



DENNIS POE

Pathophysiology and Surgical Treatment
of Eustachian Tube Dysfunction



ACADEMIC DISSERTATION

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University of Tampere, School of Medicine

Päijät-Häme Central Hospital, Department of Otolaryngology

Finland

Children's Hospital Boston, Department of Otolaryngology

USA

Tel-Aviv University, Tel-Aviv Sourasky Medical Center, Department of Otolaryngology

Israel

Supervised by

Professor Ilmari Pyykkö

University of Tampere

Finland

Reviewed by

Docent Timo Hirvonen

University of Helsinki

Finland

Professor Heikki Löppönen

University of Eastern Finland

Finland

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Distribution

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P.O. Box 617

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1 ABSTRACT

The purpose of this study was to develop methods for quantitative analysis of Eustachian tube (ET) function to supplement video endoscopy and to apply the knowledge gained to the creation of new surgical procedures to treat refractory dilatory or patulous dysfunction of the ET.

Prospective studies were performed on adult normal subjects and patients with otitis media with effusion (OME) or patulous ETs in tertiary medical centers and on human cadaver heads. Timing and metric parameters were measured from the endoscopic videos. Analyses of endoscopy with simultaneous sonotubometry were conducted in normal subjects. Patients with refractory OME underwent laser Eustachian tuboplasty (LETP) procedures to vaporize mucosa, submucosa, and cartilage, thinning the postero-medial wall of the ET. The feasibility and safety of an alternative procedure, balloon dilation of the ET was investigated in cadavers and then performed on patients with refractory OME. Patients with patulous ETs underwent surgical augmentation of the concave defect found in the antero-lateral wall.

Diagnostic analyses were done on 27 normal, 13 OME and 15 patulous subjects. Mean values for normals: angle of torus tubarius rotation 34.2° (SD 14.3) and excursion of the antero-lateral wall 35.5 % of torus tubarius height (SD 16.3). Lateral excursion wall was significantly less in patulous ET (18.7%, SD 15.1, $p=0.001$) and in OME (23.9%, SD 21.7, $p=0.048$). During sonotubometry, all showed normal endoscopy and appeared to open, but only 11/17 opened by objective criteria of 5 dB increase in signal with swallows (ave. duration 0.43 s) and 13/17 with yawns (ave. 2.03s). LETP in conjunction with tympanostomy tube was performed in 13 patients and eliminated OME in 4/11 at 6 months, 3/10 at 1 year, and 3/8 at 2 years. Balloon dilation catheters successfully dilated all cadaver ETs without significant adverse effects and average tubal volume increased from 0.16 to 0.49 cm^3 (SD 0.12). In 11 patients undergoing balloon dilation, all cases successfully dilated. 11/11 could autoinsufflate by Valsalva ($p<0.001$); tympanograms were A: 4/11, C: 1/11, or open (perforation or tube): 6/11. All atelectases resolved. There were no complications related to the dilation. 14 patients underwent patulous ET reconstruction; 1 had complete relief, 5 had significant improvement and were satisfied, 7 improved but were dissatisfied, and 1 was unchanged. There were no complications.

The ET contains a functional valve within the cartilaginous segment and its failure may lead to middle ear disorders. On video endoscopy, lateral excursion of the antero-lateral wall was reduced in OME and patulous ETs. This parameter can now be further studied in the search for pathophysiology of tubal dysfunction. Sonotubometry failed to record tubal opening in all subjects, but when it occurred it was more accurately determined than by endoscopy. The combined technology provides complimentary information and is promising for future use.

LETP was safe, without significant complications, and could improve severely refractory OME. It is promising for expanded indications in ET surgery. Alternatively, balloon dilation was shown to be safe, technically feasible and with some reasonable possibility for clinical efficacy. Randomized clinical trials of the procedure are indicated. Patulous

ET reconstruction was successful in relieving symptoms and future work is needed to improve the instrumentation and graft materials.

2 ABBREVIATIONS

CCD	Charge Coupled Device
cm	centimeter
CO ₂	Carbon Dioxide
CT	Computed Tomographic
dB	decibel
DV	Digital Video
EAC	External Auditory Canal
ET	Eustachian Tube
H ₂ blocker	Histamine receptor type 2 antagonist
KTP	Potassium-titanyl-phosphate
LETP	Laser Eustachian Tuboplasty
LVP	Levator Veli Palatini
mg	milligram
mmHg	Millimeters of mercury
MPR	Multi Planar Reconstruction
N ₂	Nitrogen
OME	Otitis Media with Effusion
O ₂	Oxygen
PETR	Patulous Eustachian Tube Reconstruction
PTA	Pure Tone Average
RMS	Root Mean Square
SCD	Semicircular Canal Dehiscence
SPSS	Statistical Package for Social Sciences
s-VHS	Super Video Home System
TVP	Tensor Veli Palatini

3 LIST OF ORIGINAL COMMUNICATIONS

The thesis is based on the following original papers, which are referred to by their numbers:

1. Poe DS, Pyykkö, I. Measurements of Eustachian tube dilation by video endoscopy. *Otol Neurotol* 2011 Jul;32(5):794-8
2. Handzel O, Poe, D, Marchbanks, R. Combined sonotubometry and slow motion video endoscopy of Eustachian tube dilation. Accepted to *Otol Neurotol*.
3. Poe DS, Grimmer JF, Metson R. Laser Eustachian tuboplasty: two-year results. *Laryngoscope*. 2007;117(2):231-7.
4. Poe D, Hanna B. Balloon dilation of the cartilaginous portion of the Eustachian tube. *Am J Otolaryngology* Apr 12, 2010
5. Poe DS, Silvola J, and Pyykkö I. Balloon Dilation of the Cartilaginous Eustachian Tube. *Otolaryngology -- Head and Neck Surgery*. 2011 April 1; 144(4): 563 - 569.
6. Poe DS. Diagnosis and Management of the patulous Eustachian tube. *Otol Neurotol*. 2007;28:668-677

4 INTRODUCTION

The Eustachian tube connects the middle ear cavity with the naso-pharynx, performs the critical roles of aeration and drainage of the middle ear cavity and protects the middle ear from reflux of sound and material from the nasopharynx. The first known mention of the Eustachian tube was in the writings of Alcmaeon of Sparta in 400 B.C., (Bluestone and Bluestone 2005) but Bartolomeus Eustachius is credited with its discovery in 1562 when he published a detailed description of its anatomy and physiologic function. (Eustachius 1944) Valsalva later described the Eustachian tube as having cartilaginous and osseous parts and he was the first to recognize the importance of the tensor veli palatini muscle in opening the Eustachian tube. (Canalis 1990) Additionally, he described the Valsalva maneuver, which remains clinically relevant to this day. Toynbee furthered our understanding of the Eustachian tube through extensive investigations of the peri-tubal muscles (Toynbee 1853) and Politzer made important contributions in recognizing the role of the Eustachian tube in middle ear pathology. (Bluestone and Bluestone 2005)

Eustachian tube dysfunction is believed to be the leading cause of otitis media, but the nature of the pathology remains undetermined. Previous work has principally focused on studying the limitations of tubal fluid dynamics through the bony-cartilaginous isthmus, which is the narrowest portion of the lumen. Despite the extensive analyses that have resulted from these efforts, tests to measure various aspects of tubal flow and pressure have failed to consistently correlate with clinical findings. Surgical treatments to widen the isthmus have not been beneficial. There is evidence that acute otitis media and otitis media with effusion are associated with inflammatory and anatomical changes in the cartilaginous portion of the Eustachian tube. We have proposed a hypothesis that the cartilaginous portion of the Eustachian tube functions as a valve and that malfunction of the valve can result in pathology or symptoms in the middle ear. Pathological changes in the tubal orifice and valve have been demonstrated to correlate closely with the presence of middle ear atelectasis or middle ear effusion. Therapy directed toward correction of the valve's function should be expected to improve otitis media and alleviate middle ear symptoms. Initial attempts to surgically widen the valve as a treatment for dilatory dysfunction and to narrow it for patulous dysfunction have met with some preliminary success.

Endoscopy of the Eustachian tube has greatly aided in the recognition of pathological changes within the cartilaginous portion. Mucosal inflammation, edema, excessive mucous secretions and external compression from the adenoid may cause functional obstruction. Dynamic dysfunction due to muscle weakness, hypercontraction, or lack of coordination between muscles can also cause functional obstruction. (Poe, Abou-Halawa et al. 2001) These observations have been made qualitatively, but the means for quantification of abnormalities is lacking.

The purpose of this study was two-fold. First, a method was sought to make quantified measurements of tubal function in conjunction with transnasal video endoscopy to determine whether the information would be useful for clinical or research purposes in elucidating the pathophysiology of dysfunction in patients. Identification or

quantification of pathology should aid in staging severity of disease and in planning for clinical treatment. Second, a hypothesis was proposed that dysfunction of the Eustachian tube most commonly involves a failure of its functional valve. The test of this hypothesis would be that the surgical methods developed to repair observed defects in the valve would result in clinical improvement of symptoms or signs of middle ear complaints.

5 REVIEW OF THE LITERATURE

5.1 EUSTACHIAN TUBE

5.1.1 Eustachian tube Anatomy

The Eustachian tube is a dynamic conduit between the middle ear and the nasopharynx. It performs aeration and drainage of the middle ear cavity and protects the middle ear material from the nasopharynx. This tubular organ performs secretory, ciliary, and dilatory functions that are required for optimal conduction of sound through the middle ear cavity. (Bluestone and Bluestone 2005)

The Eustachian tube measures approximately 31 to 38 mm in length in the normal adult. (Proctor 1973) It contains a physiological functional valve, which is closed in the passive resting position and is dilated open by active muscular exertion. Although there is no consensus on the definition of Eustachian tube dysfunction, it is taken to imply that the tubal functional valve fails to dilate open sufficiently widely or frequently to adequately ventilate the middle ear cavity. Failure of valve dilation may lead to numerous consequences within the middle ear with the most common of these being otitis media. (Bluestone, Paradise et al. 1972) Insufficient dilation of the functional valve should be more properly referred to as dilatory dysfunction to distinguish it from failure of the valve to close, which is the etiology of the patulous Eustachian tube. (Poe, Abou-Halawa et al. 2001)

As the direction of mucociliary clearance within the Eustachian tube flows from the ear to the nasopharyngeal orifice, the anatomy will be described with “proximal” referring to the middle ear end and “distal” referring toward the nasopharyngeal orifice. A cross section through the tubal lumen can be divided into superior and inferior halves and anterolateral and posteromedial halves.

The proximal one-third of the tubal length is, in effect, a bony funnel-shaped extension of the middle ear which becomes narrowest at the isthmus, the smallest aperture in the entire tube. (Sudo, Sando et al. 1997) The osseous portion is lined with a thin layer of cuboidal respiratory epithelium (Honjo, Hayashi et al. 1985) (Sando, Takahashi et al. 1994) and is a fixed conduit that is normally patent. (Hopf, Linnarz et al. 1991)

The distal 2/3 of the Eustachian tube is the pharyngeal portion, which is composed of a cartilaginous skeleton to which is attached a complex arrangement of peritubal muscles capable of a wide range of dynamic movements. The lumen is lined with respiratory epithelium that is taller, more columnar, and more ciliated inferiorly than the cuboidal epithelium in the superior one-half. (Honjo, Hayashi et al. 1985) (Sando, Takahashi et al. 1994) A submucosal layer of lymphatics and fat add to the thickness of the lining within the tubal lumen. The cartilaginous portion is normally closed in the resting position due to apposition of the mucosal walls. Closure occurs over a variable length (5-10mm segment) just a few millimeters distal to the bony isthmus where the cartilaginous

skeleton becomes flexible.(Poe, Abou-Halawa et al. 2001) *This portion that intermittently dilates to the open position is termed the “functional valve,” because it serves such a purpose.* (Poe, Pyykko et al. 2000)

There are four peritubular muscles, the levator veli palatini (LVP), the salpingopharyngeus, the tensor tympani, and the tensor veli palatini (TVP). The TVP muscle is thought to be the principal dilator of the tubal lumen. (**Figure 1a-c**) (Rood and Doyle 1978)

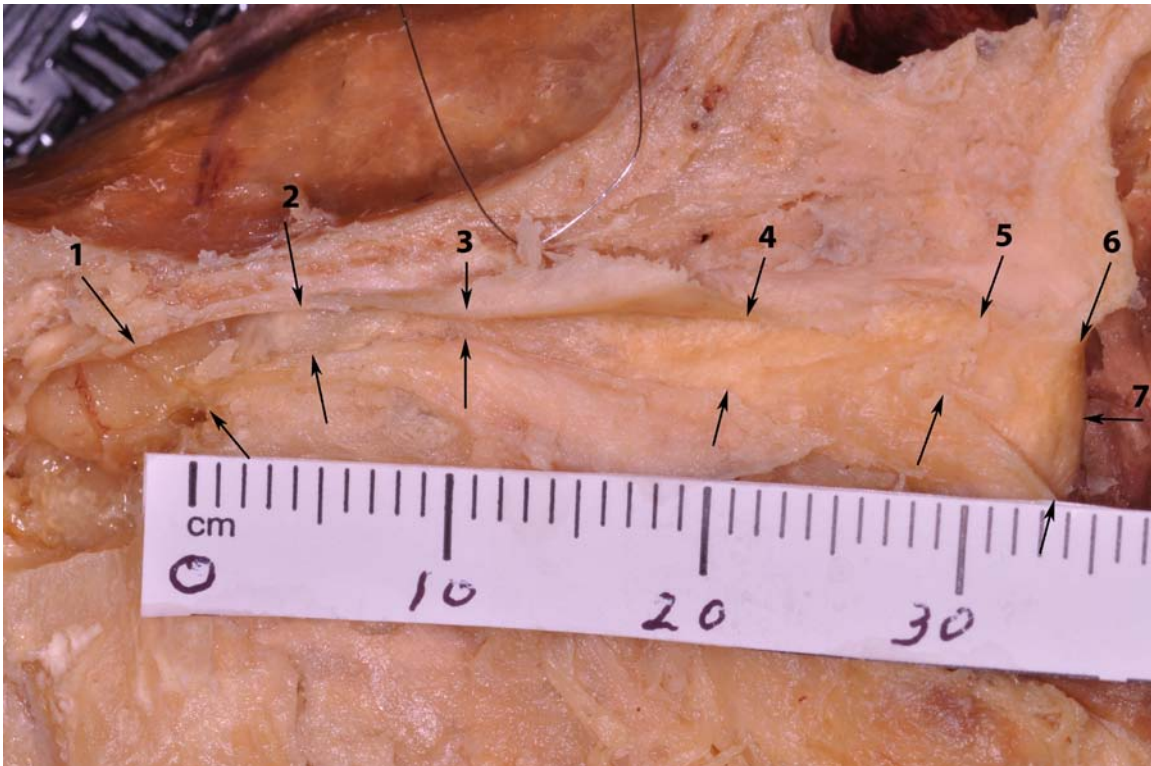


Figure 1a. Fixed cadaver dissection with a longitudinal cut through a right Eustachian tube orifice. The antero-lateral wall has been resected and the figure is oriented with superior upward. The bony orifice is labelled 1, isthmus 3, and torus tubarius 7. Scale unit marks are in mm.

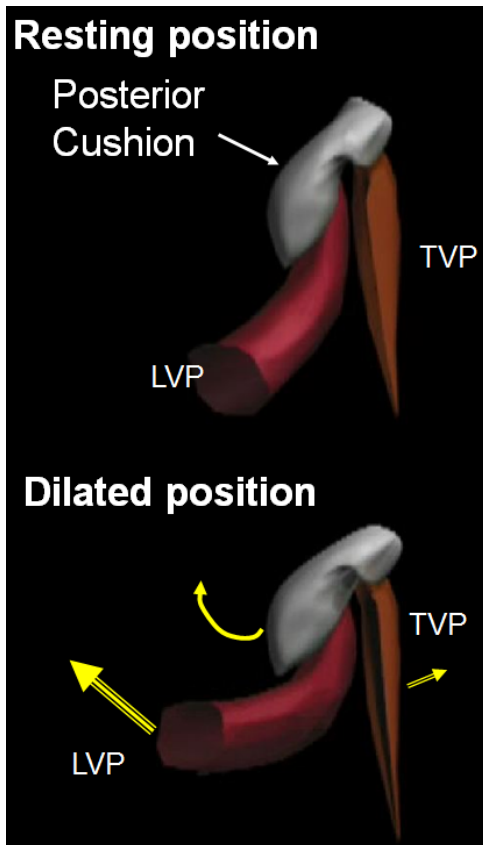


Figure 1b. Diagram of a left Eustachian tube seen from the nasopharyngeal orifice. LVP = Levator Veli Palatini muscle, TVP = Tensor Veli Palatini muscle. Posterior cushion = Torus tubarius. Artwork courtesy of Dr. Oskar Kujawski

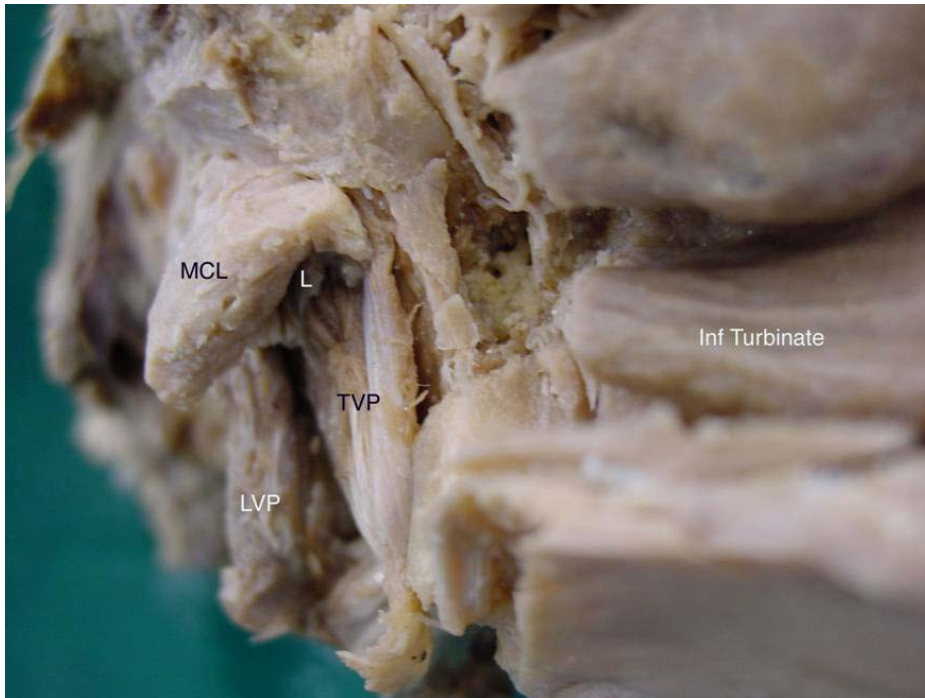


Figure 1c Fixed cadaver dissection of the nasal cavity and left Eustachian tube orifice. MCL = Medial cartilaginous lamina within the torus tubarius. Reproduced courtesy of *Laryngoscope*, 113:583-591,2003.

The LVP is a round-bellied muscle that looks like a sling running from the base of the temporal bone along the bony Eustachian tube and passing under a groove in the inferior aspect of the medial cartilaginous lamina and membranous floor of the Eustachian tube to insert into the palatal musculature. Contraction of the LVP raises the soft palate and medially rotates the medial cartilaginous lamina. (Rich 1920; Proctor 1973)

The TVP is a flat, fan shaped muscle with broad origins from the basisphenoid and includes dilator tubae muscle fibers originating from the membranous anterolateral wall of the Eustachian tube. It courses longitudinally to follow the length of the cartilaginous Eustachian tube and tapers to run under the hamulus of the palatal bone, finally inserting into the soft palate. (Proctor 1973) The relaxed bulk of the TVP contributes to the bulge in the anterolateral wall that protrudes into the lumen of the Eustachian tube and aids in its closure.(Ishijima, Sando et al. 2002; Takasaki, Sando et al. 2002) Contraction of the TVP muscle tenses the anterolateral membranous wall and distracts it laterally to dilate the tubal valve into the open position.(Rood and Doyle 1978)

5.1.2 Physiology of tubal dilation

Intermittent brief tubal dilation is most likely the principal mechanism for equilibration of middle ear pressure with the ambient atmosphere. Involuntary dilation of the Eustachian tube occurs throughout the day, typically occurring with a swallow or yawn, but it does not accompany every swallow or yawn. Barometric and chemical receptors within the

middle ear are thought to provide autonomic nervous system feedback that influences the frequency of involuntary tubal opening. (Eden and Gannon 1987; Rockley and Hawke 1992) Tubal dilation occurs in normal subjects approximately 1.4 times per minute during daytime with the duration of opening averaging 0.4 seconds. (Mondain, Vidal et al. 1997) During sleep, the frequency of tubal opening is substantially reduced.

Experiments with electrical stimulation in monkey models has shown that sequential muscular contractions initiate rotational movements of the cartilaginous framework and create tension within the anterolateral wall, which causes the effacement of its resting bulge. This effacement is the primary action that opens the lumen to the middle ear. (Bluestone and Bluestone 2005) Tubal dilation begins with the action of the LVP muscle to medially rotate the cartilaginous skeleton, primarily its mobile distal half of the medial cartilaginous lamina. (Cantekin, Doyle et al. 1979) TVP muscle contraction follows causing the resting convexity of the anterolateral wall to become effaced or even concave as the final step to transiently open the lumen. (Cantekin, Doyle et al. 1979; Honjo, Okazaki et al. 1979; Honjo, Ushiro et al. 1983; Ghadiali, Swarts et al. 2003)

It is believed that intermittent brief dilation of the tube is the principal mechanism for equilibration of middle ear pressure with the ambient atmosphere. (Sade 1984; Honjo 1988; Hergils and Magnuson 1998) Middle ear and mastoid gas exchange is an ongoing process that continually generates a net absorption of gases resulting in an increasingly negative pressure between tubal dilations. (Felding, Rasmussen et al. 1987; Ostfeld and Silberberg 1991; Ars and Ars-Piret 1994; Doyle and Seroky 1994) There is a gradient of partial pressures of gases between the middle ear gases and the venous capillary soluble gases that drives the net absorption of gas into the circulation over time as seen in table 1.

