

**This item is the archived peer-reviewed author-version of:**

Endoscopic versus transcranial procurement of allograft tympano-ossicular systems : a prospective double-blind randomized controlled audit

**Reference:**

Caremans Jeroen, Hamans Evert, Muylle Ludo, van de Heyning Paul, van Rompaey Vincent.- Endoscopic versus transcranial procurement of allograft tympano-ossicular systems : a prospective double-blind randomized controlled audit Cell and tissue banking - ISSN 1573-6814 - (2015), p. 1-6  
DOI: <http://dx.doi.org/doi:10.1007/s10561-015-9531-8>

**ENDOSCOPIC VERSUS TRANSCRANIAL PROCUREMENT OF ALLOGRAFT  
TYMPANO-OSSICULAR SYSTEMS: A PROSPECTIVE DOUBLE-BLIND RANDOMIZED  
CONTROLLED AUDIT.**

*Endoscopic procurement is the new standard technique.*

Caremans Jeroen, MSc <sup>1</sup>

Hamans Evert, MD, PhD <sup>1,2,3</sup>

Muyllé Ludo, MD, PhD <sup>1,3</sup>

Van de Heyning Paul, MD, PhD <sup>1,2,3</sup>

Van Rompaey Vincent, MD, PhD <sup>2,3</sup>

<sup>1</sup>University of Antwerp Temporal Bone Bank, Tissue and Cell Bank, Antwerp University Hospital,  
Edegem, Belgium

<sup>2</sup>Department of Otorhinolaryngology and Head & Neck Surgery, Antwerp University Hospital,  
Edegem, Belgium.

<sup>3</sup>Faculty of Medicine and Health Sciences, University of Antwerp, Campus Drie Eiken, Antwerp,  
Belgium.

Corresponding author

Vincent Van Rompaey, MD, PhD

Antwerp University Hospital

Dept. of Otorhinolaryngology and Head & Neck Surgery

Wilrijkstraat 10, 2650 Edegem, Belgium

vincent.van.rompaey@uza.be

*+32/3.821.47.30*

*+32/3.825.05.36*

## **ABSTRACT**

**Objective:** Allograft tympano-ossicular systems (ATOS) have proven their use over many decades in tympanoplasty and reconstruction after resection of cholesteatoma. The transcranial bone plug technique has been used in the past 50 years to procure *en bloc* ATOS (tympanic membrane with malleus, incus and stapes attached). Recently, our group reported the feasibility of the endoscopic procurement technique.

The aim of this study was to assess whether clinical outcome is equivalent in ATOS acquired by using the endoscopic procurement technique compared to ATOS acquired by using the transcranial technique.

**Study design:** Double-blind randomized controlled audit.

**Setting:** Tertiary referral center.

**Patients:** Patients that underwent allograft tympanoplasty because of chronic otitis media with and without cholesteatoma.

**Main outcome measures:** Allograft epithelialisation was evaluated at the short-term postoperative visit by microscopic examination. Failures were reported if reperforation was observed.

**Results:** Fifty patients underwent allograft tympanoplasty: 34 received endoscopically procured ATOS and 16 received transcranially procured ATOS. One failed case was observed, in the endoscopic procurement group. We did not observe a statistically significant difference between the two groups in failure rate.

**Conclusions:** This study demonstrates equivalence of the clinical outcome of allograft tympanoplasty using either endoscopic or transcranial procured ATOS and therefore indicates that the endoscopic technique can be considered the new standard procurement technique. Especially because the endoscopic procurement technique has several advantages compared to the former transcranial procurement technique: it avoids risk of prion transmission and it is faster while lacking any noticeable incision.

**Keywords:** Tympanic membrane – Ear ossicles – Endoscopy – Allograft – Tissue banks

## INTRODUCTION

Allograft tympano-ossicular systems (ATOS) have proven their use over many decades in tympanoplasty, ossiculoplasty and reconstruction after resection of cholesteatoma. (Van Rompaey, Farr et al. 2013) The first published account of allograft tympanoplasty was by Ned Chalat (Detroit, Michigan) in 1964. (Chalat 1964) However, the 3 transplanted tympanic membranes he reported all reperforated in the long term. In 1966, Jean Marquet (Antwerp, Belgium) published his results after transplanting allograft tympanic membranes. (Marquet 1966) He can be credited as the first surgeon to report clinically successful transplantation of tympanic membranes. Since that time, a number of surgeons have trialed both *en bloc* tympano-ossicular techniques and tympanomeatal techniques with separate ossicle interposition or columellar reconstruction. (Van Rompaey, Farr et al. 2013)

