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Restoration of middle-ear input in fluid-filled middle ears by controlled introduction of air or a novel air-filled implant

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ABSTRACT

The effect of small amounts of air on sound-induced umbo velocity in an otherwise saline-filled middle ear (ME) was investigated to examine the efficacy of a novel balloon-like air-filled ME implant suitable for patients with chronically non-aerated MEs. In this study, air bubbles or air-filled implants were introduced into saline-filled human cadaveric MEs. Umbo velocity, a convenient measure of ME response, served as an indicator of hearing sensitivity. Filling the ME with saline reduced umbo velocity by 25–30 dB at low frequencies and more at high frequencies, consistent with earlier work (Ravicz et al., Hear. Res. 195: 103–130 (2004)). Small amounts of air (~30 μl) in the otherwise saline-filled ME increased umbo velocity substantially, to levels only 10–15 dB lower than in the dry ME, in a frequency- and location-dependent manner: air in contact with the tympanic membrane (TM) increased umbo velocity at all frequencies, while air located away from the TM increased umbo velocity only below about 500 Hz. The air-filled implant also affected umbo velocity in a manner similar to an air bubble of equivalent compliance. Inserting additional implants into the ME had the same effect as increasing air volume. These results suggest these middle-ear implants would significantly reduce conductive hearing loss in patients with chronically fluid-filled MEs.

1. Introduction

Middle-ear effusion (fluid in the middle ear) is a well-known cause of conductive hearing loss, and otitis media with effusion (OME) is responsible for thousands of medical office visits each year (Lieberthal et al., 2013) and affects millions worldwide (Merchant et al., 1998b; Monasta et al., 2012). The effusion can be serous or mucoid (e.g., Cunningham and Eavey, 1993) and can be the result of middle-ear disease or other conditions that result in poor middle-ear (ME) aeration. The presence of ME effusion (and any associated ME static pressure) induces a conductive hearing loss of generally 20–40 dB in cases of acute OME (Bluestone et al., 1973; Fria et al., 1985; Merchant and Rosowski, 2003) and up to 60–70 dB in cases of chronic otitis media (COM; Merchant et al., 1998b; Merchant and Rosowski, 2013).

In cases of acute OME, the hearing loss is usually resolved when the fluid is drained to aerate the ME via myringotomy and placement of a tympanostomy tube (e.g., Bluestone and Klein, 2007). The myringotomy also relieves any static pressure difference across the tympanic membrane (TM) and improves the quality of life (Witsell et al., 2005). While conditions leading to OME often abate after normal clinical and surgical treatment, in a significant fraction of cases the effusion returns when the myringotomy is healed, and the conductive hearing loss recurs (Cassebrandt et al., 1992; Nadol and McKenna, 2005; Gaihede et al., 2007; Gulya et al., 2010; Lieberthal et al., 2013) – perhaps due to the same dysfunction in ME aeration that led to the effusion in the first place.

With COM, the standard therapy is surgical (mastoidectomy and tympanoplasty procedures), with the goals of surgery being eradication of disease, prevention of recurrence, and improvement in hearing. In the United States, over 70,000 tympanoplasty surgeries are performed annually (Ruben, 1982). While tympanomastoid surgery is successful in controlling infection with a success rate in excess of 80–90%, postoperative hearing results are more modest (Nadol and McKenna, 2005; Gulya et al., 2010): In general, long-

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List of abbreviations and variables

C	compliance of a small quantity of air
C_{Vial}	compliance of the air in the small measurement vial
c	speed of sound
COM	chronic otitis media
EAV	equivalent acoustic volume of implant
f	frequency
ME	middle ear
N	number of trials
OME	otitis media with effusion
$p(0)$	probability that the null hypothesis is true
$\mathbf{P_{EC}}$	sound pressure in the ear canal
R	correlation coefficient
ρ_0	density of air
TM	tympanic membrane
$\%TM_{air}$	percentage of TM area contacted by air
V	volume of a small quantity of air
$V_{Implant}$	volume of an implant
V^A_{Vial}	acoustic volume of the small measurement vial
$V^A_{Vial+Implant}$	acoustic volume of the small measurement vial with an implant inside
V_{MEC}	volume of middle-ear cavity
$\%V_{MEC}$	percentage of middle-ear cavity volume filled with air
$\mathbf{V_U}$	Umbo velocity
$\mathbf{\Delta V_U}$	change in $\mathbf{V_U}$ from the normal condition
$\mathbf{Y}$	acoustic admittance
$\mathbf{Y_{Vial}}$	acoustic admittance of the air in the small measurement vial

term closure of the air-bone gap to 20 dB or less occurs in only 40–70% of cases (Merchant et al., 1998a,b). The most common cause of failure of tympanoplasty to restore hearing is non-aeration of the ME due to chronic Eustachian tube dysfunction or deposition of fibrous tissue (Merchant et al., 1998a). Though balloon dilation tuboplasty has shown promise as a way to improve ME aeration by enlarging the Eustachian tube orifice (e.g., Ockermann et al., 2010; Poe et al., 2011), the long-term outcome of this procedure is still under examination. Thus, currently there is no approved long-lasting and reliable way of re-aerating the MEs of patients with COM after tympanomastoidectomy surgery.