Table 1

Partial pressures (in mmHg) measured in humans – table adapted from Sadé (Sade and Ar 1997)

	Atmosphere	Nasopharynx	Middle Ear	Venous Blood
Total	760	760	760	704
N₂	563	578	623	575
O₂	150	99	40	38
H₂O	47	47	47	47
CO₂	0.3	36	50	44

CO₂ has the highest coefficient of diffusion and is most rapidly exchanged with the net exchange passing from the venous blood to the middle ear. The next most rapid diffusion occurs with O₂, passing from the middle ear into the blood. Diffusing much more slowly into the circulation is N₂, the predominant partial pressure in both air and blood and the source of the largest gradient. It is the slow absorption of N₂ that causes the increasing

relative vacuum between ambient air and the middle ear cavity over time. (Tideholm 2003; Pau, Sievert et al. 2008) Failure to dilate for an extended period of time can lead to pathologically severe negative pressure and consequences of tympanic membrane retraction, atelectasis, and otitis media with effusion (OME).(Falk and Magnuson 1984; Doyle and Seroky 1994; Bluestone and Bluestone 2005) Indeed, intermittent dilation with opening of the middle ear may principally serve to regulate nitrogen balance.(Ars and Ars-Piret 1994)

Tubal dilation is likely naturally facilitated by the presence of surface tension lowering substances that are found in its mucus. Surfactants are produced within the tubal mucosa and probably aid in reducing the surface tension of the lumen, which reduces the work required to dilate the tube. (Birken and Brookler 1972) Although treatment with surfactants has produced reduction of passive opening pressures in Eustachian tubes and even reduced the time to resolve acute otitis media in animal models, these results have not yet been reproduced successfully in humans.(Grace, Kwok et al. 1987; Passali and Zavattini 1987; Kobayashi T 1993; Chandrasekhar and Mautone 2004)

Fluid and secretions in the middle ear are cleared by a combination of muscular pumping action that occurs with the tubal closing process (Honjo, Hayashi et al. 1985) and by mucociliary activity. (Bluestone CD 1996) Reflux of nasopharyngeal secretions into the middle ear is limited or prevented by the closed position of the resting pharyngeal Eustachian tube and by the trapped volume of gas in the middle ear and mastoid bone which creates a "gas cushion." Reflux of the sounds of breathing and vocalization are similarly blocked by the closed resting position of the pharyngeal Eustachian tube.(Bluestone CD 1996)

5.2 TESTING OF THE EUSTACHIAN TUBE

5.2.1 Eustachian tube function tests

A number of tests have been employed applying either positive or negative pressure through the external auditory canal or nasopharynx to assess Eustachian tube function. Unfortunately, none of these tests have gained widespread use as they are all lacking in clinical significance. The forced response test measures the pressure needed to passively open the Eustachian Tube and it requires a patent ventilation tube or tympanic membrane perforation. The external auditory canal is sealed and using a tympanometry probe, the pressure is increased until the Eustachian tube opens resulting in a sudden decompression. The inflation-deflation test uses a tympanometry probe to record and vary pressure as the patient swallows in an attempt to open the Eustachian tube. (Bluestone CD 2005)

Both the forced response test and the inflation-deflation test were used to evaluate pediatric patients prior to tympanoplasty in one study. Although good Eustachian tube function correlated with a favorable outcome for tympanoplasty, poor Eustachian tube function did not correlate with worse outcomes for tympanoplasty.(Manning, Cantekin et al. 1987; Choi, Han et al. 2009)

Sonotubometry takes measurements of the Eustachian tube opening using a speaker that produces a tone inside the nose and mouth. A microphone is placed within the external auditory canal such that opening of the Eustachian tube can be detected as an increase in the amplitude of sound received from the nasopharynx. (van der Avoort, van Heerbeek et al. 2005; van der Avoort, Heerbeek et al. 2006; van der Avoort, van Heerbeek et al. 2007) Difficulties with signal to noise ratio, false negatives and positives, artefacts and waveforms of uncertain importance have limited its clinical use. Sonotubometry has not necessarily predicted the presence or absence of middle ear ventilation in all cases. False negatives are a particular problem as some subjects with normal ears and no history of tubal dysfunction may fail to open with sonotubometry. (Sumi, Tsunoda et al. 2007; van Heerbeek, van der Avoort et al. 2007)

Most recently, tubomanometry has become available using impedance tympanometry measurements of the external auditory canal during swallowing. During a swallow, the mouth is closed and the nose is sealed with a probe that causes a ramp increase in nasopharyngeal pressure. The pressure stimulus is not physiologic and may take some practice for patients to learn to swallow against the rising nasopharyngeal pressure. Investigators have correlated higher tubal opening pressures with middle ear pathology, but its clinical utility remains limited. (Martin C 1999)

5.2.2 Eustachian tube endoscopy

Efforts have been made to observe the functioning of the Eustachian tube in a minimally invasive fashion using endoscopic techniques. Endoscopy of the human Eustachian tube has substantially increased our understanding of the functional processes in both normal and pathological cases. Initial work done by the insertion of microfiber-optic instruments into the tubal lumen yielded only limited information since the bony isthmus is only about 1.0-1.5 mm in horizontal diameter and 2 to 3 mm in vertical diameter. (Schuknecht and Gulya 1986) In order to pass through the narrow isthmus, endoscope diameters must be restricted to 1 mm or less, which significantly compromises the resolution of images. Only gross structures within the middle ear, such as ossicles, are recognizable and fine structures or details of movements cannot be appreciated. Direct contact of the endoscope lens with secretions and mucosal folds obscures the view within the lumen to such a degree that most reports have only been able to describe gross observations such as the presence of lesions or degree of patency. (Kimura, Yamaguchi et al. 1989; Chays, Cohen et al. 1995; Takahashi, Honjo et al. 1996; Klug, Fabinyi et al. 1999) Importantly, microendoscopy has demonstrated that the lumen of the osseous Eustachian tube may be patent in cases of active otitis media with effusion, suggesting that the pathophysiology is for reasons other than obstruction within the bony portion. (Hopf, Linnarz et al. 1991)

Larger diameter (≥ 3 mm) fiber-optic nasopharyngoscopes or rigid Hopkins rod endoscopes have been used for more detailed studies of the lumen of the cartilaginous portion of the Eustachian tube. The endoscopes were carefully positioned in the

nasopharyngeal orifice with the view directed superiorly 45 degrees and laterally 45 degrees into the lumen. This angle allowed for observation along the longitudinal axis of most of the pharyngeal portion of the tube as it rotated into the dilated position during the opening sequence. Careful observation of tubal dynamics became possible with high-resolution optics. Avoidance of direct contact with the mucosa prevented interference with the dilating mechanism and limited problems with fogging of the lens. Video recordings were made and replayed in slow motion for meticulous analysis of the dilation process and for study of normal physiology and pathophysiology. (Poe, Pyykko et al. 2000; Poe, Abou-Halawa et al. 2001; Mathew, Kuruvilla et al. 2007)

Eustachian tube endoscopy generally yielded views proximally well into the valve area during the time of maximal active dilation. The opening process was observed to begin at the nasopharyngeal orifice and to progressively dilate the lumen proximally toward the isthmus, generally straightening the resting curvature of the lumen and bringing it into full view of the endoscope. Although valve dilation was observed in detail, true opening of the lumen to communicate with the middle ear cannot be substantiated by visual means alone. Normal subjects and patients with tubal dysfunction have been studied using these techniques to establish some observed patterns of normal dynamic physiology and pathophysiology. (Poe, Pyykko et al. 2000; Poe, Abou-Halawa et al. 2001)

5.2.3 Technique of Eustachian tube video endoscopy

Patients were examined in the sitting position in an office setting. Topical spray anesthetic and decongestant, lidocaine (4%) topical mixed with equal parts of phenylephrine HCl 0.5% solution, was applied to both nasal cavities while the patient sniffed. Endoscopes were introduced into the nasal cavity and advanced along the floor and below inferior turbinate up to the nasopharyngeal orifice of the Eustachian tube. It is located just posterior to the inferior turbinate and identified by the torus tubarius (or posterior cushion). It was observed to be important to positively identify the torus tubarius and not pass it, resulting in viewing the fossa of Rosenmüller and mistaking it for Eustachian tube orifice.

The initial endoscopic (Poe, Pyykko et al. 2000) exam was done with a 3.7 mm diameter steerable flexible fiber-optic nasopharyngoscope EMF-P3 (Olympus, Tokyo, Japan). Careful inspection of the nasal cavity, nasopharynx, hypopharynx, and larynx was done to look for mucosal inflammation or lesions, especially if there was any evidence for laryngo-pharyngeal reflux or allergic disease. If the adenoid was enlarged, its proximity to the torus tubarius of the Eustachian tube was noted. Contact of the adenoid with the torus tubarius has been demonstrated to correlate with tubal dilatory dysfunction that improves following adenoidectomy. (Nguyen, Manoukian et al. 2004) Lastly, the Eustachian tube was closely examined. The optimal fiber-optic view brought the tip into the proper angle to view up the long axis of the Eustachian tube as it dilated. This angle of introduction could be obtained either from the ipsilateral nasal cavity or by introducing the endoscope along the floor of the contralateral nasal cavity and passing the tip behind the vomer.

For a more detailed examination or if slow-motion recording (Poe, Pyykkö et al. 2000) was desired, rigid endoscopes were preferred, generally using a 4-mm diameter, 30 or 45 degree view angle, Hopkins rod rigid sinus surgery endoscope (Karl Storz, Culver City CU Alber City, CA) The rod endoscopes have high-resolution images, but the fiber-optic endoscopes are easier to pass and can be steered deeper into the Eustachian tube lumen if desired.

The 30 or 45-degree rigid endoscope was introduced with the view angle looking directly laterally and passed along the nasal floor, following the inferior turbinate. After passing the posterior aspect of the inferior turbinate, the next landmark encountered was the anterior cushion of the Eustachian tube's nasopharyngeal orifice. Once at the orifice, the endoscope was rotated slightly to look superiorly into the long axis of the tubal lumen. The rigid endoscope was used with a Charge Coupled Device (CCD) camera in place and images are viewed on a video monitor. Video recordings were made with an s-VHS video or DV recorder.

The patient was initially asked to vocalize the letters "K," "K," "K," repeatedly to view the isolated action of the LVP. The "Ks" stimulated palatal elevation and medial rotation of the torus tubarius and posteromedial wall of the Eustachian tube. Swallows were done to induce normal physiological tubal dilations, and forced yawns were performed to cause maximal sustained dilations. The Eustachian tube was not expected to open with every swallow and yawn and patients were coached to feel the muscular contractions in the back of their throats to generate some dilatory efforts. Water was often provided if there were difficulties with swallowing. The procedure was repeated for the contralateral Eustachian tube orifice.

The video of tubal dilations was then reviewed and analyzed in normal time, slow motion, and even stepping through single frames that were captured at a rate of 29.97 frames per second. (Poe, Pyykkö et al. 2000; Poe, Abou-Halawa et al. 2001)

5.2.4 Endoscopy of the normal Eustachian tube

Although the technique for endoscopy has been available for decades only a few studies have systematically tried to visualize the dynamic events in the normal Eustachian tube function. The dilation process was initially studied endoscopically in thirty normal subjects (Poe, Pyykkö et al. 2000). Dilation and opening were observed to have four consistent sequential phases during a normal swallow:

1. The soft palate elevated with simultaneous medial rotation of the torus tubarius and posteromedial wall. The lateral pharyngeal wall also medialized causing transient constriction of the nasopharyngeal orifice despite the medial rotation of the torus tubarius and posteromedial wall. It was postulated that this contrary constrictive movement could be to provide momentary protection of the Eustachian tube against reflux, clearing it just prior to dilating with a swallow (**Figure 2a,b**).

2. The palate remained elevated and the torus tubarius and posteromedial wall remained medially rotated as the lateral pharyngeal wall lateralized and caused some initial dilation of the nasopharyngeal orifice.
3. The TVP began to contract in the anterolateral wall causing dilation of the lumen to propagate from the nasopharynx proximally toward the bony isthmus. The dilation occurred by excursion of the anterolateral lumen wall laterally. The elevation of the palate and medially rotated position of the torus tubarius and posteromedial wall were maintained.
4. Tubal opening occurred as the functional valve of the cartilaginous tube dilated laterally away from the stable and medially rotated posteromedial wall to create a roughly rounded aperture in the lumen. The convex bulge seen in the resting anterolateral valve wall became visibly effaced or concave to produce this final opening (**Figure 2c**).

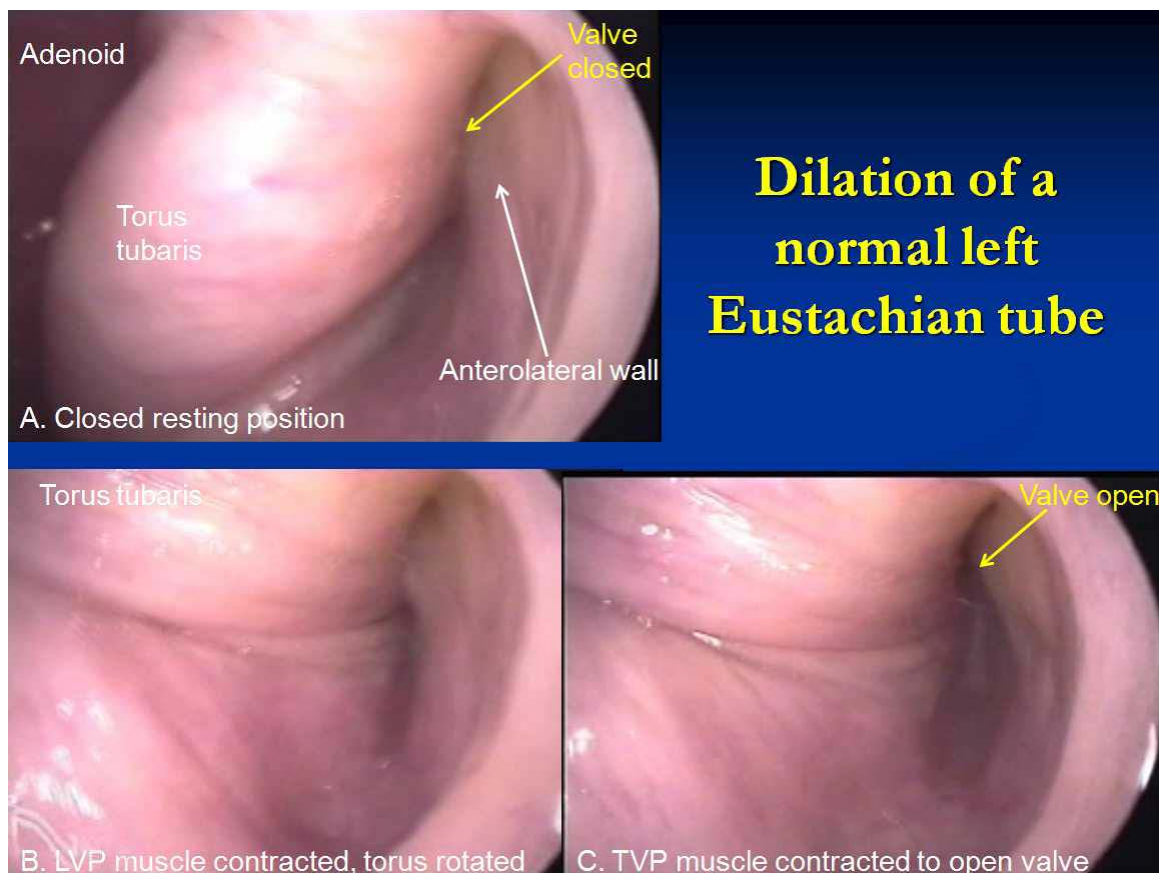


Figure 2 a- c Transnasal, 4mm, 45 degree Hopkins rod endoscopic view of left normal Eustachian tube orifice. A. Resting position (valve closed). B. Initiation of swallow. Levator veli palatini muscle has elevated the palate and medially rotated the torus tubarius. C. Tensor veli palatini has contracted dilating the valve to open position.

Closure of the tube began with the valve area and propagated distally toward the nasopharyngeal orifice. This proximal to distal closure has been previously recognized on contrast studies and hypothesized to have a pumping action to expel material from the

lumen as a protection against reflux. (Honjo, Hayashi et al. 1985) Relaxation of the anteromedial wall, torus tubarius and posteromedial wall, lateral pharyngeal wall and palate occurred in variable order or even simultaneously.

The thin mucosa and subcutaneous tissues of the normal Eustachian tubes permitted observation of the muscular contractions of the LVP and TVP. Even the ripples representing the contractions of distinct individual fibers were often appreciated in detail.

5.2.5 Endoscopy of the Dysfunctional Eustachian Tube

Only a few studies have systematically explored the use of endoscopy in the study of the Eustachian tube in patients. In one study Eustachian tube dilatory dysfunction has been defined as an inadequacy of the dilatory function that results in secondary ear pathology (Poe, Abou-Halawa et al. 2001). It may be caused by anatomical obstruction or physiologic failure due to: 1) hereditary factors as suspected in families with strong histories of ear disease, 2) mucosal inflammation causing functional obstruction or failure of dilation, 3) muscular problems that cause dilatory dynamic dysfunction and lastly 4) true anatomical obstruction due to neoplasms or other mass lesions, which are the least common cause.

The etiologies of tubal dilatory failure have been separated into obstructive and dynamic dysfunctions. Most obstructive problems were not due to true anatomical blockage, but were instead found to be the result of functional failures to either dilate the tube sufficiently widely or sufficiently frequently to adequately aerate the middle ear.

There is increasing evidence that Eustachian tube dilatory and patulous dysfunction results from pathology within the cartilaginous portion. (Hopf, Linnarz et al. 1991; Chays, Cohen et al. 1995; Poe, Abou-Halawa et al. 2001) Slow-motion video analysis was done on fifty-eight ears (in forty adult patients) with pathology suggestive of tubal dilatory dysfunction (Poe, Abou-Halawa et al. 2001). All subjects were found to have significant pathology and compromise in the tubal dilation process within the cartilaginous portion compared to (13%) of normal subjects who had only mild inflammatory changes. The pathological findings are summarized in Table 2.

Table 2

Pathological findings in 58 clinically dysfunctional Eustachian tubes

Mucosal edema	48 (83%)
Reduced anterolateral wall lateral excursion	43 (74%)
Functionally obstructive mucosal disease	15 (26%)

Defects were observed in all of the different components of the cartilaginous Eustachian tube, including cartilaginous skeleton, tubal muscles, submucosa, and epithelium of the

lumen. Edema of the mucosa and submucosa, the most common findings, reduced the diameter of the lumen and decreased the ability to open the valve region. The torus tubarius and posteromedial wall were most affected by the apparent inflammation, which could continue into the tubal lumen or sometimes stopped abruptly at the transition into the lumen. The inflammatory changes were often most prominent on the posterior surface of the torus tubarius that faced the adenoid. The mucosa and submucosa of the torus tubarius and posteromedial wall is normally thicker and contains more glands than the anterolateral wall. (Schuknecht and Gulya 1986; Poe, Abou-Halawa et al. 2001) It may be more susceptible to inflammatory changes and swelling. In severe inflammation, the torus tubarius was observed to become compressed by an enlarged adenoid during swallowing causing it to be thrust forward and blocking the tubal orifice during dilatory efforts. This type of bulbous torus tubarius has been repeatedly seen in subsequent clinical experience, especially in patients with severe allergic or laryngopharyngeal reflux disease (Poe, Metson et al. 2003). **Figure 3** shows examples of mild (Fig 3a,b) and more severe inflammation (Fig 3 c,d).

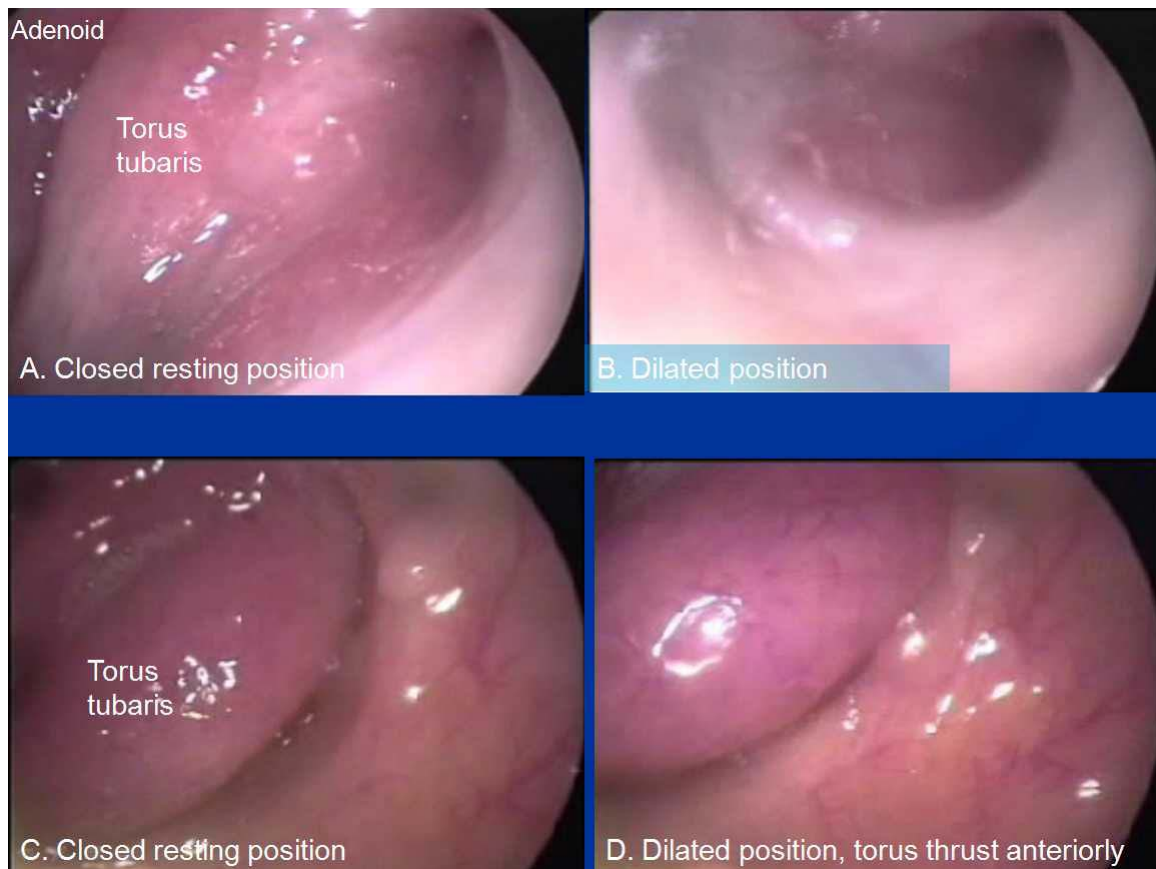


Figure 3. Transnasal, 4mm, 45 degree Hopkins rod endoscopic view of left inflamed & edematous Eustachian tube orifices

- A. Mildly inflamed torus tubarius in resting position (valve closed).
- B. Mildly inflamed torus tubarius in dilated position. (same case as 2a)
- C. Severely inflamed torus tubarius in resting position (valve closed).

D. Severely inflamed torus tubarius in dilated position. Torus tubarius is so edematous that pharyngeal constrictors and adenoids have forced it anteriorly during swallow, completely preventing dilation. (same case as 2c)

Muscular dysfunction (dynamic dysfunction) as the primary abnormality was seen in 8%. Examples were observed in which hypofunction, hypercontraction or lack of coordination between the TVP and LVP muscles caused poor dilatory efforts.

Most commonly observed was reduced TVP muscle action with decreased lateral excursion of the anterolateral wall. In some cases the TVP showed diffuse weakness or focal, apparent dilator tubae weakness, disorganized contractions, or absence of the usual dilatory wave that should normally progress from the nasopharyngeal orifice toward the isthmus. Hyperactive contraction of the TVP was also seen producing prominent ripples and longitudinal ridges of mucosa that paradoxically reduced the lumen diameter instead of dilating it.

Observations of LVP muscle dysfunction included premature relaxation of the LVP causing the torus tubarius to return to its resting position before or during the contraction of the TVP, and double contraction of the muscle which blocked the lumen during dilatory efforts.

Dilatory function appeared to depend on the coordinated action of both TVP and LVP muscles. Although LVP function is not important for tubal dilation in other primates (Cantekin, Doyle et al. 1983), it appeared to be significant in patients. The LVP may serve as a “scaffold” against which the inefficient dilatory efforts of the TVP, which only act on the anterolateral wall, are dependent. (Poe, Abou-Halawa et al. 2001; Bluestone 2008)

The authors did not find correlation between the severity or type of middle ear pathology and the severity or type of Eustachian tube pathology. It appeared that changes in the tympanic membrane and middle ear took an independent pathophysiological process once Eustachian tube dysfunction had passed some critical point.

In patulous Eustachian tubes patients demonstrated a consistent volume defect or concavity in the superior cross-sectional half of the anterolateral wall, within the valve area. Normal Eustachian tubes have a convex bulge in this location that flattens during the final stage of dilation process.