In the 1980s and the 1990s the emergence of the Human Immunodeficiency Virus (HIV) and later the variant Creutzfeldt-Jakob's disease (vCJD) - as part of the Bovine Spongiform Encephalopathy (BSE) crisis - led to the downfall of ATOS use because of fear of transmitting disease to the acceptor. However, until now there is no evidence that ATOS have ever transmitted infectious or malignant disease. (Van Rompaey, Farr et al. 2013) Allograft tympanoplasty has been continued by otolaryngologists in the Antwerp University Hospital in specific indications and our group has demonstrated the feasibility of running a tympano-ossicular tissue bank complying with European Union (EU) regulations on human allografts, confirmed by inspection and authorisation by the Belgian Federal Agency of Medicines and Health Products, the competent authority (Van Rompaey, Vandamme et al. 2012). The quality management system of the tympano-ossicular tissue bank is critical to assure that the patient receives tissue, which is safe, individually checked and prepared in a suitable environment.

The *en bloc* ATOS with complete ossicular chain can only be procured through the traditional transcranial technique as described by Schuknecht. (Merchant and Nadol 2010) Two temporal bone plugs are removed with the bone plug cutter, which is a circular oscillating saw blade. After the brain has been removed, the saw is centered on the arcuate eminence and advanced in an inferior direction until it has passed through the skull base. This plug of bone contains the bony part of the external

auditory canal, the middle ear, the bony labyrinth, the internal auditory canal, the petrous apex, part of the Eustachian tube, and most of the mastoid. (Merchant and Nadol 2010)

However, most otologists involved in allograft tympanoplasty gradually abandoned the *en bloc* ATOS with complete ossicular chain and preferred the tympanomeatal allograft. This tympanomeatal allograft without ossicles (HT) or with only the malleus attached for support (HTM) could be implanted and combined with a columellar reconstruction using the sculpted allograft incus or malleus (HIr or HMr) in case of ossicular chain erosion. (Marquet 1971, Marquet 1977, Somers, Van Rompaey et al. 2012)

Because the *en bloc* ATOS had become obsolete, the traditional transcranial technique was challenged due to its many disadvantages, including the potential risk for prion disease transmission by handling of the dura mater, particularly related to CJD and vCJD (although never reported), its esthetic invasiveness because a craniotomy had to be performed (and reconstructed) and the need to dissect the *en bloc* ATOS in the clean room after procurement which is time-consuming. (Meylan, Duscher et al. 1996) This evolution has led our group to introduce an endoscopic transmeatal procurement technique by which a HTM and separate incus are procured. (Van Rompaey, van Dinther et al. 2012, Van Rompaey, Caremans et al. 2013)

Endoscopic procurement has several advantages compared to the traditional transcranial bone plug technique: contact with the dura mater is avoided and therefore the risk of prion transmission is prevented. Moreover, it is less time-consuming - since procurement and dissection are performed simultaneously - and not esthetically invasive since the transmeatal incision is limited to the external auditory canal and therefore invisible externally. Its technical feasibility has already been reported (Van Rompaey, Caremans et al. 2013) as well as the equivalent ATOS in vitro quality, the gain in procurement time and the increase in donor number (Caremans, Hamans et al. 2015).

The aim of this study was to assess whether the clinical outcome of ATOS acquired by using the endoscopic procurement technique is equivalent to the clinical outcome of ATOS acquired by using the transcranial technique.

## **MATERIALS AND METHODS**

### *Ethics and regulations*

The study was designed and conducted according to the Declaration of Helsinki (1996). Ethic committee approval was obtained for auditing clinical outcome. The quality management system and standard operating procedures on critical activities of the tympano-ossicular tissue bank (including donor selection, procurement, preparation, laboratory investigations, preservation, storage and distribution) were reported earlier by our group. (Van Rompaey, Vandamme et al. 2012) Donor inclusion was identical in both groups and complying with Belgian national and EU regulations.