In an earlier study of mechanisms of hearing loss in OME (Ravicz et al., 2004), in which saline or silicone fluid was instilled into cadaver MEs through the Eustachian tube to mimic ME effusion, we showed that (a) reductions in sound-induced umbo velocity due to ME fluid match hearing loss in OME patients (when the effect of ME static pressure is taken into account) and (b) the reduction in umbo velocity with fluid present is produced by different mechanisms in different frequency ranges. At low frequencies (500 Hz and below), the reduction in umbo velocity is independent of the location of the fluid, and the primary effect of the fluid is consistent with a reduction in ME compliance (the ability of the TM to move in response to sound) caused by the replacement of the compressible air in the ME with incompressible fluid (Fig. 1A). A simple model predicted the reduction in umbo velocity fairly well (Fig. 1A). At high frequencies (above 1–2 kHz), the reduction is due to an increase in the effective mass of the TM by the fluid contacting it, and the same amount of fluid produces a greater reduction if it is contact with the TM than if it is in other parts of the ME remote from the TM (Fig. 1B). Completely filling the ME air spaces with fluid, which proved to be difficult to achieve, resulted in 25–35 dB reductions in TM and umbo motion across all tested frequencies. A conclusion from that study is that a small amount of air in the otherwise fluid-filled ME partly lessens the reduction in umbo velocity (Fig. 1C) and should restore some hearing. Similar conclusions were reached in live animal studies (Guan and Gan, 2013; Guan et al., 2014).

There are also clinical demonstrations that the presence of small amounts of air or other gases in the otherwise effusion-filled ME improve hearing sensitivity (e.g., Andréasson et al., 1978, 1983; Koch and Becker, 1981). To this end, some clinicians and investigators have injected air or gases with lower diffusivity into the effusion-filled MEs of patients (e.g., Koch and Becker, 1981; Andréasson et al., 1983; Silverstein et al., 1993; Silman et al., 2005). These injections produce transitory improvements in hearing that are eventually reduced to the original pathological state. The limiting factor in this transitory improvement is the time required for the air or other gas to be absorbed and replaced by fluid (Andréasson et al., 1983) — generally on the order of a few days to a few weeks.

This success in restoring hearing in fluid-filled MEs, even on a transitory basis, points out that a balloon-like implant that maintains a small air volume in the ME could provide a longer-term solution for hearing loss in chronic OME. A successful implant that provides a permanent functional air space must satisfy the following conditions (Merchant et al., 2010): (1) *Physical properties*: It must be sufficiently small to fit into the ME without hindering the motion of the ossicles or other ME structures important for hearing. (2) *Barrier properties*: It must resist diffusion of air and exudate to maintain an air-filled space in a physiological environment. (3) *Acoustical properties*: It must have sufficient acoustic compliance to allow sound waves to compress it. (4) *Biocompatibility properties*: It must resist degradation from physiological processes inside the body and must not provoke a physiological foreign-body response. Previous attempts to develop such an implant (e.g., Gaudin, 1968; Gerhardt, 1984) have failed because they have been unable to meet these conditions.

In this paper we evaluate (1) the effects of the presence and location of a small air bubble in a saline-filled ME on sound-induced umbo motion, and (2) the performance of a novel ME implant that satisfies the conditions described above. To perform this evaluation we use the temporal-bone preparation developed for our investigations of the effect of fluid on ME sound conduction (Ravicz et al., 2004). Such cadaveric temporal bone preparations have been shown to be representative of the live ear for many ME processes (e.g., Rosowski et al., 1990, 2007; Goode et al., 1993; Chien et al., 2009) and have been used to study the effects of ME fluid on hearing (Ravicz et al., 2004; Gan et al., 2006; Dai et al., 2008; Zhang et al., 2014). In this paper we further explore the effects of small air bubbles in a saline-filled cadaveric ME and determine the effects of total air volume and location on umbo velocity. We introduce one or more implants into an otherwise saline-filled ME and demonstrate that the effect of the implants on umbo velocity are comparable to that of air bubbles of similar compliance and location within the ME. These novel ME implants could restore hearing in patients with chronically non-aerated MEs.

2. Materials and methods

2.1. Preparation

The management of human data was performed in accordance with guidelines published by the U.S. Public Health Service for the use of de-identified post-mortem human material.