5.3 TREATMENT OF EUSTACHIAN TUBE DYSFUNCTION

5.3.1 Differential Diagnosis aspects of Eustachian tube

Chronic fullness in the ear associated with a normal appearing mobile tympanic membrane, absence of any retraction or effusion, and a normal tympanogram should not

be interpreted as Eustachian tube dilatatory dysfunction, especially if myringotomy fails to relieve the symptoms. Instead, a search for other causes of fullness, blockage, or otalgia is indicated and should include evaluation of temporomandibular joint dysfunction, superior semicircular canal dehiscence syndrome, patulous Eustachian tube and endolymphatic hydrops.
(Poe 2007)

Table 3
Differential diagnosis for chronic Eustachian tube dilatatory dysfunction

Allergic disease
Laryngo-pharyngeal reflux (LPR)
Hypertrophied adenoid contacting torus tubarius
Chronic sinusitis
Tubal dynamic dysfunction
Pneumonia or chronic pulmonary disease
Primary mucosal disease

- Immune deficient/suppressed
- Samter's (Aspirin sensitivity, Asthma, Nasal polyps) triad
- Wegener's or other granulomatous disease
- Other middle ear or nasopharyngeal inflammation

Anatomical obstruction with neoplasm or other lesion

5.3.2 Medical treatment of Eustachian tube dysfunction

Tubal dilatatory dysfunction appears to be predominantly due to mucosal inflammatory disease, similar to chronic sinusitis, and can be managed in most cases with medical treatment. Identification of the underlying etiology is important for success. Laryngopharyngeal reflux should be treated with dietary management, daily or twice daily proton pump inhibitors and H₂ blockers at bedtime as indicated. Refractory cases may be treated by sleeping on an inclined bed, and lastly, fundoplication can be done if necessary.(Koufman 2011)

Symptoms and signs of allergic disease should be thoroughly investigated, doing appropriate testing and dietary elimination trials as indicated. Avoidance of the offending allergen, oral antihistamines, leukotriene inhibitors, nasal antihistamines or mast cell stabilizers, nasal steroid sprays, and immunotherapy may all be pursued as required.(Kushnir 2011)

The possibilities of other underlying pathologies should be carefully considered. Recurrent infections should raise the suspicion for underlying nasal or sinus disease, immunosuppression or immunodeficiency, or primary mucosal disease (eg. Samter's triad, Wegener's and other granulomatous disorders).

Anatomical obstruction secondary to neoplasm should be ruled out, especially in cases of unilateral persistent effusion. Contrast-enhanced imaging studies are often necessary to recognize nasopharyngeal carcinoma and other malignancies. Functional obstruction due to hypertrophic adenoid tissue contacting the torus tubarius can be treated by adenoidectomy.

5.3.3 Tympanostomy tubes for dilatory dysfunction

Persistent tubal dilatory dysfunction with OME or atelectasis has been successfully managed in most cases with tympanostomy tubes with excellent long term outcomes. Some patients, however, recur with effusion or atelectasis and require multiple tympanostomy tubes over many years. Alternatively, tympanic membrane perforation or progression of atelectasis may develop and result in chronic otitis media with or without cholesteatoma.

A number of "permanent" tubes have been developed in an attempt to provide longer lasting middle ear ventilation, but they are subject to problems with crusting, infection, obstruction, unplanned extrusion and development of unwanted large perforations.(Silverstein 1994)

5.3.4 Eustachian tuboplasty on the osseus portion

Numerous surgical procedures have been developed in an attempt to correct chronic Eustachian tube dilatory dysfunction. Because the bony isthmus is the narrowest portion of the tubal lumen, all of the operations described historically have involved techniques to widen the osseous portion of the Eustachian tube. (Zollner and Beck 1955) described stenting of the tubal lumen with silk threads and in 1963 (Zollner 1963) changed to the use of a polyethylene tube. The stents had problems with extrusion and obstruction as well as a risk for internal carotid artery injury during the insertion process through the middle ear tubal orifice. (Wullstein 1960) performed the first reported case of drilling the osseus Eustachian tube from a middle ear approach and he expressed significant concern over the potential for internal carotid artery injury in future such attempts. House et al. (House, Glasscock et al. 1969) reported performing a middle cranial fossa approach for exposure to drill and widen the Eustachian tube. Misurya (Misurya 1975) performed a similar widening of the isthmus using a combined transcanal and preauricular approach. Jansen (Jansen 1985) focused on widening the posterior-superior aspect of the middle ear tubal orifice using endoscopic assistance. Charachon et al (Charachon, Gratacap et al. 1986) described a postauricular approach to widen the inferior and lateral tubal walls leaving silastic stents indwelling for 18 to 24 months. Additionally they advocated removal of most of the tensor tympani muscle to gain additional width of the bony Eustachian tube. Zini et al (Zini C 1988) performed an even wider tubal drillout involving the superior and inferior aspects of the osseous Eustachian tube in addition to removal of the tensor tympani muscle. They also left silastic stents in place for 6 to 12 months. There have been no reports of long-term success using any of these above techniques.

5.3.5 Eustachian tuboplasty on the cartilaginous portion

Given the mounting evidence from endoscopic investigations that dilatory dysfunction may commonly result from inadequate opening of the tubal valve within the cartilaginous portion, operations were proposed to widen this portion. Laser Eustachian tuboplasty (LETP) was designed to ablate mucosa, submucosa and sometimes cartilage from the posterolateral wall of the tubal lumen to widen it and facilitate the dilatory efforts of the TVP muscle. The operation was first performed by Kujawski in patients with varying degrees of OME and/or atelectasis, employing a carbon dioxide laser to ablate mucosa, soft tissue, and cartilage at the nasopharyngeal orifice. The ablation extended along the posterior wall into the tubal lumen. A retrospective report of the first 38 patients using either a carbon dioxide or 980 nm diode laser demonstrated that 81% remained free of Eustachian tube dilatory dysfunction after 36 months of follow-up. (Kujawski 2004) A subsequent prospective pilot study was conducted using a similar technique to evaluate the safety and efficacy of LETP in conjunction with a tympanostomy tube in patients with refractory OME. The procedure resulted in the absence of effusion in 7/10 (70%) patients at 6 months and 3/5 (60%) patients at 12 months. There were no significant complications. Healing appeared to occur with regrowth of healthier appearing mucosa and scar tissue. The torus tubarius and posteriormedial wall appeared thinner and with reduced inflammation compared to preoperatively. (Poe, Metson et al. 2003)

A trial of Eustachian tuboplasty using a microdebrider for tissue ablation was done in twenty patients with chronic OME and sinus disease along with their endoscopic sinus surgery; 14/20 (70%) improved subjectively and by improvement in tympanogram and or pure-tone averages. Failure correlated with higher preoperative CT sinus disease stage and with higher eosinophil counts in the biopsy specimens. (Metson, Pletcher et al. 2007)

Most recently, Eustachian tuboplasty has been done with a KTP (potassium-titanyl-phosphate) laser fiber making two or three transverse “cross hatch” cuts full thickness from the leading edge of the torus tubarius down through the mucosa and transecting the medial cartilaginous lamina nearly up to the valve. The posterior surface perichondrium was spared. The cuts were intended to alter the curvature of the medial cartilaginous lamina causing it to bow medially and widen the distal lumen and nasopharyngeal orifice. The procedure was retrospectively reported having been performed in 25 patients with varying degrees of ear blockage and abnormal tympanograms over an unspecified duration. 92% were relieved of fullness symptoms and 96% improved their tympanograms (from a baseline of types B, C, or shallow A) after a mean follow-up of 15 months. These results are promising, but longer follow-up and additional experience from other surgeons will be needed to judge the long-term importance of this new technique. (Yanez 2010)

5.3.6 Patulous Eustachian tube

The patulous Eustachian tube has been defined as an abnormal patency in the lumen that results in autophony, the auditory perception of one's own internal sounds.(O'Connor and Shea 1981)

The symptoms of the patulous Eustachian tube were first described by Jago in 1858 (Jago 1858) and recognition of the disorder as a clinical entity was reported by Schwartz in 1864. (Schwartz 1864) Jago later wrote that he had personally experienced autophony and patulous Eustachian tube symptoms. (Jago 1867) Patients typically report a feeling that their affected ear is "blocked," leading to confusion between the patulous Eustachian tube and tubal dilatory dysfunction. Autophony is often described as similar to talking into a "wind tunnel" or "barrel" and they experience an "echo" or abnormally loud perception of their voice and nasal breathing. It can occur spontaneously or be activated by exercise and prolonged talking; nasal or oral decongestants are of no benefit and may exacerbate the condition. The autophony can be very disturbing to patients and even lead to major depression and suicide.(DiBartolomeo 2009)

Autophony is usually intermittent, although in severe cases the symptoms may persist for hours at a time. It can generally be relieved, at least temporarily, by placing the head down into a dependent position or lying supine for some time. Sniffing inward against a closed nostril to generate negative middle ear pressure, ipsilateral internal jugular vein compression, and the presence of an upper respiratory infection or allergies are also known to give some temporary relief from the condition.

Confirmation of a patulous Eustachian tube on physical examination can only be done if the patient has active autophony during the exam. A brisk walk or going up and down stairs for several minutes prior to the examination may activate the symptoms. Most commonly the tympanic membrane and middle ear will appear normal, but tympanic membrane scarring, atrophy, and retraction may occur from habitual sniffing. The diagnosis can be confirmed by observation of medial and lateral movements of the tympanic membrane coincident with regular or forced nasal breathing. These patulous excursions of the tympanic membrane are best observed with the operating microscope and with the patient in the sitting position. Lying supine may cause venous congestion to close the patulous tube (Pulec, Kamio et al. 1975) and the excursions may be missed with a handheld otoscope. Excursions may be enhanced with obstruction of the contralateral nostril. (Doherty and Slattery 2003) A tympanogram may record "sawtoothed" waves synchronous with nasal breathing as a more sensitive test than microscopic observation and normal tracings should be present with breath-holding. Tympanometry may also show middle ear negative pressure or hypermobility of the tympanic membrane. (Doherty and Slattery 2003) Nasopharyngeal endoscopy into the Eustachian tube lumen will reveal a concave longitudinal defect in the superior aspect in the anterolateral wall of the tubal valve, where it should normally be convex. (Poe, Abou-Halawa et al. 2001) (**Figure 4**)



Figure 4. Transnasal, 4mm, 45 degree Hopkins rod endoscopic view of orifice of a left patulous Eustachian tube. Note concavity of antero-lateral wall extending through valve.

The patulous Eustachian tube is thought to be due to the loss of tissue within the cartilaginous portion and it has been commonly reported with weight loss, especially in chronic wasting illnesses. (Pulec and Simonton 1964) Additionally it has been associated with pregnancy, use of high dose oral contraceptives, (O'Connor and Shea 1981) and estrogen therapy for carcinoma of the prostate. (Shambaugh 1938) Associations have also been noted with conditions causing atrophy or scarring within the nasopharynx and musculature including adenoidectomy, radiation therapy, poliomyelitis, multiple sclerosis and other neuromuscular diseases, cerebrovascular accident, temporomandibular joint dysfunction, malocclusion, iatrogenic trauma, and craniofacial abnormalities. (Pulec JL 1973; Virtanen 1978; Cox 1980; O'Connor and Shea 1981) Patulous Eustachian tube symptoms have been reported following protracted otitis media, (Tsuji T 2003) especially in patients who have developed a habit of excessive nose blowing or Valsalva maneuvers. Up to one third of patients have had no identifiable cause. (Doherty and Slattery 2003) An occasional association between patulous Eustachian tube and palatal myoclonus has been noted. (Hazell 1990)

Numerous medical and surgical treatments have been reported for the patulous Eustachian tube. Patients require reassurance that although the condition may be very disturbing, it is in no way dangerous or destructive. Weight gain has been recommended by some, but it is only recommended when the patient is undernourished and underweight. Decongestants and nasal steroid sprays should be discontinued. Mucous thickening agents (Dyer and McElveen 1991), topical estrogen drops (Bluestone CD 1998), and topical irritants intended to induce mucosal edema (Bezold K 1908) may be effective, but usually only temporarily. Myringotomy with or without a ventilating tube has been reported to be helpful in half of the cases, (Pulec and Hahn 1970; Luxford and Sheehy 1982) but it appears to be most effective only in relieving the sensation of the tympanic membrane moving during breathing.

Surgical correction has been attempted by cauterization of the Eustachian tube orifice or lumen(Pulec and Simonton 1964) and removal of portions of the tubal cartilage(Simonton 1957). Topical applications with nitric acid, phenol, salicylic acid/boric acid(Bezold K 1908), were effective for approximately two weeks and required repeated treatments.(O'Connor and Shea 1981) Peri-tubal injections of paraffin caused granulomas(Zollner 1963) and gelatin sponge achieved only success for weeks to months(Ogawa, Satoh et al. 1976). Injection of the tubal orifice with Teflon® paste (Pulec and Hahn 1970) could produce enduring benefit, but serious complications including cerebral embolism from inadvertent injection into the internal carotid artery caused the manufacturer to withdraw the material for this purpose.(O'Connor and Shea 1981)

Pterygoid hamulotomy in normal cats produced middle ear effusion in 31/43 animals(Odoi, Proud et al. 1971) Combining the procedure with transposition or transection of the tendon of the tensor veli palatine muscle yielded successful results with an average of two year follow-up in 11/16 patients.(Virtanen and Palva 1982)

Lasting relief of autophony has been achieved by complete obstruction of the Eustachian tube using an angiocatheter occluded with bone wax (Bluestone and Cantekin 1981) or by cauterization of the lumen with insertion of a fat graft. (Doherty and Slattery 2003) These procedures generally require long-term middle ear ventilation with a tube. Insertion of a cartilage graft into a submucosal intraluminal pocket to add bulk to the posteromedial wall of the nasopharyngeal orifice has had some early success. (Kujawski 2004)

6 PURPOSE OF THE STUDY

The purpose of this study was to identify and quantify anatomical and physiological parameters of tubal dilation observed during video endoscopy. Based on these findings and previous work, surgical procedures were designed to alter the dimensions of the functional valve within the cartilaginous Eustachian tube to treat OME or patulous disorders. The following two hypotheses were tested in six studies:

1. The cartilaginous portion of the Eustachian tube contains a functional valve and pathology involving the valve leads to middle ear disease. Surgical dilation of the functional valve should improve otitis media with effusion.
2. The patulous Eustachian tube has a concave shape in the antero-lateral wall causing insufficiency in the functional valve.

The specific aims of the study were:

Study 1 To quantify metric and time parameters from video recordings of transnasal Eustachian tube endoscopy, establishing normal values and comparing them statistically with patients who had OME or patulous dysfunction.

Study 2 To apply a newly invented technology to simultaneously measure sonotubometry in synchrony with video endoscopy. Sonotubometry would provide objective measurements of tubal opening and endoscopy would concurrently demonstrate the phases of dilation.

Study 3 To evaluate safety, efficacy and long term data from a prospective study of Eustachian tuboplasty for medically refractory long-standing OME.

Study 4 To investigate feasibility and safety of balloon dilation technology to dilate the lumen of the Eustachian tube in a cadaver model with CT and dissection analyses of the results.

Study 5 To evaluate the safety and potential for efficacy in a prospective study of balloon dilation of the cartilaginous Eustachian tube in patients with refractory long-standing OME.

Study 6 To evaluate the role of a concave defect in the lateral wall of the functional valve as the etiology of patulous Eustachian tube with video endoscopy. Additionally, a prospective trial of surgical augmentation of the lateral wall and valve was conducted for treatment.

7 MATERIALS AND METHODS

7.1 SUBJECTS

Table 4 shows a summary of the study with a breakdown of the interventions performed in the six sub-studies that involved normal subjects, patients with OME or patulous Eustachian tubes or cadaver heads (without ear or sinus disease). The study progressed from studying video endoscopy of Eustachian tubes to the development and application of surgical methods for correcting the observed pathology.

Video endoscopy was obtained in all subjects and analyzed for various parameters or pathology. Endoscopy on contralateral normal ears was not performed if the subject declined the exam. Video software was used to make quantitative measurements from recorded examinations. (study 1) Sonotubometry was performed to make additional measurements of tubal opening by simultaneously combining it with endoscopy (study 2). Patients with long-standing refractory OME who were found on endoscopy to have prominent mucosal thickening from inflammation in the functional valve of the Eustachian tube underwent laser resection of intraluminal tissue for dilation of the valve and orifice (laser Eustachian tuboplasty) (study 3). An alternative method for dilation of the valve using sinus balloon technology was explored in cadaver specimens (study 4) and in patients with long-standing refractory OME (study 5). For patulous Eustachian tubes, a leak in the functional valve was sought and the antero-lateral wall was surgically augmented to close the defect (study 6).

Table 4 shows an overview of the interventions and number of subjects investigated. All subjects were adults 18 years or older.

Study	Interventions	Disease	<i>n</i> (ETs)	<i>n</i> (subjects)	<i>n</i> (Total ETs)
1	Video endoscopy Analysis of timing parameters Analysis of metric parameters -	Normal subjects	24	15	68
		Otitis media with effusion	20	13	
		Patulous ET	24	15	
2	Video endoscopy sonotubometry	Normal subjects	18	18	18
3	Video endoscopy Laser Eustachian tuboplasty	Otitis media with effusion	13	13	13
4	Video endoscopy CT scan Balloon dilation of Eustachian tube Video endoscopy CT scan with contrast in lumen Anatomical dissection	Normal unembalmed cadaver heads	16	8	16
5	Balloon Dilation of ET	Otitis Media with Effusion	11	11	11
6	Video endoscopy Patulous ET Reconstruction	Patulous ET	14	11	14

7.2 METHODS

7.2.1 MEASUREMENTS OF EUSTACHIAN TUBE DILATION BY VIDEO ENDOSCOPY (STUDY 1)

Measurement of torus tubarius and antero-lateral wall timing and movements.

Recorded examinations from Eustachian tube 4 mm Hopkins rod 30 degree (Karl Storz, Tuttlingen, Germany) endoscopic examinations in the office were studied and measurements were taken by reviewing video and still frames with OsiriX DICOM viewer software v.3.7, (Geneva, Switzerland). Magnification of images increases exponentially in proximity with a target and presents a problem for measuring lengths without references in the image. To resolve this issue, measurements were made in reference to the height of the torus tubarius, which is an easily recognizable landmark.

Lengths were calculated as a percentage of the torus tubarius height. Torus tubarius heights were visualized at roughly similar magnifications between patients and the absolute measured lengths were statistically compared. The height of the torus tubarius was measured in pixels in both the resting position and in the maximally medially rotated position during dilatory efforts. The average of these values was used as the torus tubarius unit of measurement.

The angle of rotation of the torus tubarius was calculated by the software. The maximum lateral excursion of the anterolateral wall (by TVP muscle action) within the orifice and the height of maximal palatal elevation (inferior to the torus tubarius) were measured as percentages of the torus tubarius unit. Durations of the dilatory sequence, time to rotate the torus tubarius medially and the duration of apparent opening of the valve were measured directly from the time line in Final Cut Pro video processing software (Apple, Cupertino, CA) Measurements were evaluated statistically with SPSS 17.0 statistical software package (IBM, Chicago, IL). Independent samples Mann-Whitney U tests were employed using $p < 0.05$ for the level of significance.

7.2.2 SYNCHRONOUS ENDOSCOPY AND SONOTUBOMETRY OF THE EUSTACHIAN TUBE (STUDY 2)

Subjects underwent endoscopic nasopharyngoscopy with sonotubometry. The examination utilized a novel device to record synchronous and simultaneous sonotubometer and digital video recordings of transnasal endoscopy (MMS-S10-EV Eustachian Tube Analyser, Marchbanks Measurements Systems, Lymington, UK).

Figure 5



Figure 5. A. Shows Eustachian tube Analyser in the office. B. Shows the nasal speaker and ear transducer in position in a subject.

Endoscopy was performed as previously described using a rigid 45 Hopkins rod endoscope (Karl Storz, Tuttlingen, Germany) or flexible nasopharyngoscope (Pentax, Montvale, NJ) fitted with a single chip analog charge coupled device (CCD) video camera (Karl Storz). Sonotubometry was performed with the speaker placed into the nostril contralateral to the Eustachian tube to be studied. A microphone was placed in the ipsilateral external auditory canal (EAC) and sealed against the EAC walls. The endoscope was passed through the ipsilateral nasal cavity. The nasal speaker was set to produce a 7 kHz tone at 100 dB SPL for a duration of 6.0 seconds. The nasal probe tone signal was detected by the EAC microphone, amplified, passed through an RMS converter, onto a true log dB amplifier and finally to a 12 bit analog to digital converter. Video recording was done at 29.97 frames per second and calibrated to the sonotubometer with a measured variance of +/- 20 ms. Recordings were made during swallows to observe physiological dilation of the Eustachian tubes and with forced yawns for sustained maximal efforts. During each 6.25 seconds long video clip, subjects could typically perform two swallowing efforts, at times three. Normal individuals do not dilate their Eustachian tube to open with every swallow. Dilation of the functional valve was observed on endoscopy by the coordinated actions of the LVP contraction holding the torus tubarius in a medialized position against which the TVP subsequently dilated the antero-lateral wall to produce a rounding of the valve to the fully dilated position. Dilation of the valve to the open position was determined by the observation of a 5 dB rise in the dB SPL in the microphone signal from the sonotubometer that coincided with the muscular effort.

7.2.3 EUSTACHIAN TUBOPLASTY TO WIDEN THE EUSTACHIAN TUBE ORIFICE AND FUNCTIONAL VALVE (STUDY 3)

Laser debulking of the luminal surface of the torus tubarius and postero-medial wall up to or including the valve was performed to widen the aperture in patients with long-standing refractory OME. The study was a prospective continuation of a pilot trial to add longer term follow-up in an expanded cohort. The outcomes were presence or absence of effusion on otomicroscopic exam and tympanogram type A, B or C.

13 of 16 patients operated met criteria for the study having had at least a five-year history of chronic otitis media with effusion (OME). They had each undergone at least two prior tympanostomy tube placements with recurrence of the effusion immediately following extrusion of each of the tubes. 8 of the 13 patients were originally presented in the preliminary LETP study (Poe, Metson et al. 2003) and their subsequent data is included in this report. The average follow-up was 26 months (range, 14 to 34 months). The patients served as their own historical controls.

All patients underwent preoperative transnasal endoscopic slow-motion video analysis of their Eustachian tubes and were found to have disease within the cartilaginous portion consistent with a functional obstructive disorder.

All patients were treated for a minimum of eight weeks with nasal corticosteroids and medical therapy for allergic or laryngopharyngeal reflux disease was given if indicated by signs or symptoms. Failure to show improvement of OME following medical management was the final inclusion criterion. Audiograms and tympanograms were performed preoperatively.

Surgery was performed unilaterally, on the worse ear if the condition were bilateral.

The study protocol was approved by the institutional (ethical) review board of the Massachusetts Eye and Ear Infirmary, Boston, MA, USA. All patients were provided appropriate information regarding study design and had signed informed consents.

Eustachian tuboplasty surgical technique

Patients were placed in the supine position, maintained with general anesthesia, and orally intubated. **Figure 6**



Figure 6: Operative setup for left-sided LETP with tonsil mouth gag in place and nasal endoscope in the left nostril. An optional endoscope holder is fixed to the mouth gag.