### *Procurement techniques*

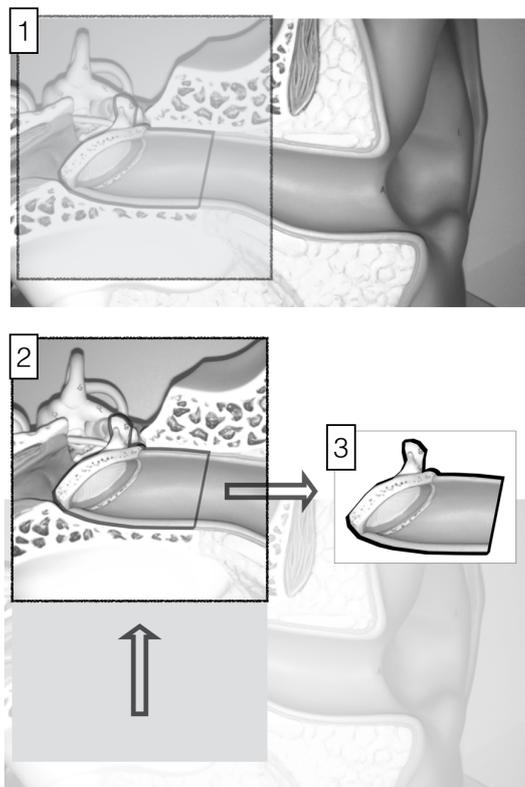
Transcranial procurement was performed using the traditional bone plug technique as described by Schuknecht and represented in figure 1A. (Merchant and Nadol 2010) Through the craniotomy two temporal bone plugs are obtained, and fixated in a buffered 2.7 – 4.0% formaldehyde solution with pH 5 - 6. In a cleanroom, ATOS are dissected from the temporal bone plugs and preserved in new formaldehyde solution.

Transmeatal procurement is performed using the endoscopic technique as described by our group and represented in figure 1B. (Van Rompaey, Caremans et al. 2013) The 30° angled rigid Hopkins rod nasal endoscope, portable Tele Pack X with telecam camera head (Karl Storz, Tuttlingen, Germany), Rosen knife, angled microforceps and microhook were used.

1. The meatal cuff is incised using a Rosen knife. The cuff is released circumferentially from the bony canal using a Rosen knife.
2. The fibrous annulus is released from the bony annulus and the mucosa is incised using a Rosen knife or Thomassin/Fisch dissector. The chorda tympani is cut.
3. The incudostapedial joint is separated and the incus is released from the malleus head using a microhook. The incus is procured using an angled microforceps.

4. The allograft, consisting of a 360° meatal cuff, the fibrous annulus, the tympanic membrane and the malleus, is procured by clenching the malleus neck or head with a microforceps and gently pulling the allograft through the external auditory canal.
5. The cuff is manually unfolded and then further unfolded in saline water. When the allograft has retrieved its natural form, it's fixated in a buffered 2.7 – 4.0 % formaldehyde solution with pH 5 – 6.

### A. Transcranial procurement



### B. Endoscopic procurement

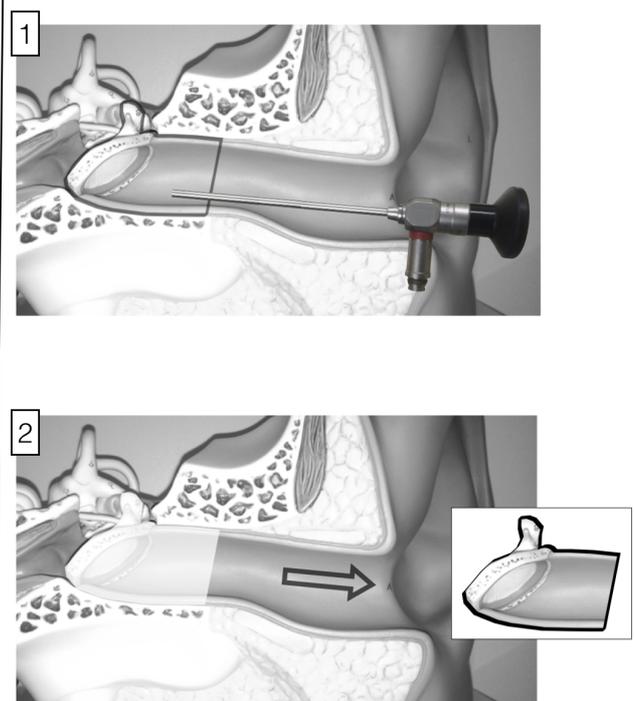


Figure 1

### Quality control

The in vitro quality of the newly procured allografts is verified in a cleanroom by an accredited ENT surgeon. The allografts are rinsed in sterile water and then checked under the microscope. In order to prevent cross-contamination, new sterile gloves and a new forceps are used for each donor. When the ATOS have been checked, they are put in a new recipient filled with buffered formaldehyde solution. The quality of the allograft is based on the quality of the eardrum (tympanosclerosis, weak spots,

perforations), the quality of the cuff (length, fissures, form) and the integrity of the fibrous annulus. All ATOS listed as 'good quality' can be used for any indication in ear surgery. Other ATOS may still be used but only for specific indications.

