/j.heares.2016.03.005.
4. McKnight C.L., Doman D.A., Brown J.A., Bance M., Adamson R.B. - Direct measurement of the wavelength of sound waves in the human skull. *J Acoust Soc Am.*, 2013;133(1):136-145. doi:10.1121/1.4768801.
5. Jakob A., Bornitz M., Kunlish E., Zahnert T. - New aspects in the clinical diagnosis of otosclerosis using laser Doppler vibrometry. *Otol Neurotol.*, 2009;30(8):1049-1057. doi: 10.1097/MAO.0b013e31819e622b.
6. Mota C., Danti S., D'Alessandro D., Trombi L., Ricci C., Puppi D., Dinucci D., Milazzo M., Stefanini C., Chiellini F., Moroni L., Berrettini S. - Multiscale fabrication of biomimetic scaffolds for tympanic membrane tissue engineering. *Biofabrication*, 2015;7(2):025005. doi: 10.1088/1758-9050/7/2/025005.
7. Woodfield T.B., Moroni L., Malda J. - Combinatorial approaches to controlling cell behaviour and tissue formation in 3D via rapid-prototyping and smart scaffold design. *Comb Chem High Throughput Screen.*, 2009;12(6):562-579.
8. Seonwoo H., Kim S.W., Kim J., Chunje T., Lim K.T., Kim Y.J., Pandey S., Choung P.H., Choung Y.H., Chung J.H. - Regeneration of chronic tympanic membrane perforation using an EGF-releasing chitosan patch. *Tissue Eng Part A.*, 2013;19(17-18):2097-2107. doi: 10.1089/ten.TEA.2012.0617.
9. Teh B.M., Marano R.J., Shen Y., Friedland P.L., Dilley R.J., Atlas M.D. - Tissue engineering of the tympanic membrane. *Tissue Eng Part B Rev.*, 2013;19(2):116-132. doi: 10.1089/ten.TEB.2012.0389. Epub 2012 Nov 29.