Ventilation of the ipsilateral middle ear was achieved by placing a 0.9-mm-silicone mini-Baxter tympanostomy tube in 10 cases, or by removing an obstructed permanent tympanostomy tube and leaving the tympanic membrane perforation in 2 cases. Myringotomy alone was performed in one case. Middle ear effusion was aspirated. A 30° 4-mm-diameter nasal endoscope was placed through the ipsilateral nasal cavity to visualize the tubal orifice. A tonsil mouth retractor was placed and surgical instruments were passed transorally. Local infiltration using 1% lidocaine with 1:100,000 epinephrine was performed in the tubal orifice. The medial cartilaginous lamina within the torus tubarius was identified and palpated as a landmark. A 980-nm contact-tip diode laser (Biolitec, East Longmeadow, MA) with settings of 7 W power, continuous pulse mode with 0.2 seconds on and 0.8 seconds off was used in the first six cases. The diode laser was on loan and after its return to the manufacturer, an argon laser (HGM, Medical

Laser Systems, Salt Lake City, UT) with settings of 3 W, 0.2 sec pulse duration, continuous mode was used in the subsequent five cases. Vaporization of mucosa and submucosa to expose the underlying cartilage was done to create a wedge shaped defect on the intraluminal surface of the torus tubarius and postero-medial wall. Submucosal vaporization was done in the valve region sparing the mucosa. **Figure 7**

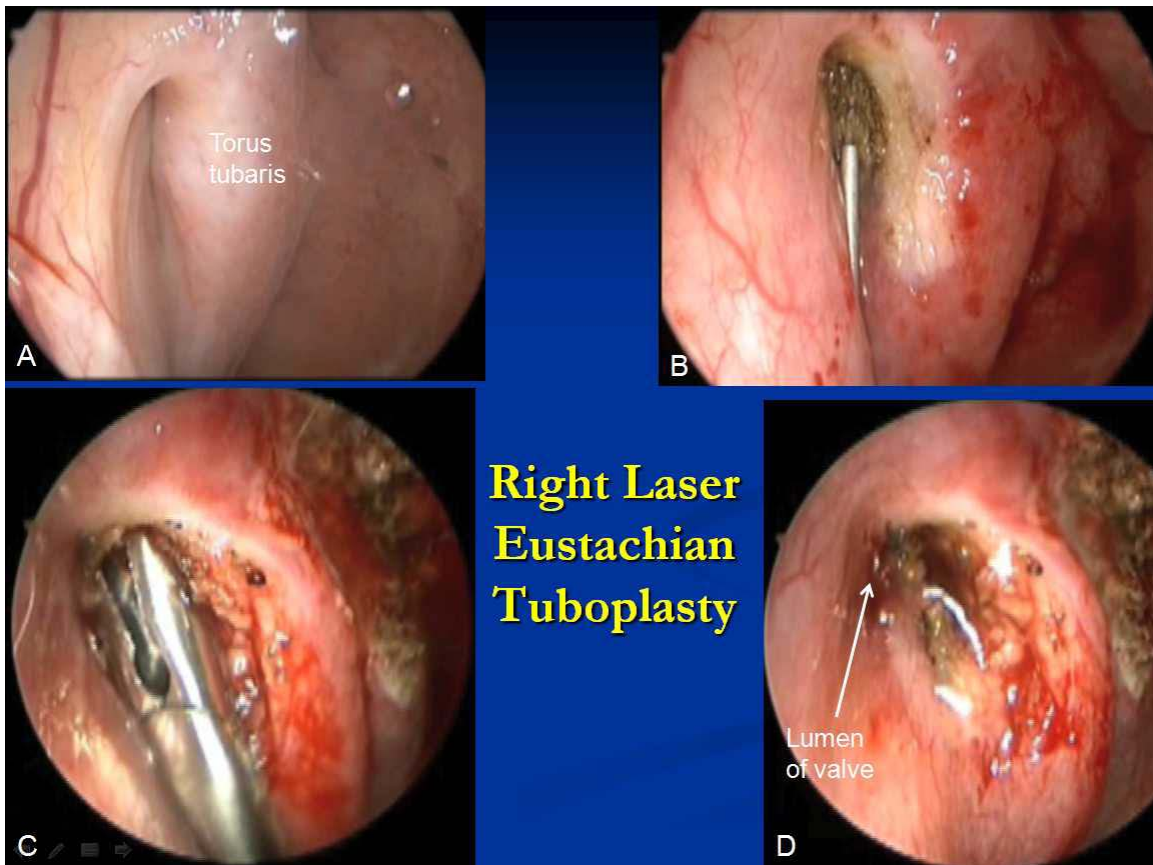


Figure 7 LETP. A. Preoperative image shows significantly thickened inflammatory changes in the mucosa of the torus tubarius with bulging into the lumen. B. Argon laser vaporization of mucosa and submucosa of postero-medial wall to expose the medial cartilaginous lamina with sparing of the antero-lateral wall. C. Resection of cartilaginous bulge from torus tubarius. D Completed resection. Note intact valve mucosa but removal of underlying submucosa.

The resection was confined to the postero-medial wall avoiding injury to the antero-lateral wall. The medial cartilaginous lamina was thinned when it protruded into the lumen. The extent of surgical excision was determined by the degree of bulk seen at the pre-operative slow-motion video analysis, In two patients, mucosal biopsies of the torus tubarius were obtained at the time of LETP and several months postoperatively.

Patients were followed with audiograms, tympanograms, and microscopic examination of the ears for 6 months, 1 year, and yearly intervals thereafter. Two year follow-up is

reported as the three year follow-up data was insufficient due to lack of patient follow-up. Patients who were suspected of having reflux disease were continued on omeprazole 20 mg orally daily for at least 6 weeks after surgery. Failure of LETP was determined if OME recurred as diagnosed by oto-microscopic examination.

A tympanostomy tube placement or myringotomy was performed to assure that patients had at least the same temporary benefit that had been experienced with previous tubes. As a pilot study, the goal was to establish whether the novel procedure could have a demonstrable effect in altering patients' refractory OME history, in which a tube had been previously placed at least two times and the effusion had promptly recurred each time.

7.2.4 FEASIBILITY AND SAFETY EVALUATION OF BALLOON DILATION OF THE EUSTACHIAN TUBE IN CADAVERS (STUDY 4)

Unembalmed adult human cadaver half-heads underwent baseline axial computed tomographic (CT) scans (CereTom® OTOScan, NeuroLogica Corporation, Danvers, MA) in the supine position with 0.625 mm slice thickness. Endoscopic photographs of the nasopharyngeal orifice of the Eustachian tube were obtained at baseline and at each stage of the procedures using 0° and 30° angled, 4mm diameter Hopkins rod endoscopes fitted with a three chip CCD video camera (Karl Storz, Tuttlingen, Germany). Instruments were passed through the nasal cavity to simulate an actual surgical procedure to the maximum extent possible.

The sinus balloon dilation system (Acclarent, Inc., Menlo Park, CA) was employed for dilation of the cartilaginous portion of each Eustachian tube. The guide catheter was inserted just into the tubal nasopharyngeal orifice and a Relieva Vigor™ sinus guidewire was threaded through the catheter into the lumen of the Eustachian tube lumen and advanced under fluoroscopic guidance using a C-Arm to reach the bony isthmus. The guiding catheter was removed and imaged again with CT. A 6 or 7 mm diameter x16mm length Relieva Solo™ sinus balloon catheter was passed over the guide wire until reaching resistance near the bony-cartilaginous isthmus. The balloon typically protruded from the tubal orifice approximately 2 – 3 mm. The guidewire was removed and the balloon was inflated to 12 atm for one minute, after which it was deflated and removed. Endoscopic assessment of the dilation was performed immediately after dilation. CT scans were then obtained approximately 15 – 60 minutes afterwards, placing the ½ heads into a lateral decubitus position with the tubal orifice facing upwards and the orifice was filled with Omnipaque contrast solution, 300mg I/ml (GE Healthcare, Princeton, NJ) in order to accurately visualize and quantify the dimensions and volumes post-dilation.

Careful assessments were made to inspect for any adverse effects from the dilation including endoscopic inspection, surgical dissection of the cartilage, muscles, soft tissues and adjacent temporal bone, basisphenoid, or pterygoid plates, and detailed review of the CT scans.

A final trial of dilation was performed in four Eustachian tubes of two unembalmed whole cadaver heads under endoscopic guidance to best simulate surgical conditions. After dilation, close endoscopic inspection was done to assess for any evidence of adverse effects, including a visual survey of the mucosa and palpation of the posterior cushion to inspect for excessive mobility. **Figures 8 a-c**

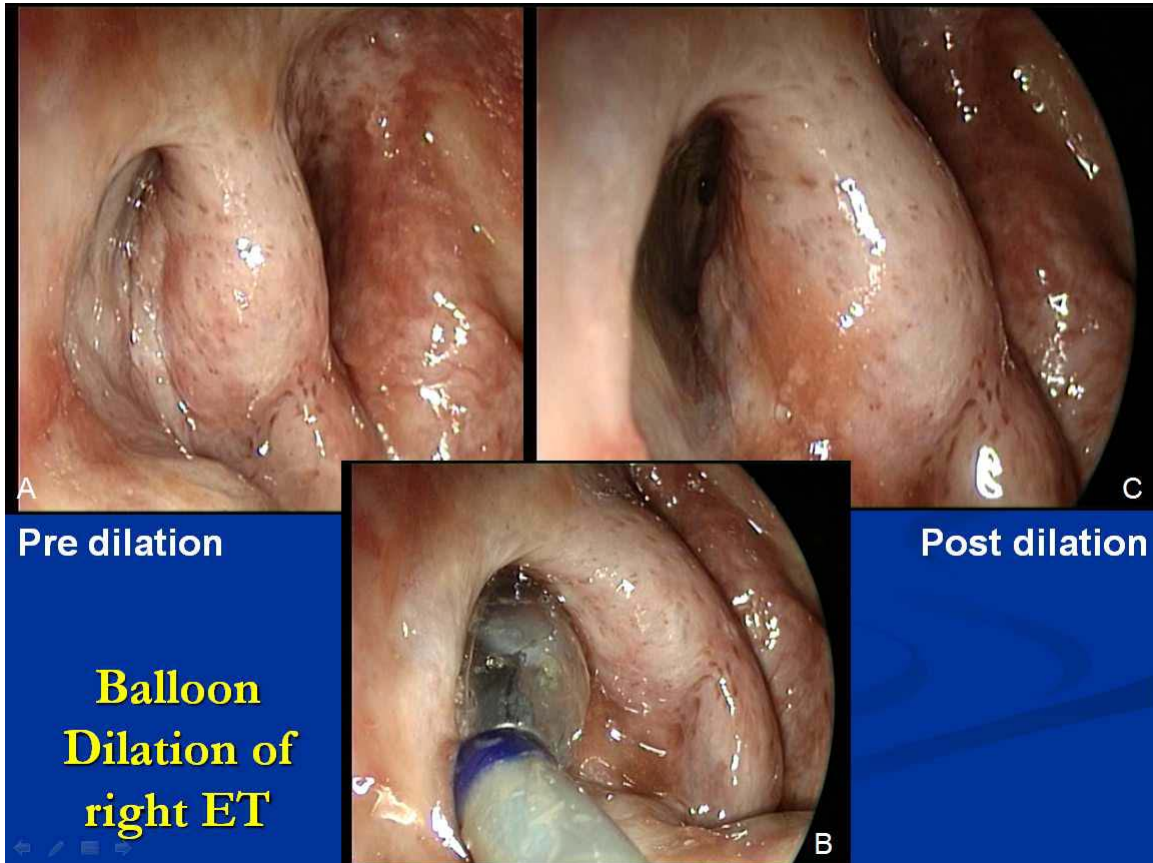


Figure 8 A. Endoscopic view of right Eustachian tube in cadaver at baseline. B. 7mm x 16 mm sinus dilation balloon is inflated in position. C. Tubal lumen post dilation.

CT scans were additionally analyzed to determine the dimensions and volume of the cartilaginous Eustachian tube pre- and post-dilation. Cross sectional areas with respective major and minor axis diameters at approximately 4 mm intervals, and volumes were computed using OsiriX software (OsiriX Foundation, Geneva, Switzerland).

A curvilinear line representing the longitudinal axis of the Eustachian tube was used to create 2D Curved MPR (Multiplanar) perpendicular reconstructions from which the length of the longitudinal axis could be measured as well as the cross-sectional areas and lengths of the major/minor axes of the oval shaped cross sections. Volumes were calculated by manually outlining a region-of-interest on each axial slice and using the volume estimation algorithm.

7.2.5 BALLOON DILATION OF THE CARTILAGINOUS EUSTACHIAN TUBE (STUDY 5)

Patients with unilateral or bilateral persistent OME for \geq five consecutive years, broken only by tympanostomy tubes or tympanic membrane (TM) perforation were evaluated as candidates for ET surgery. None of the subjects could insufflate their ears with a Valsalva maneuver. Otomicroscopy and tympanometry were done bilaterally. Video rigid or fiberoptic endoscopy of the Eustachian tube with slow motion review demonstrated mucosal inflammation as the predominant finding, indicating dilatory dysfunction of the ET as opposed to dynamic (muscular) dysfunction. The techniques for endoscopic examination and a scoring system for rating mucosal inflammation have been previously reported. (Poe, Metson et al. 2003). The mucosal inflammation score was modified to separate mild and moderate disease and remains unvalidated. The score consisted of 1 = normal mucosa; 2 = mild edema and or erythema, with or without increased mucus; 3 = moderate edema and erythema with significant compromise of dilation of the lumen during swallows and yawns; 4 = severe edema and erythema with inability to dilate the lumen open. Preoperative high resolution computed tomography (CT) scans were obtained to rule out anatomical anomalies of the ET or cranial base and dehiscence of the internal carotid artery into the tubal lumen.

Candidates for surgery were offered the option of continuing their current management or undergoing a procedure consisting of unilateral balloon dilation of the cartilaginous ET. In the case of bilateral disease, the side with the worst ear pathology was selected.

Outcomes included the ability to self-insufflate air through the ET with a Valsalva maneuver, rating of mucosal inflammation at the tubal orifice as seen by endoscopy, otomicroscopic findings of OME/TM retraction/normal and tympanogram curves types A/B/C.

Informed consent was obtained and the protocol was approved by the Ethical Committee (equivalent to USA IRB) for the Päijät-Häme Central Hospital, Lahti, Finland (Balloon Dilation of the ET R09054). All cases were performed by the second author at that secondary referral hospital and some were assisted by the first author.

Surgical technique

Patients were induced and maintained under general anesthesia with endotracheal intubation in the supine position. Topical Oxymetazoline hydrochloride decongestant was applied to the nasal cavities. A 30 degree Hopkins rod endoscope (Karl Storz, Culver City, CA) was introduced through the ipsilateral or contralateral nasal cavity. Video images were displayed on a monitor (Karl Storz, Tuttlingen, Germany).

Similar to the rationale in Study 3, as this was a pilot study of safety and exploration of possibility for efficacy, a tympanostomy tube was inserted in the two cases with OME at the time of the surgery so that patients could experience immediate symptom

improvement as with prior tympanostomy tube procedures. The remaining cases had a tube, perforation, or atelectasis.

The sinus balloon dilation system (Acclarent, Inc., Menlo Park, CA) was employed to dilate the cartilaginous portion of the ET. A curved guiding catheter with a tip angle of 70 degrees was passed through the nasal cavity with the tip placed just into the ET nasopharyngeal orifice. A 7 mm diameter x 16mm length Relieva Solo™ sinus balloon catheter was passed through the guiding catheter and atraumatically into the ET orifice until reaching the first mild resistance as it approached the narrowest diameter at the bony-cartilaginous isthmus. The balloon typically protruded from the tubal orifice about 2 – 3 mm.

The balloon catheter lumen was left open to allow for air escape from the proximal (toward the middle ear) ET during inflation. The balloon was inflated with sterile water up to 12 atm for one minute after which it was deflated and removed.

The immediate effect on widening of the lumen of the ET was judged qualitatively from intraoperative videos reviewed following the surgery and by palpation of the torus tubarius. The degree to which the functional valve was opened by the dilation and remained open was estimated by the increase in apparent depth of view into the lumen of the ET. As the mucosal surfaces are normally in apposition in the valve, the length of persistent opening of the valve could reflect the immediate result of the dilation. The effectiveness of the dilation was rated as none if there were no visible change, small if the apparent increase in distance seen was estimated at < 4 mm, medium for ≥ 4 mm without seeing the isthmus, and patent if the valve was dilated open and the isthmus was visible.

All patients were treated on an out-patient basis. Follow-up exams were scheduled for one and six months post-op and were planned to include otomicroscopy, tympanogram, endoscopy of the ET, demonstration of attempt to do a Valsalva maneuver and a repeat rating of the mucosa of the ET lumen. Valsalva maneuvers were neither coached nor practiced. Subjects were merely asked to perform these maneuvers during their office visits.

Statistical analysis was done with using SPSS 17.0 statistical software package (IBM, Chicago, IL) with 2-tailed Fisher's exact test performed using $p < 0.05$ for significance. The patients were used as their own historical controls, given their long-standing disease.

7.2.6 IDENTIFICATION OF THE PATULOUS EUSTACHIAN TUBE DEFECT AND SURGICAL CORRECTION WITH AUGMENTATION OF THE LATERAL WALL. (STUDY 6)

Patulous Eustachian tube reconstruction (PETR) was performed in patients who had been symptomatic for a median of 6 years and had failed conservative management. Second-sided procedures were staged. Slow motion video endoscopy was done to inspect for a

defect in the functional valve of the Eustachian tube. The outcome measure was a self-reported assessment of the patient's autophony scored as: 1) complete relief, 2) significant improvement, satisfied, 3) improvement, dissatisfied, 4) unchanged, 5) worse.

PETR surgical technique

PETR was performed as an outpatient procedure under general anesthesia using a combined endoscopic trans-nasal and trans-oral approach similar to that described for LETP above. Autologous nasal septal or tragal cartilage or AlloDerm™ acellular cadaveric dermal implant (Life Cell Corp., the Woodlands, TX) were used for graft materials. Under endoscopic guidance, a 200 micron fiber-delivered argon ion laser (HGM Co) with settings of 3.5 W and 500 ms or a diode pumped KTP laser (Iridex Co.) with settings of 1500 milliwatts and 500 ms were used to make the incision and initial dissection into the submucoperichondrial plane along the roof of the Eustachian tube lumen. The incision was made circumferentially along the superior half of the nasopharyngeal orifice and carried deeply to expose the medial and lateral cartilagenous laminae.

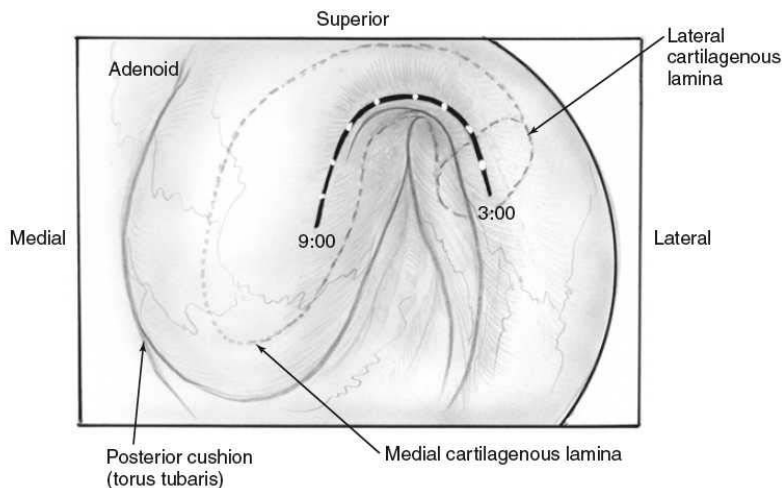


Figure 9 PETR in a left Eustachian tube. The incision and underlying cartilagenous landmarks are demonstrated.

Sharp and blunt dissection with curved instruments was done to develop the submucoperichondrial flap creating a pocket inferior to the cartilage roof and the pocket was dissected up well into the valve.

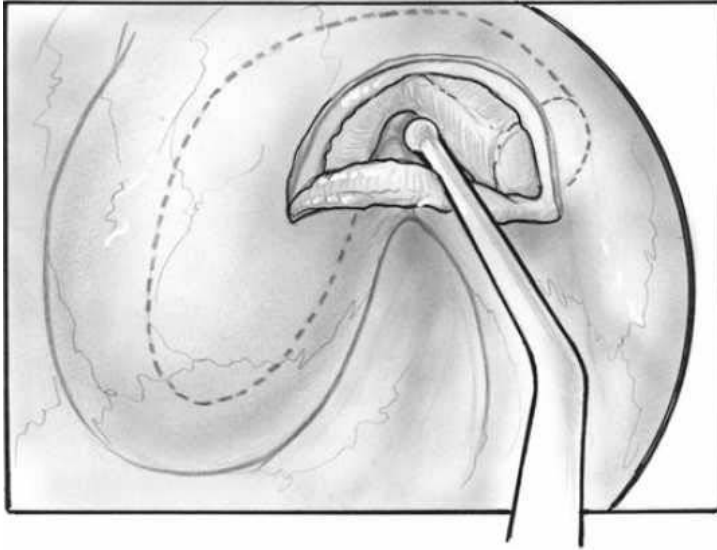


Figure 10 Blunt dissection of the submucoperichondrial flap.

The resultant pocket was filled with multiple wedges of autologous cartilage grafts or with Alloderm™ implant measuring between 1 x 1cm to 1 x 2cm. Sufficient graft material was placed into the pocket to overcorrect the concave defect in the anterolateral wall anticipating a 50 to 60% loss of graft volume postoperatively. The mucosal wound was closed with sutures.

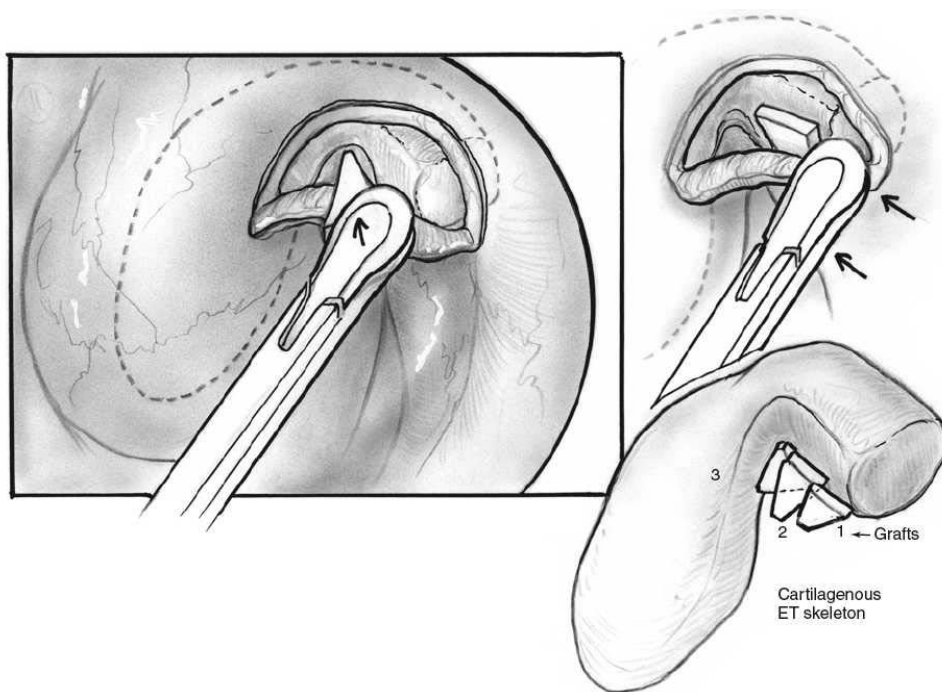


Figure 11 Positioning of cartilage graft wedges into the pocket.

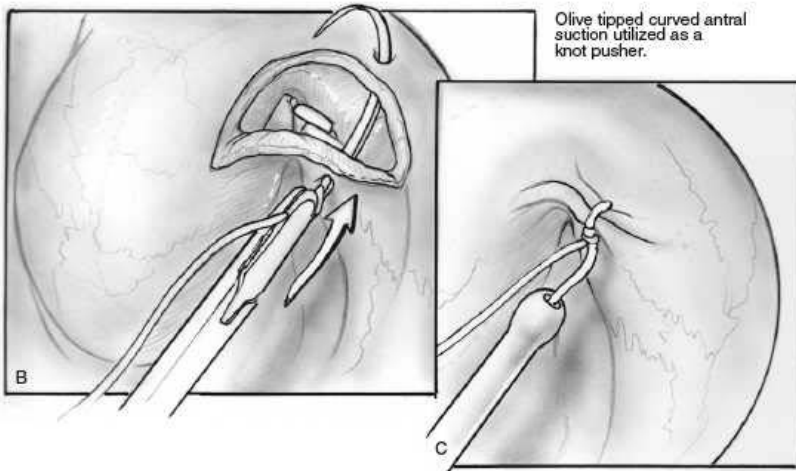
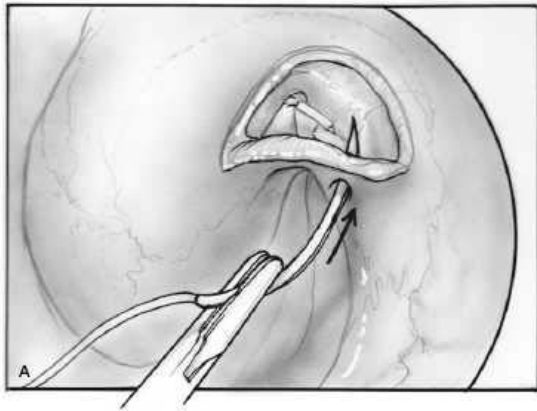


Figure 12 Positioning of cartilage graft wedges into the pocket.