#### *Patient characteristics and study design*

All consecutive tympanoplasty cases were included where ATOS were used to reconstruct the tympanic membrane, i.e. subtotal or total perforation, pars tensa cholesteatoma and attical cholesteatoma. The tympanoplasty procedures were performed by eight different surgeons in the Antwerp University Hospital from November 2013 to November 2014 using the same surgical technique.

Patients were randomized to the transcranial or the transmeatal ATOS by the tympano-ossicular tissue bank technician blinded to the patient characteristics. The surgeon was unaware of how the ATOS was procured, during surgery as well as during clinical follow-up. The data were unblinded after obtaining the 3-month prospective electronic case report forms of the last included patient.

#### *Outcome measures*

The graft take-rate was evaluated at three months postoperatively. We used the Ear Audit case report forms to collect data prospectively. This is a prospective audit and database tool, also known as the Common Otology Database, designed to assess clinical outcome in different types of middle ear surgery, including myringoplasty, ossiculoplasty, cholesteatoma surgery and stapes surgery (Van Rompaey, Yung et al. 2009, Van Rompaey, Yung et al. 2010). The surgeon checked whether the tympanic membrane was intact or not - re-perforation was considered a failure - and whether there were any minor adverse events like myringitis or anterior blunting.

#### *Statistics*

A p-value of 0.05 or less was considered as statistically significant. The Pearson Chi Square test was used to compare stochastic variables in 2 nonparametric groups.

## **RESULTS**

Fifty patients underwent allograft tympanoplasty: 34 received endoscopically procured ATOS (group A) and 16 received transcranially procured ATOS (group B). Group A included 21 male and 13 female subjects, age ranging from 6 to 81 years (median, 31 years); group B included 10 male and 6 female subjects, age ranging from 6 to 73 years (median, 43 years). Follow-up ranged from 5 weeks to 43 weeks, median follow-up was 11 weeks. One patient from group A was lost to follow-up. One case of reperforation was observed in group A, in the endoscopic procurement group. One case developed anterior blunting in group A, which is considered a minor adverse event. No adverse events were observed in group B.

We did not observe a statistically significant difference between the two groups in failure or minor adverse events (p value 0.495).

## DISCUSSION

In this study, we have observed clinical outcome (i.e. graft take-rate) in allograft tympanoplasty using either endoscopic (97% epithelialized tympanic membranes) or transcranial procured ATOS (100% epithelialized tympanic membranes). This difference might be caused by the higher number of endoscopically procured allografts. Because these graft take-rates are higher than those reported in cases where autologous materials were used for tympanoplasty (i.e. 93%), we consider both techniques to be equivalent (Andersen 2014).

The endoscopic procurement technique has several obvious advantages compared to the transcranial technique. Because the end product is procured immediately from the donor rather than dissected from the procured temporal bone plug later in the cleanroom, endoscopic procurement is significantly less time-consuming. An earlier study performed by our group reported a median procurement time of the left and right ATOS at 172.5 minutes in the transcranial procurement (including dissection time in the cleanroom) and 85 minutes in the endoscopic procurement. (Caremans, Hamans et al. 2014) Meanwhile, procurement time in the endoscopic procurement technique has further decreased. There is also an important impact on the safety of ATOS: since the dura mater is not manipulated during endoscopic procurement, the potential risk of transmitting prions is reduced to zero. Finally, the endoscopic technique does not require donor site reconstruction because there is no visible incision. The latter has two major consequences: first of all, the endoscopic procurement technique is more acceptable to cooperating hospitals and donor relatives; moreover, potential donors that were formerly excluded for transcranial procurement because hair was lacking to adequately conceal the incision (a relative contraindication), can now be considered for the endoscopic technique resulting in a significant increase of 189% in donor number. (Caremans, Hamans et al. 2015)

There are some challenges for the endoscopic technique as well. It can be performed by a technician, but intensive training is required. Experience with ATOS dissection from a temporal bone plug or middle ear surgery in general is helpful, but handling the endoscope is not self-evident for the technician. Donors with a very curved auditory canal may present difficulties with visibility and

accessibility by the instruments. And finally, when dissecting ATOS from a temporal bone plug stored in buffered formaldehyde solution, the ATOS have already been fixated in their natural form. Since the endoscopically procured ATOS have not been fixated, it is important to unfold and relax them patiently to their natural shape before fixation in the buffered formaldehyde solution.