8 RESULTS

8.1 MEASUREMENTS OF EUSTACHIAN TUBE DILATION BY VIDEO ENDOSCOPY (STUDY 1)

Heights of the torus tubarius for the unit of measure

There were no statistically significant differences in the heights of the torus tubarius between the groups, which consisted of normal controls, patients with OME and patients with patulous Eustachian tube.

Duration of Eustachian tube dilatory cycle

There were no statistically significant differences between the groups regarding the duration of any portions of the tubal opening and closing cycle. The mean cycle time was 995 ms for normal subjects. There was a trend toward a longer cycle time with patulous tubes at 1276 ms.

Torus tubarius rotation time measured the duration from initiation of its medial rotation to its maximally rotated position and there were no significant differences between the groups.

Opening time of the valve represented the duration that the functional valve appeared to be dilated open or made maximal efforts to dilate. The opening time for normal subjects was 10.5 ms and there was a trend for prolongation of the opening time in dilatory dysfunction Eustachian tubes at 15.1 ms.

Linear and angular measurements in the Eustachian tube dilatory cycle

There were no significant differences between groups regarding height of elevation of the palate. Elevation in normal subjects was 34.8% of torus tubarius height.

Lateral excursion of the antero-lateral tubal wall, the distance traveled due to TVP contraction, was significantly reduced in dilatory dysfunction (23.9% of torus tubarius height, $p=0.015$) and even more reduced in patulous Eustachian tube (18.7%, $p= 0.001$) in comparison to normals (35.5%).

The mean angle of rotation of the torus tubarius during dilation for normals was 34.2° and there was no significant difference from the other groups.

The important results are summarized in **table 5** at the end of this section 8 and the complete results with statistical analyses are in the Study 1 article (Poe and Pyykkö 2010)

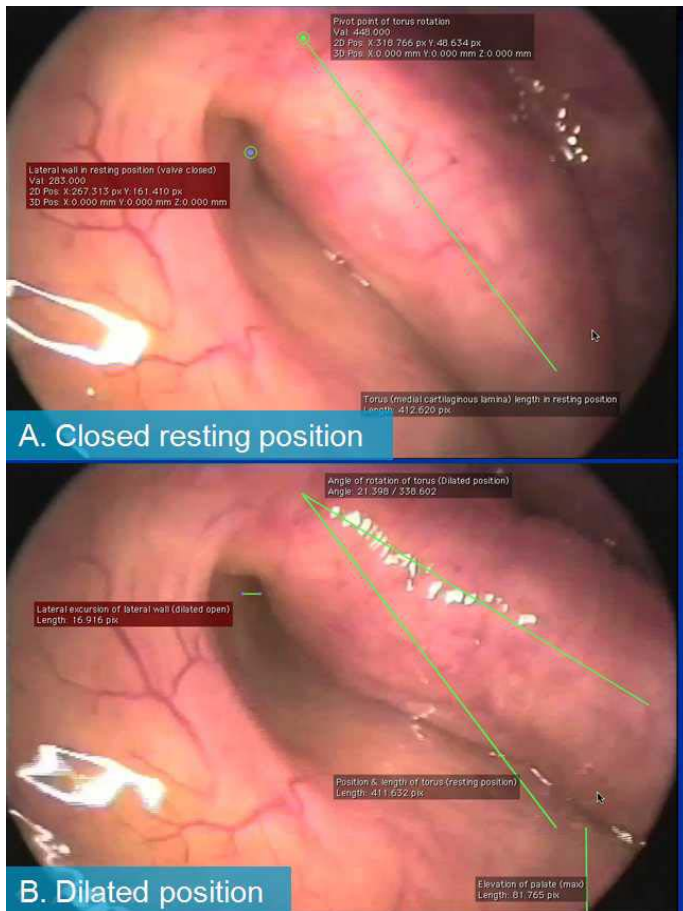


Figure 13 shows the parameters measured on the closed and dilated position still frames that were grabbed from the video endoscopic exam.

8.2 SYNCHRONOUS ENDOSCOPY AND SONOTUBOMETRY OF THE EUSTACHIAN TUBE (STUDY 2)

Sonotubometer measurements

Quantitative results of the sonotubometer measurements during swallow or yawn maneuvers to open the Eustachian tube are summarized in **table 5**. The number of subjects that appeared to open the ET, as observed by endoscopy, or objectively opened it, as recorded by a ≥ 5 dB signal increase by sonotubometry, is shown in the first column for each maneuver. The duration and amplitude of the sonotubometer signal increases are listed within the same cell below the number of subjects that opened their Eustachian tubes.

One subject was excluded from data analysis due to increases in sound intensity with tubal opening significantly larger than for other subjects. Six out of the remaining seventeen (35.3%) subjects failed to demonstrate a voluntary ability to develop objective opening with swallowing during the study. For the 11/17 that did open the Eustachian

tube during swallows, successful opening was variable (range 10-100% of openings per swallows). Four subjects opened their Eustachian tubes with every swallow (i.e. 100% openings per swallows). The average duration of tubal opening during swallows as measured by sonotubometry was 0.44 seconds, and the average increase in sound intensity reaching the EAC was 9.2 dB. Yawning resulted in a higher percentage of instances of tubal opening compared to swallowing and only four subjects (23.5%) could not open the Eustachian tube during a forced yawn. The average opening time was 2.03 sec and the intensity of sound recorded in the EAC increased by an average of 10.1 dB.

Correlation between sonotubometer results and video endoscopy

There was a 100% correlation between sonotubometric detection of a significant rise in dB SPL to indicate tubal opening and endoscopic observation of valve dilation to the open position. On the contrary, endoscopic observations of valve dilation did not correlate with a dilation to open on the sonotubometry in 1/11 cases. Assuming the sonotubometry to be the “gold standard,” this yields a specificity of 0.92.

A negative sound pressure wave was recorded in a number of instances, immediately preceding a swallow related opening. In **figure 14** recorded from subject 8, a bubble of nasal secretions is seen in the Eustachian tube orifice; the sonotubometer recording reflects a closed Eustachian tube. Upon swallowing figure b shows the bubble to be inflated and the sonotubometer records a reduction in the sound intensity reaching the EAC. These findings are compatible with air being pushed from the Eustachian tube into the nasopharynx.

The results are summarized in **table 5**.

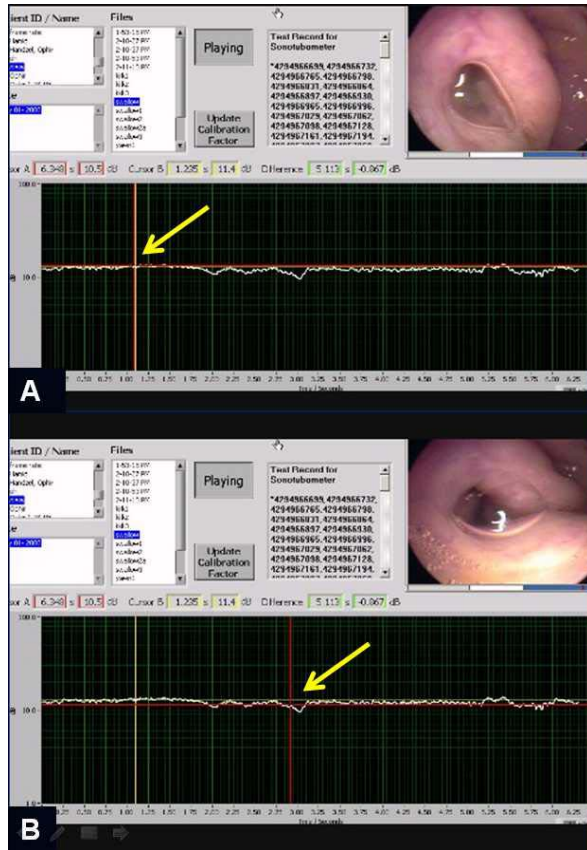


Figure 14. Sonotubometer and video endoscopy demonstrating an air bubble being forced out of the tubal lumen between resting baseline A and action of the pharyngeal constrictor and LVP muscles to initiate a swallow in B.

8.3 LASER EUSTACHIAN TUBOPLASTY (STUDY 3)

8.3.1 Outcomes of laser Eustachian tuboplasty

The outcomes for LETP are summarized in **table 5**. In the preoperative assessment, 9/13 cases had effusion filling the middle ear and 4/13 cases had a mixture of atelectasis and effusion. Laryngopharyngeal reflux was diagnosed in 9/13 (69%) and allergic rhinitis in 10/13 (77%). LETP in combination with tympanostomy tube eliminated OME in 4/11 of the patients at 6 months, 3/10 at 1 year, and 3/8 at 2 years.

Comorbidities

Comorbidities were associated with failures in the 1 year results. The difference between successful and failed LETP patients showed statistically significant correlation with the presence of reflux disease (0% vs. 40%, respectively, $p=0.01$) or allergic disease (10% vs. 30%, respectively, $p=0.05$). At two years, there was no significant difference between

successful and failed LETP patients with the presence of either reflux (10% vs. 30%, respectively, $p=0.10$) or allergic disease (10% vs. 20%, respectively, $p=0.20$) by chi square analysis.

Audiometry results

Successful LETP + tympanostomy tube patients demonstrated a statistically significant difference in their mean pre-treatment pure tone average (PTA) (35.3 dB) and post-treatment PTA at 1 and 2 years (12.9 dB and 20.8 dB, respectively, $p=0.028$). There was no statistically significant worsening of the PTAs in either the successful or failed groups.

Histology

Pre- and post-operative histological examinations were obtained in two patients. Preoperatively there was severe inflammation with hemorrhagic changes. The pseudostratified columnar mucosa was hypertrophied and without cilia. There was a severe inflammatory infiltrate within the submucosa and mucosa. The post-operative specimen showed some moderate inflammation and hypertrophy with return of a ciliated epithelial border. The inflammatory infiltrate did not involve the mucosa. There was fibrosis in the submucosal layer but the overall thickness of the mucosa and submucosa was substantially reduced compared to preoperatively.

Postoperative endoscopy

Comparison of endoscopic examinations preoperatively **Figure 15 A,B** and postoperatively in **Figure 15 C,D** showed that the wounds healed with a stellate-shaped scar over a scaphoid loss of volume in the postero-medial wall adjacent to the valve. The result was a wider tubal orifice and distal portion of the valve in nearly all cases, including failures.

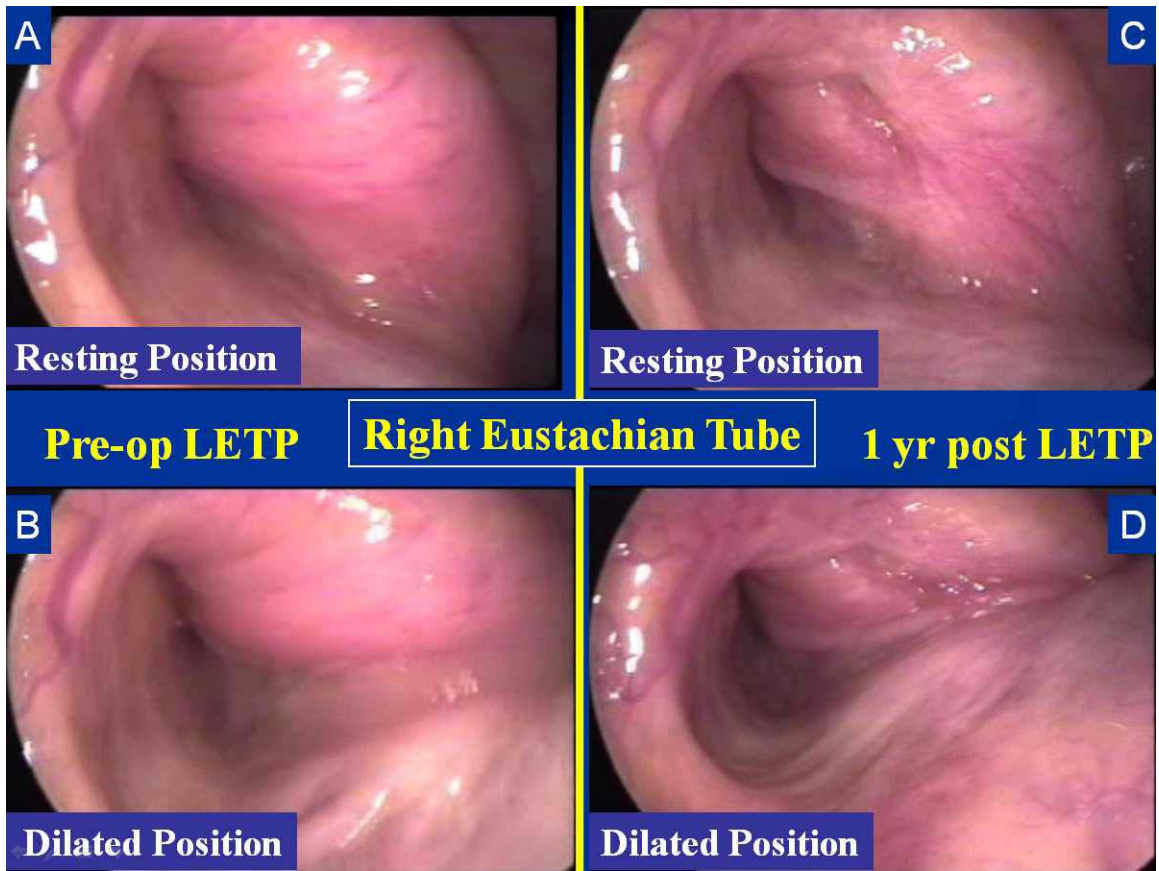


Figure 15 showing pre LETP and 1 year post LETP office endoscopic exams of the right Eustachian tube

Complications were insignificant and were limited to one soft intranasal synechia and a small synechia between the posterior surface of the torus tubarius and the adjacent adenoid mucosa. Two other patients developed a small red granuloma in the center of the resected area of mucosa that were treated with nasal corticosteroid spray for six weeks and the granulomas subsided completely. There were no instances of epistaxis, nasal obstruction, significant pain or intraluminal adhesions or strictures. There were no patulous Eustachian tubes as a result of LETP.

8.4 BALLOON DILATION OF THE CARTILAGINOUS PORTION OF THE EUSTACHIAN TUBE: INITIAL SAFETY AND FEASIBILITY ANALYSIS IN A CADAVER MODEL (STUDY 4)

Dilation outcomes

Successful balloon dilation was achieved in all Eustachian tubes without any major adverse effects. Dilation of the 12 Eustachian tubes in the ½ heads was accomplished with a 7 mm diameter balloon in 8 (66.7%) and with a 6 mm balloon in 4 (33.3%). In most cases, the inflated balloon locked securely into position leaving approximately one-

third of the 16 mm length protruding distally from the orifice. In all cases, the dilation caused medialization of the torus tubarius, medially rotating the free portion of the medial cartilaginous lamina.

Post dilation measurements

Average intraluminal volumes of the cartilaginous Eustachian tube increased from pre-dilation 0.16 cm³ to post-dilation 0.49 cm³ (increase of +357%), ($p < 0.001$).

Measurements of the post dilation lengths of the cartilaginous portion of the Eustachian tube averaged 26.3 mm (SD 1.7830, range 23.3 – 29.0) Cross sectional areas were measured at approximately 4 mm intervals through the cartilaginous Eustachian tube with the results depicted in **Figure 16**.

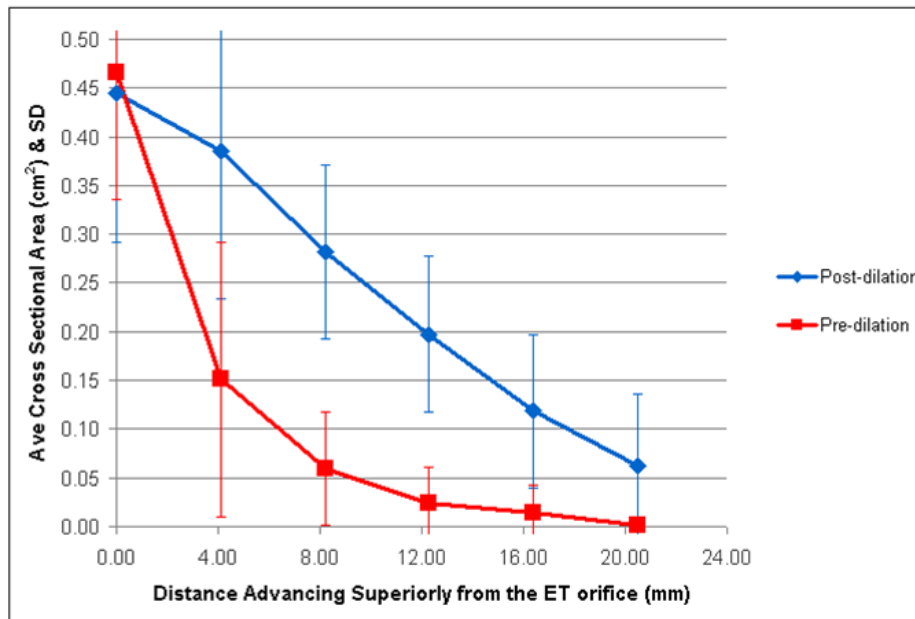


Figure 16 shows average cross sectional areas of the post-dilated Eustachian tube at distances from the nasopharyngeal orifice specified on the x-axis. The greatest effects of dilation are seen from 4 mm to 16 mm.

At the Eustachian tube orifice (0 mm distance) and at the bony cartilaginous junction (ave 26.3 mm), there were no significant differences between pre- and post-dilation areas ($p = 0.61$ and $p = 0.54$ respectively). At the remaining distances, post-dilation areas were significantly larger ($p < 0.001$ for each distance).

Adverse effects

There were minor adverse effects in three Eustachian tubes, which were limited to lacerations of the luminal mucosa. There were no other soft tissue or bony injuries in the ½ head or whole head specimens.

The results are summarized below in **table 5**.

8.5 BALLOON DILATION OF THE CARTILAGINOUS EUSTACHIAN TUBE

Demographics

There were 11 patients (5M, 6F) ages 33-76 years (average 51.8) having had previous tympanostomy tubes (ave 4.7). The preoperative status and post operative results are summarized in **Figure 17** and the Valsalva outcomes are summarized in **table 5**.

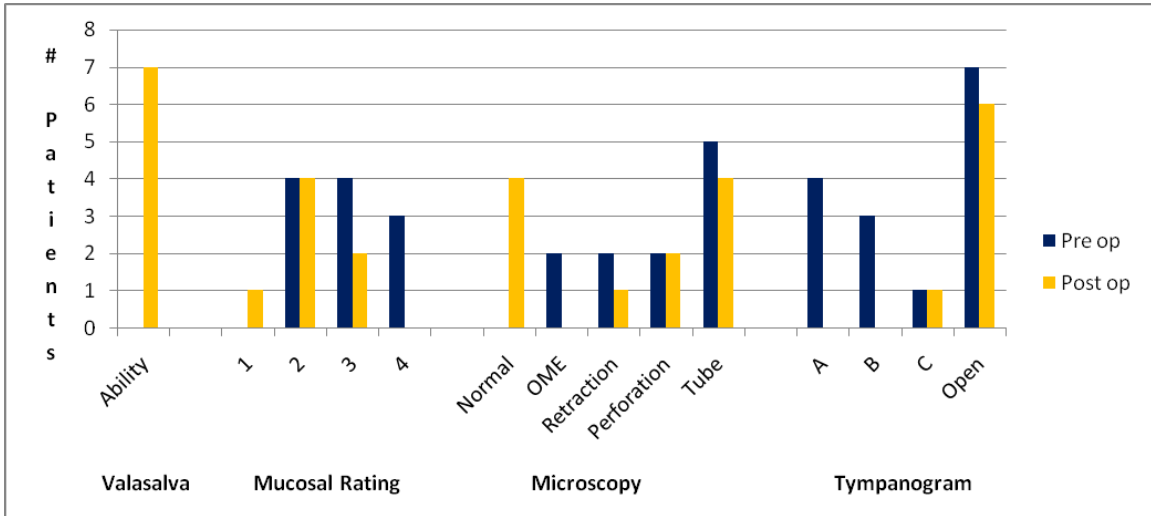


Figure 17 shows the pre operative status and post-operative results after the balloon dilation procedure. Follow up range 6 – 14 months (mean 9.2) A

Dilation outcomes

Balloon dilation results are summarized in **Table 6**.

Table 6**Balloon Dilation**

Case #	Side	Atm	Dilation effectiveness	Mucosal tear	Adjunctive procedure	Comment
1	R	12	Medium	Yes	remove tube	
2	L	12	Patent	Yes	remove tube	
3	L	10	Medium			
4	L	8	Small			Balloon slipped out by end of dilation
5	L	8	Small		remove tube	Balloon protruded 30%
6	L	12	Patent			
7	L	12	Patent			Balloon protruded 30%
8	L	12	Medium		insert tube	
9	L	10	Medium	Yes		Dilation repeated x1
10	L	12	Patent	Yes		
11	L	12	Patent	Yes	insert tube	

The balloon typically protruded out of the orifice by 25 to 30%. It was monitored during inflation and the guide catheter adjusted to hold it in position if it began to slip out more than 30%.

Dilation of the ET occurred successfully in all cases. The dilation effectiveness was small in the 2 cases inflated to 8 atm, medium in the 2 cases dilated to 10 atm, and dilated to fully open in 5/6 (83.33%) cases inflated to 12 atm. The full dilation associated with 12 atm was significant ($p = 0.048$). The position of the posterior cushion was not altered and there was no increase in flexibility to suggest cartilaginous fractures. There was no persistent bleeding.

Complications

A mucosal laceration within the lumen of the ET occurred in 5/11 (45.5%) and 4 of the 5 had been inflated to 12 atm. The lacerations were limited to the mucosa, were less than 5 mm in length, and were considered to be clinically acceptable (minor adverse effect). Bleeding from the lacerations was very limited and of brief duration. All of the patients had a mild sore throat after surgery that resolved within two days.

There were no major adverse effects. All mucosal lacerations had healed without scarring. There was no evidence of injuries, synechial bands, narrowing of the lumen or patulous ETs. There was no post-op epistaxis.

A C 6-7 contralateral radiculopathy occurred in one patient thought to be due to the neck extension required for endotracheal intubation. It fully recovered. There were no complications related to the balloon dilation. No patients developed patulous ET symptoms (including autophony), even transiently. There were no cases of reflux otitis.

8.6 DIAGNOSIS OF THE PATULOUS EUSTACHIAN TUBE AND PATULOUS EUSTACHIAN TUBE RECONSTRUCTION (STUDY 6)

Patulous Eustachian tube defect in the antero-lateral wall

Slow motion video endoscopy of the cartilaginous Eustachian tube demonstrated a concave (scaphoid) defect in the superior aspect of the anterolateral wall within the functional valve in all patients, supporting previous findings.

Outcomes of PETR

Nasal septal cartilage was used in the first case but bleeding from the septum drained over the tubal orifice slowing the procedure and prompted the use of Alloderm implant in the subsequent 12 cases. Over the course of the study, progressively wider and longer submucoperichondrial pockets were created to accommodate larger implants or grafts with deeper insertion into the valve region in an attempt to improve the outcomes. The use of tragal cartilage in the last case was intended to minimize the loss of graft volume in the healing period. Results are shown in the **table 7**.

Results of PETR (Table 7)

N = 14 Eustachian tubes, follow-up 3 – 30 mo, Ave 15.8 mo

<u>Outcome</u>	<u>Number</u>
Complete relief	1 (7%)
Significant improvement, satisfied	5 (36%)
Improvement, dissatisfied	7 (50 %)
Unchanged	1 (7%)
Worse	0
Total Satisfied	6 (43%)

Complications 0

Complications of PETR

There were no significant complications or persistent OME. One patient developed OME for two weeks. Patients typically experienced two to three days of oro-and nasopharyngeal pain that was well controlled by oral analgesics. All of the patients

experienced immediate and complete relief of their autophony postoperatively, but 67% developed some recurrence of symptoms over time. **Figure 18** shows pre- and postoperative images of a patulous Eustachian tube.

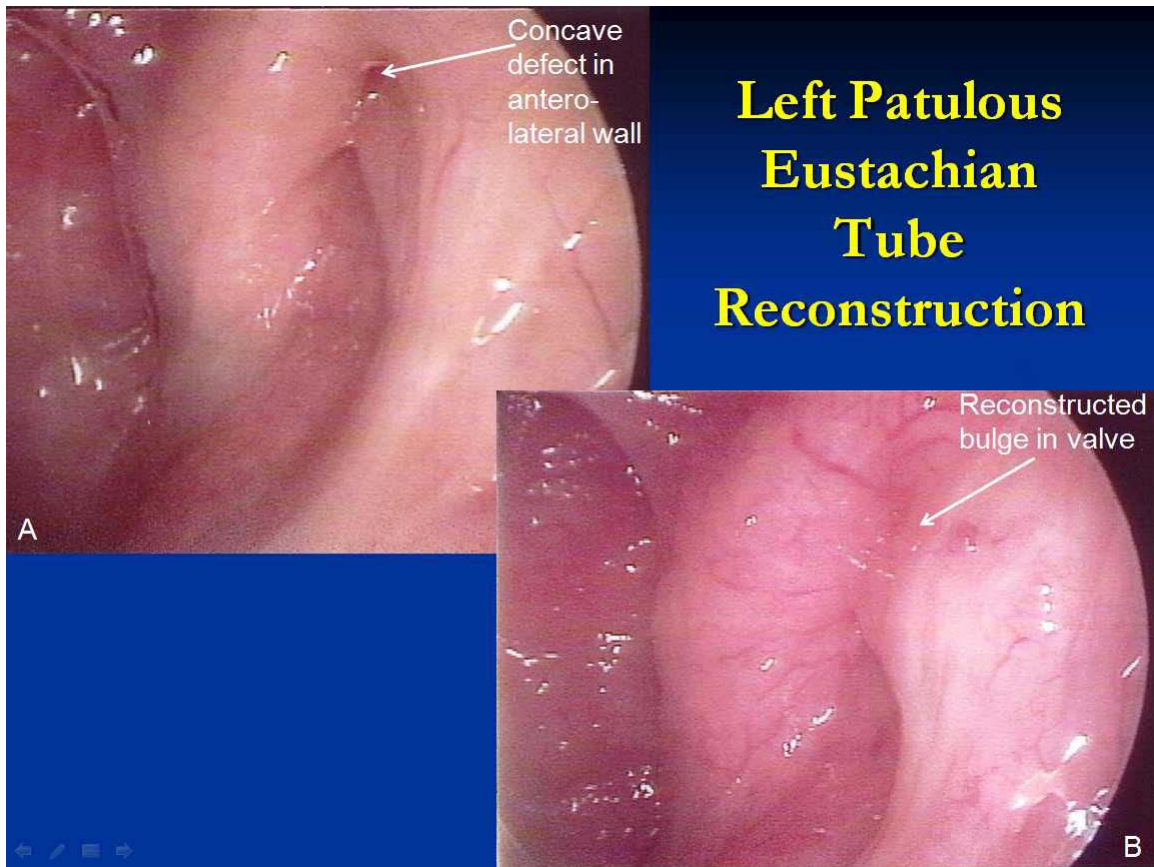


Figure 18 Endoscopic views of left patulous Eustachian tube before surgery and one year post surgery. Note the reconstructed convexity to the antero-lateral wall of the valve.

Diagnostic confounders: SCD (semicircular canal dehiscence) syndrome - patients with autophony

18 adult patients who were referred with symptoms of aural fullness or autophony of their voice similar to the complaints with patulous Eustachian tube were confirmed instead to have dehiscence of the superior (or in one case posterior) semicircular canal. Most patients experienced autophony of their voice but none of them heard their breathing sounds similarly amplified. 50% of the patients had significant improvement or resolution of their symptoms in the supine position or with Valsalva maneuver.

Table 5 shows a summary of the significant results from the above six studies.

Study	Intervention	Diagnostic and pre-operative results						Post procedure results		
		n	Normal	n	OME	n	Patulous	No OME	OME	Patulous symptoms
1	Dilation cycle (ms)	24	995.0	14	1082.9 p=.411	21	1276.2 p=.183			
	Torus tubarius rotation (ms)	23	175.7	14	154.38 p=.563	21	276.29 p=.660			
	Valve open (ms)	23	10.5	20	15.1 p=.563	24	14.1 p=.930			
	Angle of torus tubarius medial rotation (degrees)	24	34.2	20	29.9 p=.875	24	31.0 p=.592			
	Excursion of lateral wall (% torus tubarius height)	24	35.5	20	23.9 p=.015	24	18.7 p=.001			
	Palatal elevation (% torus tubarius height)	24	34.8	20	37.00 p=.664	24	30.6 p=.307			
2	Endoscopy, apparent opening with swallow	17	17							
	Sonotubom.swallow Time open (sec)		11open 0.44							
	Sonotubometry yawn Time open (sec)		13open 2.03							
3	LETP + tube/myr 6 mo follow up			13	OME present			4/11	7/11	0
	12 mo follow up							3/10	5/10	0
	24 mo follow up							3/8	4/8	0
4	Balloon dilation ave ET volume (cm3)	16	0.1565					0.4944		
	Video endoscopy	16	Normal					3 mucosal lacerations		
	CT scan	12	Normal					No injuries		
	Anatomical dissection	12						No injuries		
5	Balloon dilation ET+tube/perf ≥6 mo follow up			11	OME present			7 Able to Valsalva	4 Inconsistent Valsalva	0
6	Patulous ET endoscopy - Concave defect present antero-lateral wall					14	14 (100%)			
	Patulous ET Reconstruction							6 (43%) Satisfied	0	8 (57%) Unsatisfied or no change

9 DISCUSSION

9.1 TESTS OF THE HYPOTHESES

The purpose of this study was to test two hypotheses regarding the functioning of the cartilaginous portion of the Eustachian tube.

The Eustachian tube was demonstrated to have postero-medial and antero-lateral wall mucosal surfaces which are in opposition in the resting position and dilate open by muscular action, functioning as a valve between the nasopharynx and the middle ear. This was consistently shown in the endoscopic findings in normal subjects in studies 1 and 2. Mucosal inflammation with edema was noted in all of the patients with OME who underwent LETP in study 3. Impairment of the opening of the functional valve was demonstrated objectively in the reduction of the lateral wall excursion measured in study 1. Opening times were accurately measured by sonotubometry in study 2, but dilation efforts seen on endoscopy were not consistently associated with tubal opening by sonotubometry. The cartilaginous portion of the Eustachian tube operates like a functional valve and pathology involving the valve may lead to middle ear disease.

LETP results in study 3 indicated that surgical dilation of the functional valve is possible and might improve otitis media with effusion. The results of LETP with a mini short duration tympanostomy tube or myringotomy appear to have supported this hypothesis with improvement in 4/11 patients in whom repeated tympanostomy alone had previously failed. It is notable that the procedure did produce lasting results in some patients who had previously had chronic OME for over five years duration. The balloon dilation procedure in study 4 demonstrated that significant dilation of the tubal valve is feasible with that technology.

The second hypothesis, that the patulous Eustachian tube has a concave shape in the antero-lateral wall causing insufficiency in the functional valve, was supported by the results of studies 1, 2, and 6. Study 1 found that the lateral wall excursion was markedly reduced, probably due to either loss of tissue volume or possible hypertonic contraction of the TVP muscle at rest. Sonotubometry in study 2 effectively simulated a defect in the valve during prolonged yawns in which subjects held their valves in the dilated position for as much as 2 seconds. Study 5 found endoscopic evidence for a concave defect in the antero-lateral wall in all patients and surgical augmentation of the wall to restore the normal convex shape was initially curative in all cases.

The detailed analysis of Eustachian tube function provided further evidence to support the hypothesis that the cartilaginous portion of the Eustachian tube contains a functional

valve and that pathology involving the valve may lead to middle ear disease. Previous work has failed to show any correlation between otitis media and pathology within the osseus Eustachian tube (Hopf, Linnarz et al. 1991; Chays, Cohen et al. 1995), nor has surgical enlargement of the osseus tube successfully relieved middle ear disease.(Wullstein 1960; House, Glasscock et al. 1969; Charachon, Gratacap et al. 1986; Zini C 1988). The function of the valve can now be quantified by videoendoscopy and sonotubometry, which add valuable new tools for future study. The impaired valve can now be modified surgically with tissue reduction or augmentation.

9.2 LIMITATIONS OF THE STUDY

This study contained a number of weaknesses. It introduced a number of new techniques for analysis of the functional valve of the Eustachian tube and a number of new procedures for treatment. However, the subject cohort was different for each study which reduced the ability to make comparisons across the groups and reduced the statistical power of the study. As the surgical trials were all pilot studies, the small patient numbers could be justified to demonstrate safety and potential for clinical efficacy, but there were no control groups for these trials and patients served as their own historical controls. Larger trials with controls will be necessary to make valid statistical comparisons against existing therapy. A validated rating scale was not available for clinical staging of Eustachian tube disease, which makes it difficult for comparison of the present results with other studies. Because the procedures were novel, there was a learning curve with improvements and modifications in technique during the course of the study. As the laser Eustachian tuboplasty and balloon dilation procedures were novel, the interventions were combined with tympanostomy tubes, myringotomy or existing perforation, all of which added a significant confounding factor in the interpretation of the results. However, the patients selected for these pilot studies had long historical courses of OME broken only by tympanostomy tubes and always promptly recurring upon extrusion. Therefore, in these very refractory cases, when some benefit appeared to occur, it suggests that the novel intervention may have altered the course of the pathology. The evidence is sufficient to justify further controlled trials.

9.3 COMMENTS ON MEASUREMENTS OF EUSTACHIAN TUBE DILATION BY VIDEO ENDOSCOPY (STUDY 1)

Findings of decreased lateral wall excursions within the functional valve of the Eustachian tube correlated with OME and patulous dysfunction (Study 1). For dilatory dysfunction, reduced lateral wall excursions could be due to increased thickness of the wall from inflammation or from muscle weakness. From previous work, functioning of the LVP muscle appears to be a critical factor in successful dilation of the Eustachian tube in humans (Poe, Pykko et al. 2000; Poe, Abou-Halawa et al. 2001; Bluestone 2008), but the exact degree of LVP movement as seen by the angle of torus tubarius rotation or palatal elevation did not correlate with tubal failure. It appears that LVP action is important to fix the torus tubarius as a rigid scaffold against which the TVP

muscle action can pull the lateral wall away for tubal opening, but amount of excursion is not critical

The highly significant ($p=0.001$) and markedly reduced excursion of the lateral wall in patulous Eustachian tube is most likely due either to lack of the lateral cartilaginous lamina combined with a loss of soft tissue volume or hypertonicity of the resting TVP muscle. Loss of the protrusion of the lateral cartilaginous lamina, thin submucosa, and loss of Ostmann's fat were common findings at surgery in Study 5, but not universally present, supporting some speculation that TVP hypercontraction may be a factor in some cases. EMG evaluations to evaluate this hypothesis would be useful for further study.

There were several limitations to this study. The measurements were all limited to endoscopic observations and lacking in precise quantification. The sample sizes could be enlarged to improve the statistical analyses. The study analyzed the maximum excursion of the antero-lateral wall and not the excursion of the valve wall itself, which would be useful to investigate in the future. The etiology of decreased lateral wall excursions was not analyzed for evidence of muscle weakness versus inflammatory changes.

9.4 COMMENTS ON SYNCHRONOUS ENDOSCOPY AND SONOTUBOMETRY OF THE EUSTACHIAN TUBE (STUDY 2)

This study was a first attempt to combine endoscopic observation with a device capable of quantitative measurements of some aspect of tubal physiology. Sonotubometry was investigated as a means to passively measure tubal opening, avoiding the nonphysiological stimuli of tubomanometry, forced air testing and other tests of passive opening pressures. These other tests have not adequately predicted clinical tubal function or success and failure of tympanoplasty. (Manning, Cantekin et al. 1987)

The simultaneous and synchronous measurement of sonotubometry and video endoscopy of tubal function proved to be clinically feasible and immediately beneficial in providing complementary information not previously available with either technology alone. The test was simple to perform and had no side effects. The duration of tubal opening by sonotubometry averaged 0.44 seconds, which was in agreement with the previously published value of 0.43 seconds. (Mondain, Vidal et al. 1997) These numbers were longer than the opening time generated by endoscopic visualization alone in Study 1 of 0.11 seconds, indicating that some opening probably occurs higher in the valve than can be observed before the valve becomes fully visibly dilated. Sonotubometry is likely the more accurate means for establishing when the valve truly opens to the middle ear and measuring its duration. Sonotubometry does not provide any information about tubal pathology, however, and endoscopy is critical in assessing the quality of the mucosa and muscle movements. Endoscopy may be able to shed some light on sonotubometry findings that previously have not been understood or were dismissed as artefacts. The negative deflection before opening in some sonotubometer tracings appeared to be caused by brief compression of the Eustachian tube lumen by pharyngeal constrictors and palatal

elevation just prior to dilation. It supports the theory of a pumping action of the Eustachian tube prior to dilation as a means of minimizing reflux into the middle ear.(Honjo, Hayashi et al. 1985; Poe, Pyykko et al. 2000) There is also a pumping action generated by the progressive closure of the functional valve from superiorly (proximal) to inferiorly (distal from the ear)(Honjo, Hayashi et al. 1985) that did not correspond to a change in sonotubometry, possibly because it is generated by a different mechanism.

Limitations

The limitations of this study were the small number of subjects tested in this pilot trial and the numbers should be expanded for normals and then systematically used to investigate patients with tubal dysfunction. Larger numbers will allow for statistical analyses that were not possible in this study. There remains the problem that people do not consistently dilate their Eustachian tubes open with every swallow, nor can everyone dilate their tubes voluntarily, even despite strong efforts. Failure to open the Eustachian tube was seen in 6 subjects during swallowing and 4 subjects during yawns, yet none of these individuals had any history of tubal dysfunction or ear disease. Consequently, failure to generate voluntary opening during the course of sonotubometry does not imply tubal dysfunction by itself.

9.5 COMMENTS ON EUSTACHIAN TUBOPLASTY TO WIDEN THE EUSTACHIAN TUBE ORIFICE AND FUNCTIONAL VALVE (STUDY 3)

The first hypothesis to be tested in this overall study was that surgical dilation of the nasopharyngeal orifice and functional valve should be expected to improve otitis media with effusion. The results supported the hypothesis. Surgical widening of the tubal orifice and medial wall of the valve was effective in relieving OME with lasting benefits in 3/8 patients that had truly refractory disease preoperatively. There were three other patients who were counted as failures, but had actually improved to the point that their effusions were only intermittent and they considered themselves to be substantially improved. All of the patients experienced initial benefit but they had tubes or a myringotomy with the intervention. Failures occurred over time, but not necessarily immediately after extrusion of the tubes, probably due to recurrence of inflammation from their original underlying pathology. Failures did correlate with allergic and reflux disease in the one year follow-up results. The numbers may have been sufficiently small by the two year follow-up that the statistics were less meaningful. It is probable that, similar to chronic sinus disease, failure to eradicate the cause of underlying pathology will lead to a significant rate of return of mucosal disease. The patients for this trial were intentionally selected for their atypically severe and medically refractory OME, so that the low success rate was not surprising. It is hoped that the results will be improved in subsequent trials to include less severely affected patients who may have more intermittent OME, atelectasis, or problems with scuba diving and flights.

The reason for success in improving OME is unclear. It is believed that there could be a mechanical advantage in debulking of the postero-medial wall, widening the orifice and valve area and thus facilitating the ability of the TVP muscle to dilate the valve open by

lateral excursion of the antero-lateral wall. As seen in Study 1, that excursion may be compromised in patients with OME and dilatory dysfunction. It is also possible that the operation is excising irreversibly diseased mucosa and allowing new mucosa to regrow. The pathology showed healing with fibrosis (filling in the crater created by the laser) and restoration of healthier epithelium with the net thickness of the tissue reduced from preoperatively, largely due to the reduction in inflammation and thickness of the epithelial layer. If the underlying etiology for inflammation has been adequately treated, the new tissue can be thinner and healthier than the original. However, if the source of inflammation has not been eliminated, the condition can relapse. The surgeon must diligently search for the underlying etiology and maintain treatment as necessary to prevent recurrence.

The etiology of disease in the functional valve is not fully understood. For dilatory dysfunction, mucosal inflammation is the most common finding (Poe, Pyykko et al. 2000; Poe, Abou-Halawa et al. 2001), but the cause of tubal failure can be multifactorial. It can be on the basis of hypertrophy causing thickening the walls of the lumen, especially in the torus tubarius and postero-medial wall in which the mucosa and submucosa are naturally thicker and contain more secretory glands.(Sando, Takahashi et al. 1994) A thicker wall reduces the diameter of the lumen and increases the work necessary for the TVP muscle to dilate the lumen to a fully open position. Furthermore, inflammatory mediators may impair mucociliary function, upregulate mucus production, and propagate retrograde into the middle ear to directly cause inflammatory changes there as well.

Numerous inflammatory mediators have been demonstrated to be upregulated in the middle ears and nasopharynxes of patients with otitis media, the origin of the inflammation is unknown and deserves further research.(Lesmeister, Bothwell et al. 2006; Matkovic, Vojvodic et al. 2007; Skotnicka and Hassmann 2008) Allergic disease has been reported as a possible cause (Luong and Roland 2008) and this was supported by the correlation between atopy and failure of LETP in Study 3. Laryngopharyngeal reflux also correlated with failure of LETP in that study. Biofilms have been identified in the middle ears (Hall-Stoodley, Hu et al. 2006) and adenoids (Kania, Lamers et al. 2008) of patients with otitis media and should be studied as a possible source of inflammation.

Adenoid disease could have the effect of harbouring inflammation that spreads to the adjacent Eustachian tube, but it also has been shown to directly compress the torus tubarius anteriorly and laterally during swallowing with the result of closing the tubal orifice during the time it should be dilating. (Poe, Abou-Halawa et al. 2001) These may explain the benefit of adenoidectomy in improving OME and recurrent acute otitis media, especially when the adenoid is in close contact with the torus tubarius. (Gates, Avery et al. 1988; Nguyen, Manoukian et al. 2004)

Indications for LETP surgery

Patients who have had maximal medical therapy for their underlying pathology and who benefit from tympanostomy tubes, yet after extrusion continue to have irreversible mucosal disease with persistent atelectasis, difficulty with airplane flights or diving, or intermittent or persistent OME, may be candidates for Eustachian tuboplasty. Slow-motion video endoscopy should demonstrate mucosal disease causing functional obstructive dysfunction with inadequate dilation of the lumen. A trial of LETP in a series of dynamic (muscular) dysfunction has not yet been done.

Contraindications for surgery

Primary middle ear disease that is not caused by tubal dysfunction, such as recurrent thick proteinaceous “glue” ear that repeatedly occlude tympanostomy tubes, is a contraindication to surgery as are radiation therapy for nasopharyngeal cancer and extensive nasal or nasopharyngeal mucosal disease with an underlying, uncontrolled inflammatory process.

Surgical planning

Video endoscopy is reviewed preoperatively to determine the extent of Eustachian tube, nasal, sinus, and nasopharyngeal disease. Tissues become engorged in the supine position intraoperatively and may not accurately reflect the actual disease. More extensive disease or compromise of the lumen warrants more aggressive removal of soft tissue medial cartilaginous lamina.

Limitations

The greatest limitation of the study was the small patient size, but this represented a first prospective pilot trial intended to demonstrate safety and the possibility for efficacy of a new procedure. Larger numbers of patients will be needed to generate more meaningful statistics for analysis. There was bias in selecting patients with maximum severity of disease, which likely led to a poorer success rate than might have been achieved with less severely affected patients. Determination of the area and depth of tissue to be resected has not been scientifically studied and needs to be defined. Laser vaporization of tissue was chosen for its precision but was slow and causes thermal injury that could lengthen the healing process.

The treatment results were confounded by the concurrent placement of a tympanostomy tube or myringotomy in conjunction with the laser Eustachian tuboplasty. However, having established that laser Eustachian tuboplasty may be beneficial, it is now indicated to perform a study in which laser Eustachian tuboplasty alone is compared with a control group.

Concurrent use of antihistamine or omeprazole for patients with allergic or reflux disease respectively could have introduced a confounding factor in interpreting the results of

Eustachian tuboplasty combined with the tympanostomy tube. However, these medications had been used preoperatively for six weeks without altering the effusion and the use was felt to be indicated for their chronic underlying disorder.

9.6 COMMENTS ON FEASIBILITY AND SAFETY EVALUATION OF BALLOON DILATION OF THE EUSTACHIAN TUBE IN CADAVERS (STUDY 4)

This study in cadavers looked at the feasibility and probability of safety of performing balloon dilation of the tubal orifice and valve before considering proceeding to a clinical pilot trial. The balloon dilation technology was developed to fracture the bone around sinus ostia to enlarge them (Bolger and Vaughan 2006; Kuhn, Church et al. 2008; Weiss, Church et al. 2008) and the principle of application was different for use in the Eustachian tube, where there is no thin bony orifice. There was no attempt to dilate the bony isthmus or any portion of the temporal bone course since it is not the likely source of pathology and could risk injury to the internal carotid artery. Rather, the intent was similar to that of soft tissue endovascular or other lumina, in which the vessel is expanded, collagen rearranged, and the endothelium stretched or lacerated to heal with a wider lumen. (Mestres, Ninot et al. 1985; Ahrendt, Pitt et al. 1998; Ebeid, Sarris et al. 2001) The balloon was intended to principally expand the valve region in order to facilitate dilation to open by the TVP.

The results demonstrated clear success in significantly dilating the Eustachian tubes between 4 mm and 16 mm from the tubal orifice, which included the region of the functional valve located at approximately 5 to 13 mm. It did not significantly dilate either the flexible nasopharyngeal orifice or the rigid portion as it approached the isthmus. Volume of the Eustachian tubes was increased from an average of 0.1565 to 0.4944 cm³ which represented an increase in volume of 357%.

The procedure did not present significant technical challenges and the balloons fit reasonably well into the Eustachian tubes during dilation, occasionally protruding out as much as 50%. If a 7mm diameter balloon did not adequately remain in place during the dilation, a six mm balloon was satisfactory.

There were no major adverse injuries, such as bony fractures or injuries to the internal carotid artery. Minor adverse injuries were limited to lacerations of the mucosa of the lumen in three cases, which is an expected outcome of procedure and may be desirable. Potential safety and efficacy of the procedure was demonstrated to be satisfactory to proceed with clinical trials.

There was a roughly 15 – 60 minute period between the dilation and the CT scans that could have allowed for some relaxation of the tissues. The cadavers were not fixed and had tissues very similar in handling to live patients. However, the increased resilience of the perfused tissues in a live patient would likely tend to relax more after dilation than the cadaver tissues. In practice, there is an impression that the dilation in patients does not

appear to leave as large of a persistent dilation as was seen in the cadaver study, but this has not been accurately measured to date.