## **CONCLUSION**

This study demonstrates equivalence of the clinical outcome of allograft tympanoplasty using either endoscopic or transcranial procured ATOS and therefore indicates that the endoscopic technique can be considered the new standard procurement technique. Especially because the endoscopic procurement technique has several advantages compared to the former transcranial procurement technique: it avoids risk of prion transmission and it is faster while lacking any noticeable incision.

## **ACKNOWLEDGEMENTS**

We would like to thank all additional ENT surgeons involved in the reported allograft tympanoplasty cases: Paul Govaerts, Anouk Peeters, Jozef Claes, Carl Van Laer and Erwin Koekelkoren.

## FIGURE LEGENDS

**Figure 1.** Schematic representation comparing the transcranial technique with the endoscopic technique for ATOS procurement. A. When using the transcranial procurement technique, a craniotomy is performed to approach the temporal bone from the middle fossa side (1). The temporal bone plug is created by using a circular oscillating saw blade (2). After removal of the temporal bone plug, the ATOS can be dissected in the cleanroom (3). B. When using the endoscopic procurement technique, the ATOS are approached through the external auditory canal assisted by the 30° nasal endoscope (1). The ATOS can be dissected directly from the bony external auditory canal to remove the end product (2).

## REFERENCES

- Andersen SA, Aabenhus K, Glad H, Sørensen MS (2014) Graft take-rates after tympanoplasty: results from a prospective ear surgery database. *Otol Neurotol* 35:e292-7.
- Caremans J, Hamans E, Muylle L, Van de Heyning P and Van Rompaey V (2015) Endoscopic procurement of allograft tympano-ossicular systems: valuable to replace the Schuknecht bone plug technique? *Cell Tissue Bank* 16:91-96.
- Chalat N (1964) Tympanic Membrane Transplant. *Harper Hosp Bull* 22:27-34.
- Marquet J (1966) Reconstructive micro-surgery of the eardrum by means of a tympanic membrane homograft. Preliminary report. *Acta Otolaryngol* 62:459-464.
- Marquet J (1971) Human middle ear transplants. *J Laryngol Otol* 85:523-539.
- Marquet J (1977) Historical notes on homografts. *Otolaryngol Clin North Am* 10: 479-485.
- Merchant S and Nadol J (2010) Schuknecht's Pathology of the Ear. Ontario, Canada, McGraw-Hill.
- Meylan P, Duscher A, Mudry A, Monnier P (1996) Risk of transmission of human immunodeficiency virus infection during tympano-ossicular homograft: an experimental study. *Laryngoscope* 106:334-337.
- Somers T, Van Rompaey V, Claes G, Salembier L, van Dinther J, Zarowski A, Offeciers E (2012) Ossicular reconstruction: hydroxyapatite bone cement versus incus remodelling: how to manage incudostapedial discontinuity. *Eur Arch Otorhinolaryngol* 269:1095-1101.
- Van Rompaey, V, Caremans J, Hamans E, Muylle L, Van de Heyning P (2013) Endoscopic procurement of tympano-ossicular allografts: alternative to the transcranial or retroauricular technique. *Cell Tissue Bank* 14:511-514.
- Van Rompaey, V, Farr M, Hamans E, Mudry A, Van de Heyning P (2013) Allograft tympanoplasty: a historical perspective. *Otol Neurotol* 34:180-188.
- Van Rompaey, V, van Dinther J, Somers T, Vanhoof L, Maes M, Schatteman I, Offeciers E (2012) "Transmeatal Procurement of Allograft Tympano-Ossicular Systems: Preliminary Report (Alternative to the intracranial bone plug technique by Schuknecht). *Int Adv Otol* 8:154-157.

Van Rompaey, V, Vandamme W, Muylle L, Van de Heyning P (2012) Temporal bone bank: complying with European Union directives on human tissue and cells. *Cell Tissue Bank* 13:231-240.

Van Rompaey, V, Yung M, Claes J, Hausler R, Martin C, Somers T, Offeciers E, Pytel L, Skladzien J, Van de Heyning P (2009) Prospective effectiveness of stapes surgery for otosclerosis in a multicenter audit setting: feasibility of the Common Otology Database as a benchmark database. *Otol Neurotol* 30:1101-1110.

Van Rompaey, V, Yung M, Van de Heyning P (2010) Auditing in middle ear surgery, feasibility of the common otology database. *B-ENT* 6:189-194.