Limitations

Limitations of the study were that it was conducted on cadaver tissue and the results in a clinical trial cannot be fully predicted. The sinus balloons were not manufactured for this purpose and could be modified to optimize the instruments for Eustachian tube surgery. The possibility for success in a clinical trial is completely unpredictable based on this study, which could only be expected to look at the technical ability to do the operation and the potential for mechanically induced side effects. Even if initially successful in improving otitis media, there is no ability to predict the duration of the benefits. The balloons carry a significant expense and the duration of clinical success will be important in determining if this operation will become clinically acceptable.

9.7 COMMENTS ON BALLOON DILATION OF THE CARTILAGINOUS EUSTACHIAN TUBE (STUDY 5)

This study applied the lessons learned from Study 4 to a pilot clinical trial and demonstrated that balloon dilation of the ET is technically feasible in patients and can be performed without significant adverse effects. The 7 mm sinuplasty balloon fit reasonably well into the tubal lumen and dilated the functional valve effectively, tending to slip out in a minority of cases. In the majority, the balloon actually “locked” into position fitting to the inside curvature of the medial cartilaginous lamina that is contained within the posterior cushion. Protrusion of the balloon up to 30% was common and of no concern. Slippage of the balloon out of the ET could be limited by bracing the shaft of the guiding catheter against the floor of the nose for stability.

Balloon dilation in this pilot study demonstrated evidence for effectiveness intraoperatively, with an immediate widening of the functional valve, and postoperatively, with persisting benefits that included improvement in the ability to insufflate the ET and ear with a Valsalva maneuver 11/11 (100%), resolution of OME in all of the 5/11 (45.4%) patients with an intact TM, and a reduction in inflammation of the mucosa of the ET from a mean of 2.91 to 1.73. Although tympanostomy tube or perforation was present in all cases, the baseline inflammation had been in place despite prior tubes or perforation. The mechanism for reduction in inflammation is uncertain. It could be speculated that it may be due to compression injury to the mucosa and submucosa with healing by healthy epithelium or perhaps the compression has served to strip out sources of inflammation, such as biofilms. It is also possible that temporary aeration of the middle ear could cause downstream reduction in ET inflammation and a future controlled study comparing tympanostomy tubes vs. balloon dilation should evaluate the ET for mucosal changes in both groups. Dilation of the cartilaginous ET could widen the lumen thereby reducing the work required for the muscles, especially the Tensor Veli Palatini muscle (TVP), to

fully open the lumen on demand. It is known that balloon dilation of vascular stenoses creates tearing of the intima and sometimes the media,(McElhinney, Reddy et al. 2000) with healing occurring by scar filling in the gaps thus maintaining the widened lumen. (van den Brand, Essed et al. 1992) Compression of irreversibly injured hypertrophic mucosa and submucosa may permit healing with thinner and healthier layers. Histology following laser Eustachian tuboplasty showed return of normal ciliated epithelium and thinner submucosa. (Poe, Grimmer et al. 2007)

Balloon dilation appeared to most effectively dilate the mid portion of the cartilaginous ET, which corresponds to the functional valve, and this is likely due to the combination of the tapered shape of the balloon at each end, the flexibility of the loose cartilage at the orifice, and the rigid circumferential cartilage at the isthmus. These results correlated well with the cadaver Study 4 (Poe and Hanna 2010)

The targets of 12 atm inflation pressure for one minute duration were taken from previous sinus experience and from the preclinical cadaver trial, since, to our knowledge, this was the first clinical trial of balloon dilation of the ET. There was a greater tendency for mucosal laceration with the 12 atm pressure and this may actually be a desirable goal, given the experience with endovascular dilation.

The cases were done throughout the year so no seasonal bias in results would be anticipated in this study.

Adverse events

There were no major adverse events or complications related to the balloon dilation. Pain was predominantly related to the endotracheal intubation and there were only minimal complaints of pain localized to the nasopharynx or radiating to the ear.

Potential complications

The potential for complications is considerable, including fatal injuries to the internal carotid artery. (O'Connor and Shea 1981) Familiarity with the surgical anatomy is important. No attempt should be made to dilate the bony ET, as it is not usually the site of pathophysiology and the carotid artery courses to share the infero-medial wall of the ET within the temporal bone. From the nasopharyngeal orifice, the ET lumen takes a slight medial curve initially, then courses toward the temporal bone and becomes progressively narrow. Care should be taken to slowly advance the balloon catheter atraumatically to follow the lumen without laceration of the mucosa, which could cause bleeding or create a false passage toward the carotid injury. The balloon dilation procedure would not be recommended for a patient with an inferior carotid dehiscence and a CT scan is currently recommended.

Additional risks could be circumferential stricture, fracture of the medial cartilaginous lamina, injury to the TVP or Levator Veli Palatini muscles, hemorrhage into the pterygoid space, instrumentation of the middle ear and patulous ET. Guidewires can

pass into the middle ear and should be avoided.(Poe and Hanna 2010) From the nasopharyngeal orifice, the isthmus is 20 mm from the ET and the middle ear orifice 36 - 38 mm. (Sudo, Sando et al. 1997; Poe and Hanna 2010) The isthmus should be sufficiently narrow that the balloon catheter would not normally pass through and advancement should cease when meeting gentle resistance. Entry into the middle ear could occur with a widely patent anomalous isthmus or by excessive force of introduction.

Limitations of the study

There were several weaknesses of this study. It used the patients as historical controls and suffers from that bias. Insufflation of the ET by Valsalva maneuver is an imprecise measure of tubal function that does not necessarily predict sufficiency of middle ear aeration. However, it did reflect a significant change in this study. There is the possibility that there can be a learning curve in performing the maneuver, but these patients had five or more years of symptoms and had attempted the maneuver many times over the course of their ET dysfunction.

There was a lack of objective tests for ET function. Although such tests have not been shown to have clear clinical correlation (Manning, Cantekin et al. 1987), they would have provided additional basis for comparison of pre- and post-operative results. An ET mucosal rating scale was employed, but is only now undergoing validation testing. Some of the patients still had tympanostomy tubes in place at the termination of this study and it remains to be seen if they recur with OME in the future. A tube could have an influence on the outcomes, relieving negative pressure, draining effusion and facilitating a Valsalva maneuver. As none of the patients could perform a Valsalva maneuver previously while they had tubes, the outcome of ability to perform a Valsalva maneuver represented a real change.

All of the patients expressed an initial improvement in their symptoms in their new ability to be able to perform a Valsalva maneuver, which they perceived as a significant benefit. A disease-specific instrument for quantifying quality of life for ET disorders is being developed, but is not yet available.

The pathogenesis of OME in children is different from adults and is being investigated. At present, we have not considered performing this procedure in pediatric patients.

If balloon dilation of the ET were ultimately demonstrated to be effective with sustained benefits, it would be a useful and minimally invasive alternative to tympanostomy tubes in patients with chronic OME. Careful selection of patients with medically refractory dilatory dysfunction of the ET should be done. The procedure may also prove to be beneficial to patients with atelectasis or scuba or flight barotrauma. It remains to be determined whether the procedure should be performed in children.

9.8 COMMENTS ON IDENTIFICATION OF THE PATULOUS EUSTACHIAN TUBE DEFECT AND SURGICAL CORRECTION WITH AUGMENTATION OF THE LATERAL WALL. (STUDY 6)

This study added strong evidence to support the second hypothesis of this overall work, that the patulous Eustachian tube contains a concave defect in the antero-lateral wall that includes the functional valve. Such a defect was observed in all cases and surgical augmentation completely relieved all complaints of autophony, at least initially. The edema from surgical trauma undoubtedly contributed temporarily to the closure of the functional valve, but this effect would be expected to have subsided by six weeks post-operatively. This operation provides an opportunity to improve or relieve autophony without completely blocking the lumen, which typically would mandate long-term tympanostomy tube ventilation. (Bluestone CD 1998; Doherty and Slattery 2003)

This study also supported the findings of reduced lateral wall excursions in the valve seen endoscopically in patulous Eustachian tubes as the thickness antero-lateral wall was often reduced compared to normals. A substantial reduction in the bulge of the lateral cartilaginous lamina into the lumen and decrease in Ostmann's fat pad volume were commonly noticed. With the antero-lateral wall chronically positioned laterally, a decreased excursion with TVP muscle contraction would be expected. It could also be speculated that chronic hypercontraction of the TVP muscle could be a possible etiology in some patients, but there was no direct evidence from the present study to confirm this hypothesis. However, the large lateral excursion observed in Study 1 in patulous Eustachian tubes could support this hypothesis.

The procedure was technically challenging to perform initially and required learning new techniques for dissecting and suturing with curved instruments under endoscopic guidance. Improved instruments designed for this procedure will be helpful in its performance.

The long-term success rate of the procedure was lower than desired and this was thought to be principally due to excessive resorption of the AllodermTM implant and early failure to make the submucoperichondrial pocket sufficiently deep into the valve. There is also a need to prevent the graft from mobilizing distally toward the nasopharyngeal orifice and out of the valve due to gravity and the forces of the muscle action on the valve that tend to pump the graft distally.

A similarity between aural complaints of patients with semicircular canal dehiscence (SCD) (Minor, Solomon et al. 1998) and patulous Eustachian tube was recognized for the first time during the course of this study and prompted a retrospective comparison of their presenting signs and symptoms. SCD syndrome patients will complain of autophony of their voice and other bone conducted sounds due to the inner ear mechanics of the "third window" phenomenon. They will not typically complain of hearing their breathing sounds grossly amplified as opposed to patulous Eustachian tube patients, who hear their breathing sounds equally amplified as their voice. SCD syndrome patients will also have some degree of other components of the syndrome to include conductive hearing loss or

lower than normal bone conduction threshold and vertigo, among other possible complaints. Patulous Eustachian tube patients will demonstrate lateral and medial excursions of their tympanic membrane with forced nasal breathing as observed by otomicroscopy or tympanometry while they have active autophony.

Limitations

There were several limitations to this study. The number of patients was small, but again, this was an initial report of a trial of a novel procedure, with the main intent to establish the safety and efficacy of the concept. There was a significant bias in using a self-reporting of autophony for the outcome, but this was necessary as a number of the patients came from a distance and did not wish to return for follow-up visits unless necessary. The subjective self rating of “satisfied” or “dissatisfied”, in particular, could be biased by placebo effect. However, these patients tend to be exceedingly sensitive and intolerant of their symptoms making it unlikely that there was a significant placebo effect. There was a significant learning curve to the operation and improved success rate with later cases. Alloderm™ implants underwent a significant amount of resorption over time likely leading to late failures. Cartilage grafts are likely a better choice for a durable graft and would be preferred for future use. Additionally, Alloderm™ is from a cadaver source and could theoretically carry prions or other pathogens.

9.8 FUTURE ASPECTS

This study provided new methods for the diagnostic evaluation of Eustachian tube dysfunction that can be used to advance clinical and research work. The new operations investigated provided some potential surgical relief to patients with medically refractory disease, but they also raise new questions about the mechanisms of efficacy and new directions for basic research for possible medical therapy. LETP may be beneficial more for removing irreversibly injured mucosa than for widening the lumen. Study of the pathophysiology of the mucosal disease is needed. Graft augmentation of patulous defects may only be adding volume to a progressive local wasting condition or muscle hypertonic disorder. Study of the underlying etiology is needed.

Future research that would add to the endoscopic measurements in Study 1 could use EMG to study TVP muscle function as it correlates with lateral valve wall movements. This study focused on OME and patulous Eustachian tubes and could be expanded to include atelectasis and patients with aero- or barotrauma. Endoscopic observations could benefit from technology to calibrate the field using lasers to measure the distance from the objective lens to the target and to project a unit of measure onto the video monitor that would continually change as the distance varies. Correlation between endoscopy and other means for assessing tubal function should be studied.

Combined sonotubometry and endoscopy in Study 2 revealed an issue with false positive results in which normal Eustachian tubes may fail to open during a testing session.

Further study will be needed to determine how frequently this type of false positive occurs and whether patients can be quickly taught to generate a good dilatory effort with some instruction aided by the video endoscopy for feedback. There was an instance in which endoscopy suggested tubal opening but it was not confirmed by sonotubometry. Sonotubometry alone has artefacts that are difficult to sort out in the absence of endoscopy. Therefore, it is likely that the combination of a normal endoscopic exam and normal sonotubometry will be more strongly predictive of normal tubal function. Continued research with this combination tool will shed more light on the ability to dilate open or not when some degree of pathology is found with endoscopy. It is hoped that imaging may become more helpful in the future, especially with cine-MRI, but present resolution remains insufficient for detailed examinations.

LETP should be studied in greater numbers with expanded indications to include non-fixed atelectasis, difficulty with airplane flights or diving, or intermittent or persistent OME. A randomized controlled trial would be preferable with stratification of risk factors, such as allergic disease, reflux disease and smoking. Investigation into the pathophysiology of tubal inflammation must continue to help identify possible preventive measures or better medical means to treat dilatory dysfunction of the Eustachian tube. We are presently looking for evidence of bacterial biofilms within the tubal orifice. Such therapy would be continued as needed following surgery to prevent recurrences. With a better understanding of the etiology of tubal inflammatory disease, LETP on medically refractory disease could be more focused on removal of irreversibly diseased mucosa, removal of hypertrophic submucosa, or resecting cartilage or weakening the spring of the cartilage, whichever would be indicated. Investigation into the optimal means to accomplish the required resection could be better focused.

Balloon dilation of the Eustachian tube, the subject of Studies 4 and 5 is now being applied in expanding clinical use in patients with dilatory dysfunction in Finland, Germany, UK and USA., although data for efficacy remain lacking. The long term results of these early trials will be anticipated. A multicenter randomized controlled trial is needed before routine clinical use of this technology can be recommended and such a trial is currently being organized by the author. The size of the balloon, atmospheres of pressure of inflation, and duration of inflation all need to be studied for optimized results. If the procedure shows some success, it will need to be clarified if the benefit would be due to widening of the lumen diameter or due to mucosal or submucosal injury and regrowth of healthier tissue.

Further investigation for the etiology of the patulous Eustachian tube, the topic of Study 6, is needed. In the event of loss of tissue volume, it might be aided with medical treatment if the underlying cause could be ascertained. Hyperactivity of the TVP muscle could be investigated with EMG and if present, treated with speech therapy or precise botox injections. In the event of failure after patulous Eustachian tube reconstruction, subsequent augmentation of recurrent defects by injections with hydroxyapatite, minced cartilage or insertion of shims into the concave defect within the lumen have been effective in relieving autophony for some period. Further work needs to be done on the long term efficacy of these procedures and possible better materials.

10 SUMMARY AND CONCLUSIONS

This study found evidence to support the hypothesis that surgery designed to alter the Eustachian tube's functional valve within its cartilaginous segment may at least temporarily influence dilatory or patulous dysfunction.

New tools for anatomical and physiological assessment of the function of the valve were presented that will help to quantify and stage the pathological effects that are observed during endoscopy. Endoscopy has been shown to be most beneficial in demonstrating anatomy and pathology, but it has not been accurate in predicting function or severity of tympanic membrane or middle ear disease. This information will be important in planning intervention with the new procedures introduced in this study.

Study 1

Parameters were quantitatively measured from video endoscopy during tubal dilation to include lateral excursion of the antero-lateral wall of the valve, medial rotation of the torus tubarius, palatal elevation and durations of the dilation cycle, torus tubarius rotation time and valve opening time. Lateral excursion of the antero-lateral wall, which occurs due to action of the TVP muscle as the final phase in dilation, was reduced in patients with OME and even more reduced in patients with patulous Eustachian tubes. This potentially useful parameter can now be further studied in the search for pathophysiology of tubal dysfunction.

Study 2

A novel instrument to simultaneously record sonotubometry in synchrony with video endoscopy was tested in normal subjects and demonstrated that the two different technologies provide important complimentary information. Endoscopy cannot accurately identify true opening of the functional valve and underestimated the duration of valve opening, which was precisely measured with sonotubometry. Sonotubometry showed failure to open in some subjects despite normal endoscopic dilatory examinations suggesting that voluntary opening is not always readily feasible and does not necessarily imply tubal dysfunction. The results using this combination of technology are promising for future clinical and research work.

Study 3

Laser Eustachian tuboplasty, an endoscopic-guided procedure to thin the postero-medial wall and widen the tubal orifice and valve was evaluated for effectiveness in treating patients with medically refractory OME. The hypothesis that LETP with tympanostomy tubes could improve OME was supported. The procedure was safe, without significant complications and was performed in an outpatient setting. It can be indicated for OME, non-adherent atelectasis, or difficulties with diving and flights after failure of medical therapy and tympanostomy tubes. Failures of LETP were associated with inability to control underlying medical conditions such as atopic or reflux disease and idiopathic recurrent OME could also be a factor, but this was not specifically analyzed. The future

role of the procedure will depend on studies with long-term follow-up and expanded patient numbers. A randomized controlled trial is indicated.

Study 4

Balloon dilation of the Eustachian tube was proposed as a new procedure to widen the functional valve. Safety and feasibility issues were tested in a cadaver model and some estimates were made of possible efficacy. Sinus dilation balloons successfully widened the valve region in all of the Eustachian tubes tested without any major adverse effects. Techniques were worked out to perform the procedure in patients and clinical trials were deemed appropriate.

Study 5

Balloon dilation of the Eustachian tube, along with a perforation or tympanostomy tube, demonstrated safety and feasibility in an initial pilot trial in patients with refractory otitis media with effusion. Initial results have been promising and show potential for clinical efficacy in these severely dysfunctional Eustachian tubes, lending more evidence that therapy directed at the cartilaginous Eustachian tube may be effective in treating otitis media. A randomized controlled trial with long term follow-up is now indicated.

Study 6

A concave defect in the antero-lateral wall of the Eustachian tube's functional valve was consistently found in all patients with patulous Eustachian tubes. A surgical procedure to augment the defect, restoring a convex bulge was devised and employed in affected patients. The results supported the hypothesis that correction of the concave defect would eliminate the patulous symptoms. The procedure was safe, done on an outpatient basis, and without complications. Although complete relief was obtained in all cases initially, return of symptoms occurred over time in the majority of cases, likely due to resorption of the implant material. Future surgery will be done with cartilage grafts, which would be expected to be a more enduring material.

Future aspects:

New quantitative methods for the assessment of Eustachian tube function have been introduced and tested in this study. They can be used for the assessment of individual patients and for further research into the nature of disorders. These tools should now be consistently applied to the additional patients with dilatatory or patulous dysfunction in larger and more comprehensive studies that could also make comparisons with some traditional tests of tubal function. Underlying medical etiologies should be sought, treated and repeat testing done to assess for changes in Eustachian tube function. Medical failures from this well studied group could then move on to controlled trials of interventions. LETP can be effective, but medical control of inflammation remains important for long-term success. Balloon dilation is a minimally invasive technique with significant potential and it remains to be seen whether it is effective in more patients and over what duration. Patulous Eustachian tubes likely evolve over time creating

challenges for surgical intervention. Improved tissue grafts such as cartilage and variably sized intra-luminal shims will be important.

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Measurements of Eustachian Tube Dilation by Video Endoscopy

*†‡Dennis S. Poe and *Ilmari Pyykkö

**Department of Otolaryngology, Tampere University Medical School, Tampere University Central Hospital, Tampere, Suomi, Finland; †Department of Otology and Laryngology, Harvard Medical School; and ‡Department of Otolaryngology and Communications Enhancement, Children's Hospital Boston, Boston, Massachusetts, U.S.A.*

Objectives:

1. To create techniques for measurement of parameters of Eustachian tube (ET) dilation as observed with video endoscopy.
2. To study correlations of the parameters between healthy subjects and patients with ET dysfunction to determine if they may be important for clinical or investigational use.

Study Design: Prospective study in an academic center. 3 groups of adults: healthy subjects, otitis media with effusion (OME), patulous ET.

Intervention: Video software analyses were performed on video recordings from subjects' transnasal endoscopy to measure parameters of the tubal dilation cycle.

Results: 24 ETs of 15 healthy subjects, 24 ETs of 15 patulous ET and 20 ETs of 13 OME patients. Mean values for healthy subjects: cycle time 995 ms (SD 404.7), valve opening time 10.5 ms (SD 6.34), torus rotation time 176 ms (SD 151.5 and

angle of torus rotation 34.2° (SD 14.3). Palatal elevation, measured as a percentage of torus height was 34.8% (SD 16.6) and excursion of the antero-lateral wall 35.5 % (SD 16.3). Lateral excursion of the antero-lateral wall was significantly less in patulous ET (18.7%, SD 15.1, $p = 0.001$) and in dilatory dysfunction (23.9%, SD 21.7, $p = 0.048$). The other parameters were not statistically different between healthy subjects and patients.

Conclusion: Lateral excursion of the ET's antero-lateral wall was significantly reduced in OME and patulous ET patients compared with healthy subjects. Evaluation of the excursion of the lateral wall of the ET, which is due to TVP muscle action, may be an important parameter for further clinical and research study. **Key Words:** Eustachian tube—Eustachian tube dysfunction—Eustachian tube test—Otitis media—Otitis media with effusion—Patulous Eustachian tube—Tuba aperta.

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Anatomic and physiologic dysfunctions of the Eustachian tube (ET) are believed to be major contributing factors in the pathogenesis of otitis media. Failure of tubal function should be more precisely divided into two categories. Dilatory dysfunction refers to inadequacy of the opening process or insufficiently frequent dilation for proper aeration of the middle ear, and it is thought to be the principal cause of most chronic ear diseases. Additionally, failure of the immune defense system may contribute to inflammatory changes with upregulation of mediators and mucus production or lymphoid tissue reactions that lead to middle ear disease. Patulous dysfunction is the failure of the ET to assume its normal closed position, resulting in a chronic dilated state that permits reflux of sounds and material from the nasopharynx toward the ear (1). There is evi-

dence that reflux may contribute to otitis media in children (1), yet adults with patulous ET dysfunction rarely have active chronic ear disease.

ET dilatory dysfunction was once thought to be due to restrictions within the osseous portion, which includes one-third of the tubal length. The bony cartilaginous isthmus is the site of the narrowest diameter along the length of the ET (2). However, submillimeter endoscopy of the ET showed that there is rarely any pathology within the bony portion, and it is usually patent, even in cases of otitis media with effusion (OME) (3,4). Transnasal endoscopy into the lumen of the cartilaginous portion of the ET with video recording to permit slow-motion analysis revealed that the cartilaginous portion of healthy adult ETs functions as a valve, which is closed in the resting position and requires muscular action to dilate open (5). This functional valve represents the approximately 8-mm length within the midportion of the cartilaginous ET in which the mucosal surfaces are in apposition at rest.

Address correspondence and reprint requests to Dennis S. Poe, M.D., Department of Otolaryngology, Children's Hospital Boston, 333 Longwood Avenue, Boston, MA 02115; E-mail: dennis.poe@childrens.harvard.edu

Tubal dilation is usually associated with strong swallows and yawns and occurs in 2 principal phases beginning with palatal elevation, including activation of the levator veli palatini (LVP) muscle. Within the nasopharynx, the palate is seen to elevate with simultaneous elevation and medial rotation of the torus tubarius (posterior cushion of the tubal orifice). The distal part of the functional valve opens up during this phase, but the lumen remains closed proximally. The medial rotation is maintained as a scaffold against which the relatively inefficient final dilator of the ET, the tensor veli palatini (TVP) muscle subsequently contracts. TVP action exerts a laterally directed pull on the anterolateral wall of the tubal lumen that results in dilating the valve to its fully opened position. Valve closure occurs initially proximally and is completed distally in the nasopharyngeal orifice (6).

Systematic endoscopic observations of tubal function in patients with chronic OME and atelectasis (other than attic retractions) have found very close correlation with the presence of significant pathology within the valve of the ET (7). The types of pathology have been classified into obstructive versus dynamic disorders. Obstructive disorders can be caused by mucosal hypertrophy and inflammation in the majority of cases but can also be due to deformities in the ET cartilaginous skeleton, adenoid hypertrophy impinging on the torus tubarius, and least commonly due to anatomic blockage from neoplasms. Dynamic disorders are failures of the muscular actions of the LVP or TVP muscles principally because of hypoactive contraction but occasionally from hyperactive contraction causing a blockage or a failure of the LVP to sustain its action during TVP contraction (7). Initial attempts at staging using observed gradations of mucosal hypertrophy, muscular movements, and overall valve dilation are qualitative and remain unvalidated (8). Medical and surgical therapies for ET dysfunction are being developed and introduced, raising a need for the ability to quantify the findings in ET dysfunction and to provide a staging system for observed pathology.

In the present work, we sought to measure several parameters of tubal dilation that could be observed from video endoscopic recordings to seek correlations with dilatory or patulous dysfunction in comparison to healthy subjects. Quantified measurements of the anatomy would be desirable, but magnification varies greatly with the distance of a target from an endoscope tip. Although direct measurements are currently not practical, measurements relative to the height of the torus tubarius can be used to provide some basis for quantification. In this fashion, we measured palatal elevation, the lateral excursion of the anterolateral wall of the ET due to TVP contraction, and the medial rotational angle of the torus tubarius. Additionally, the durations of portions of the dilatory process were measured.

METHODS

Patients and healthy subjects were examined while awake and sitting in an office setting of a major tertiary medical center. The technique for video recording of ET endoscopy has been

previously reported in detail (5,7). Briefly, subjects had topical spray anesthetic and were examined with fiberoptic or rigid angled nasal endoscopes fitted with a video camera and a recording system. Subjects were asked to perform a series of swallows with the endoscopes positioned immediately anterior to the nasopharyngeal orifice of the ET and directed into the lumen. As tubal opening does not occur with every swallow and the strength of tubal opening varies with individual swallows, analyses were done on the swallow from the series that demonstrated maximal dilatory efforts.

Three groups of subjects were examined. One group included healthy subjects that had no history of recurrent or persistent otitis media. The second cohort was composed of patients with chronic OME. The third group included patients with patulous ET complaints, including autophony of their voice and breathing sounds. These patients had demonstrable tympanic membrane excursions synchronous with nasal breathing as objective confirmation of the diagnosis immediately before the endoscopy. Recorded examinations were studied by observers who were blinded to the subjects' clinical status, and measurements were taken by reviewing video and still frames with OsiriX DICOM viewer software v.3.7, (Geneva, Switzerland). The height of the torus tubarius was measured in pixels superiorly, taking the fixed pivot point adjacent to the basisphenoid and extending along its longitudinal axis to the inferior tip of the medial cartilaginous lamina's bulge, in the inferior-most aspect of the torus tubarius. The height was measured in both the resting position and in the maximally medially rotated position during dilatory efforts and drawing lines through the longitudinal axis of the cartilage in both positions (Figs. 1 and 2). The angle of rotation was calculated by the software. The average of these heights of the torus tubarius was then used as a unit of measurement against which additional measurements were made. Using this relative "torus" unit, errors in absolute measurements that would be introduced from changes in distance from the endoscope to the ET orifice between video frames would be eliminated. The maximum lateral excursion of the anterolateral wall (by TVP muscle action) within the orifice and the height of maximal palatal elevation (inferior to the torus) were measured as percentages of this torus unit. Lastly, the duration of the dilatory sequence and the duration of apparent opening of the valve were measured directly from the time line in Final Cut Pro video processing software (Apple, Cupertino, CA, USA) that

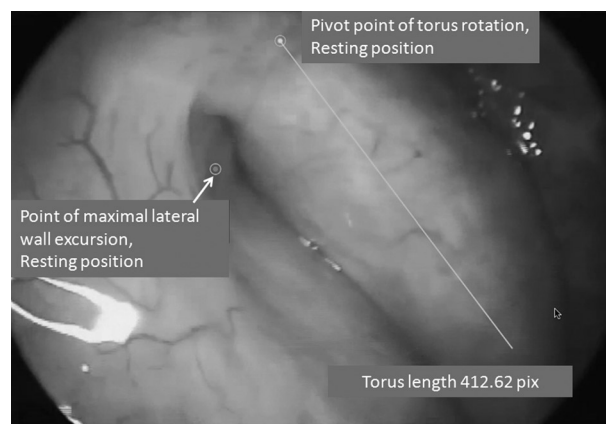


FIG. 1. Forty-five-degree transnasal endoscopic view of the right ET nasopharyngeal orifice in resting closed position. Reference points and lines are created, with measurements taken and superimposed on the still frame image.

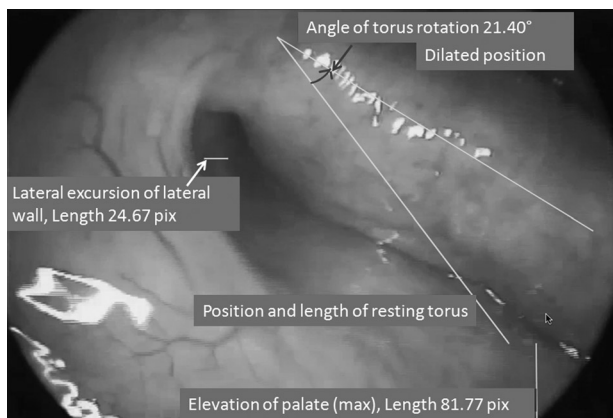


FIG. 2. Same ET as in Figure 1, dilated open position. Lengths and angle of torus tubarius rotation have been measured and indicated.

was used to create Quick-time videos to be imported into OsiriX. Patients with active patulous ET symptoms during the examination could demonstrate a failure of the valve to close, so the “opening” time was measured between the initiation of the anterolateral wall movement and the relaxation of the wall. Measurements were evaluated statistically using SPSS 17.0 statistical software package (IBM, Chicago, IL, USA). Independent samples 2-tailed *t* tests were applied using $p < 0.05$ for the level of significance.

Patients and subjects gave their informed consent to the study, which was approved by the institutional ethical review board (permission number R09021 University of Tampere, KI/1998 Karolinska Institutet).

RESULTS

Patient demographics are summarized in Table 1. Healthy subjects had no history of any chronic ear disease or middle ear effusion. There had been no temporary inflammation or retraction of the tympanic membrane during upper respiratory infections within the past 2 years.

There were no statistically significant differences in the heights of the torus tubarius between groups, despite the differences between fiberoptic and rigid endoscopic images and some variations in the distance from the endoscope to the tubal orifice.

ET measurement data and statistical analyses are presented in Table 2. Comparisons of mean time measurements of tubal dilation in healthy subjects and patients with OME or patulous ET are in Figure 3. Means of the measured movements with tubal dilation are compared between healthy subjects and patients with OME or patulous ET in Figure 4.

TABLE 2. Eustachian tube measurements

		n	Mean	Standard deviation	Significance (2 tailed) versus normal
Healthy = 0, Chronic otitis media with effusion = 1, Patulous = 2					
Open time of valve (ms)	0	23	10.50	6.336	
	1	20	15.06	9.959	0.076
	2	24	14.07	11.913	0.208
Torus rotation time (ms)	0	23	175.65	151.472	
	1	14	154.28	141.948	0.673
	2	21	276.19	336.072	0.201
Cycle time (ms)	0	24	995.00	404.722	
	1	14	1082.85	671.799	0.617
	2	21	1276.19	593.148	0.067
Palatal elevation (% torus height)	0	24	34.80	16.573	
	1	20	36.99	16.969	0.667
	2	24	30.64	17.030	0.396
Excursion of the lateral wall (% torus height)	0	24	35.50	16.306	
	1	20	23.86	21.659	0.048
	2	24	18.67	15.056	0.001
Angle of rotation of torus tubarius (degrees)	0	24	34.20	14.350	
	1	20	29.90	14.323	0.328
	2	24	31.02	18.022	0.502

Assumptions $\alpha = 0.05$ and $\beta = 0.2$ and standard deviations are sufficiently large that a 50% minimum difference was applied.

CSS indicates critical sample size for power of statistics.

Duration of ET Dilatory Cycle

There were no statistically significant differences between any of the groups regarding the duration of any portions of the ET opening and closing cycle. The mean cycle time, the duration from the initiation of dilation to completion of closure, was 995 ms for healthy subjects. There was a trend toward a longer cycle time with patulous ET, 1,276 ms ($p = 0.067$), but it did not rise to significance.

Torus rotation time measured the duration from the initiation of the torus' medial rotation to its maximally rotated position. This represented the time to achieve full contraction of the LVP muscle but did not include the subsequent sustained contraction while the TVP contracted. There were no significant differences between groups regarding torus rotation times.

“Open time” of the valve represented the duration that the valve seemed to be dilated open or made maximal efforts to dilate. This measure corresponded to contraction and relaxation of the TVP muscle. The open time for healthy subjects was 10.5 ms. There was a trend for prolongation of the open time in dilatory dysfunction ETs at 15.1 ms ($p = 0.076$) that did not reach significance.

Tubal Movements During Dilation

There were no significant differences between groups regarding height of elevation of the palate, which included

TABLE 1. Demographics

Group	No. of Eustachian tube	No. of subjects	Age range (yr)	Mean age (yr)
Healthy	24 (15 right, 9 left)	15 (9 males, 6 females)	30–64	43.4
Chronic otitis media with effusion	20 (10 right, 10 left)	13 (8 males, 5 females)	18–75	41.5
Patulous	24 (11 right, 13 left)	15 (7 males, 8 females)	18–81	41.7

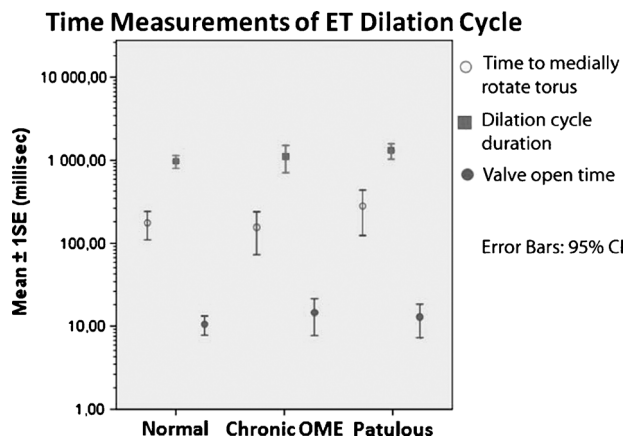


FIG. 3. Mean time measurements of tubal dilation in healthy subjects and patients with OME or patulous ET. Total duration of the opening and closing cycle, rotation of the torus tubarius to its maximum medialized position, and time of valve open are indicated.

the floor of the ET. This movement corresponds to the action of the palatal muscles initially and is then joined by the LVP. Elevation in healthy subjects was 34.8% of the torus tubarius height.

Lateral excursion of the anterolateral wall of the ET, the distance traveled because of TVP contraction, was significantly reduced in dilatory dysfunction (23.9% of the torus height, $p = 0.048$) and even more reduced in patulous ET (18.7%, $p = 0.001$) in comparison to healthy subjects (35.5%).

Mean angle of rotation of the torus tubarius during dilation for healthy subjects was 34.2 degrees, and there was no significant difference from the other groups.

DISCUSSION

This study analyzed quantifiable parameters of tubal movements observed by endoscopy to aid in understanding its pathophysiology and to determine whether these parameters would correlate with patulous or dilatory dysfunction and provide clinically useful measurements. The most significant abnormalities occurred with the excursion of the anterolateral wall of the functional valve, which, in comparison to healthy subjects, was approximately half the distance in patulous ET patients and about two-thirds in dilatory dysfunction patients.

Video endoscopy of the ET is a useful tool for studying the pathology affecting the nasopharyngeal orifice and lumen of the cartilaginous portion, which likely play roles in the pathophysiology of otitis media. Ordinary endoscopy may reveal gross pathology, but when the cause of tubal dysfunction is not immediately apparent with observation in real time, slow-motion playback is very helpful for recognizing smaller defects and subtle movement abnormalities.

Insufficient opening of the valve seems to be caused by mucosal inflammation and thickening in the majority of

cases. Pure muscular abnormalities (dynamic dysfunction) occur in a much smaller minority (5,7). Some of the dynamic disorders, such as early relaxation of the LVP muscle before the TVP muscle begins to contract, can be quite subtle and only discernable with slow-motion video.

The patulous defect is a visible concavity in the usually convex anterolateral wall of the ET valve. It seems to be due to the TVP muscle or a deficiency in volume that may be due to loss of thickness in the mucosa, submucosa, Ostmann’s fat pad, or lateral cartilaginous lamina (9). In patulous ET patients, the reduction in the anterolateral wall movement could be due to several reasons: hypertonic basal tone of the TVP muscle resulting in little additional movement with dilatory efforts, weak or thin TVP, loss of other soft tissue, or cartilage leaving a volume defect that is already dilated with little additional room for further excursion. The exact cause may vary between patients, and further studies, such as electromyogram (EMG) recordings, will be necessary to clarify the cause in each case. Most of the patulous patients demonstrated a lack of lateral cartilaginous lamina and lack of soft tissue volume in the anterolateral wall. Hypertonic functioning of the TVP muscle cannot be adequately determined by endoscopic observation, but the concave contour of the anterolateral wall provides some support for chronically increased TVP tone contributing to patulous ET by active retraction.

Dilatory dysfunction cases showed reduced excursions of the anterolateral wall as well but likely for different reasons. The wall often was noticeably inflamed and thickened, making it more difficult for the TVP to move the increased bulk of the wall. There also could be weakness of the TVP in some cases in which the mucosa seemed healthy, but the movement was reduced. Direct measurement with EMG would be necessary to confirm such cause.

Movements that were dependent on LVP action, such as palatal elevation and angle of torus rotation, did not show any significant differences between healthy subjects

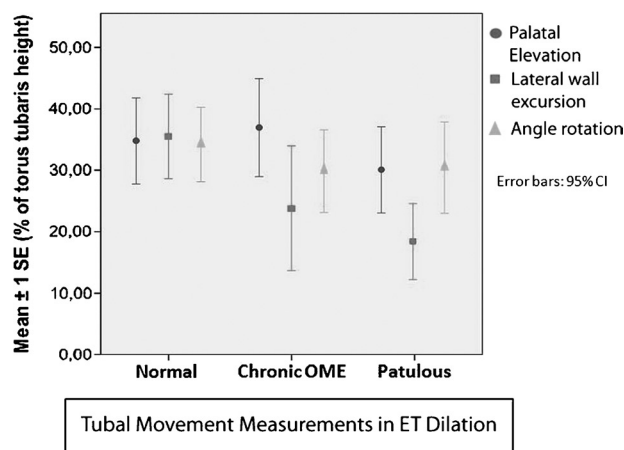


FIG. 4. Means of the measured movements with tubal dilation in healthy subjects and patients with OME or patulous ET. Palatal elevation and the anterolateral wall lateral excursion measured in percentage of torus tubarius length and angle of rotation of the torus measured in degrees.

and patients with ET dysfunction. It is likely that the LVP muscle serves to initiate tubal dilation, opening the nasopharyngeal orifice of the ET to create the scaffold against which the TVP muscle can dilate the valve open (5). Failure of the LVP action can be associated with the development of OME (7), but this study demonstrates that the extent of LVP action is not too critical a factor.

The durations of portions of the dilatory cycle did not show any significant differences between groups. Initiation of dilation with rotation of the torus was a mean of 176 ms in healthy subjects. Once rotated, the TVP contraction commenced, holding the valve in the maximally dilated or "open" position for a mean of 10.5 ms, which is a significantly shorter duration than previously reported of 430 ms (10). Their evaluation was made by sonotubometry as opposed to visual inspection and may indicate that the sonotubometry is more sensitive in detecting opening before the endoscopic aperture is sufficiently wide to observe it. As the actual opening of the valve could not be confirmed endoscopically, further study would be needed comparing with sonotubometry or other techniques to determine true patency. We observed a trend toward longer open time in dilatory dysfunction cases with a mean of 15.1 ms. It is possible that there is an increased duration of effort exerted by the TVP muscle to dilate the valve when it is compromised by inflammatory mucosa. The overall length of the ET dilatory and closing cycle was a mean of 995 ms in healthy subjects. There was a trend for longer duration in patulous ET cases with 1,276 ms that is of uncertain importance.

The present study has a number of weaknesses that limit its interpretations, most important of which was that the measurements were all limited to endoscopic observations. The standard deviations were sufficiently large that much larger sample sizes would be needed to detect small differences between the healthy subjects and the patients. Measurements of the total cycle time, time to rotate the torus tubarius to its fully medial position, open time of the valve, excursion of the palatal elevation, and angle of torus rotation did not show significant differences between groups; however, these parameters might become significant in a larger cohort, and this could be studied in the future. Comparisons were not made with severity of ear pathology, although this has previously been shown to lack any correlation with severity of ET pathology (7). This study analyzed the maximum excursion of the anterolateral wall and not the excursion of the valve wall itself, which would be useful to investigate in the future. Correlation with ET function tests, EMG recordings, sonotubometry, or other quantitative methods to measure tubal function were not performed and would be useful for further research. The ET dysfunction groups had a wider age distribution than the control group and could add some bias to the results. A more similar age distribution would be desired in a sub-

sequent study with a larger cohort. However, the strength of this article is that it provides a new means to make quantitative endoscopic measurements and used them to help describe the muscular events in detail in ET during the dilatory cycle.

This study has highlighted the importance of the TVP muscle's action to cause lateral excursion of the anterolateral wall of the valve during dilation of the ET. When the muscle wall is thick with inflammation or the muscle action is reduced sufficiently to compromise tubal opening, it may lead to atelectasis or OME. Lateral excursion of the wall is relatively easy to see with endoscopy and could be evaluated qualitatively as part of a grading scale or quantitatively as was done in this study using open source downloadable software (OsiriX).

CONCLUSION

Measurements were made of ETs from video endoscopic recordings taken during the dilatory and closing process in healthy subjects and patients with either patulous ETs or dilatory dysfunction. Lateral excursion of the ET's anterolateral wall was significantly reduced in dilatory dysfunction patients and even more reduced in patulous ET patients. Evaluation of the excursion of the lateral wall of the ET, which is due to the TVP muscle action, may be important to observe during clinical endoscopy of the ET, and it may be quantified for investigational purposes.

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Corresponding Author: Ophir Handzel, M.D.

Corresponding Author's Institution: Tel-Aviv Sourasky Medical center, Tel-Aviv University

First Author: Ophir Handzel, M.D.

Order of Authors: Ophir Handzel, M.D.;Dennis Poe, MD;Robert J Marchbanks, PhD

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Abstract: Abstract

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Subjects and Methods: Eighteen healthy subjects underwent endoscopic nasopharyngoscopy with simultaneous, synchronous sonotubometry. This pilot study utilized a novel device. Each subject was documented performing three maneuvers: pronouncing the consonant "k", swallowing and yawing.

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Conclusions: Simultaneous synchronous endoscopy and sonotubometry may improve the accuracy of either performed separately as an ET function measurement tool. Sonotubometry may prevent a false positive endoscopy (ET viewed as open, but no functional patency achieved). Endoscopy can lower the threshold considered as positive for sonotubometry. A negative pressure wave recorded by sonotubometry may reflect the ET role of clearing the middle ear of secretions towards the nasopharynx. This novel measurement technique provided additional evidence that the tensor veli palatini muscle provides the final opening action of the ET.

Synchronous Endoscopy and Sonotubometry of the Eustachian Tube: A Pilot Study

Ophir Handzel, MD¹, Dennis Poe, MD^{2,3}, Robert J, Marchbanks, PhD⁴

1. Department of Otolaryngology/Head and Neck, Oro-Maxillary Surgery, Tel-Aviv Sourasky Medical center, Tel-Aviv University, Tel-Aviv, Israel

2. Children Hospital of Boston, Department of Otolaryngology, Harvard Medical School, Boston, MA

3. Department of Otolaryngology, Tampere University Medical School and Central Hospital, Finland

4. Neurological Physics Group, Department of Medical Physics and Bioengineering, Southampton University Hospitals NHS Trust, Southampton SO16 6YD, UK

Corresponding author: Dennis Poe, MD,

E-mail address: Dennis.Poe@childrens.harvard.edu

Author Contributions

Ophir Handzel - study design, execution of the research project, data analysis and writing of the manuscript; **Dennis Poe** - study design, execution of the research project, review and critique for data analysis and manuscript; **Robert J, Marchbanks** - study design, review and critique of manuscript.

Disclaimer

Authors RJM and DP are co-inventors of the ET Analyser and they have filed a provisional patent application for the device. RJM is the owner of the company that has manufactured the device.

Introduction

Eustachian tube (ET) function plays a critical role in the maintenance of homeostasis within the normal middle ear cleft. Tubal dysfunction is a major factor in the etiology of middle ear diseases, such as acute and chronic otitis media, the creation and progression of cholesteatoma and resultant hearing loss. Great advances have been made in the reconstruction of ears injured by chronic pathology, but persistent tubal dysfunction remains a leading cause for surgical failure.¹

The ability to record objective measurements of ET function that would be clinically relevant is highly desirable, but has yet to be achieved. Existing tubal function tests are still unable to predict failure in tympanoplasty.² Reliable quantitative measurements are critically needed to aid in the investigation of pathogenesis of ET disorders and to enhance our ability to assess normal and abnormal function. A clinical ET function test would be useful in the preoperative assessment of candidates for ear surgery, aiding in the selection of patients and in appropriate tailoring of operations. It is needed to better evaluate responses to medical or surgical treatment, as a tool in the investigation of otitis media, and to aid in the evaluation of less well defined entities such as otalgia from flight or scuba barometric changes, autophony from patulous tubes, and nonspecific otalgia.

Endoscopy of the nasopharynx allows a direct examination of the pharyngeal orifice of the ET and in most cases a view into the tubal lumen. Much has been learnt from endoscopic observation of the ET: The sequence of muscular activity resulting in dilation of the ET has

been detailed,³ and pathologies of the orifice identified.¹ Video recording and slow motion recording has allowed for more detailed examination.⁴ Endoscopy is limited to subjective description of the observed structures and motion and a practical grading scale for pathology has yet to be produced. Dilation of the functional valve of the tubal lumen can be reliably observed, but actual complete opening of the full length cannot be assessed by endoscopy. The valve refers to the portion of the mucosal surfaces within the ET lumen that are in apposition during the resting position and dilate open during tubal ventilation.³

Sonotubometry is a technique by which sound emitted by a speaker seated in the nose is recorded by a microphone placed in the external auditory canal. Opening of the ET is recorded as an increase in the intensity of the recorded sound.⁵⁻⁸ However, the interpretation of sonotubometry results is complicated by the presence of uncertain findings and both false negatives and positives, thus it does not reliably predict middle ear ventilation.⁹

In this report we describe for the first time, a method of recording ET function by simultaneous and synchronous video endoscopy and sonotubometry. By applying this technique to normal volunteers we hope to better elucidate the mechanisms of ET opening and to shed some light on the limitations inherent in performing endoscopy and sonotubometry separately. Correlation of these synchronized findings would be expected to aid in the interpretation of sonotubometry data and add to the understanding of some previously unexplained results. Sonotubometry confirmation of dilation of the ET valve to the open position would be compared to the endoscopic observation of valve dilation to ascertain the reliability of the endoscopic assessment of complete tubal opening.

Materials and methods

Eighteen healthy subjects underwent endoscopic nasopharyngoscopy with simultaneous synchronous sonotubometry. None had a history or findings on physical examination suggestive of ET dysfunction, chronic ear or sinus pathology. The group included eleven females and seven males, their ages ranging from 23 to 52 years old. Each subject gave their informed consent to the study and it has been approved by the local research ethics committee (Tel-Aviv Sourasky Medical Center code 0621-10-TLV).

The examination utilized a novel device capable of recording synchronous and simultaneous sonotubometer and digital video recordings of transnasal endoscopy (MMS-S10-EV Eustachian Tube Analyser, Marchbanks Measurements Systems, Lymington, UK). Figure 1 illustrates the display of the ET analyser. The results from the sonotubometry are shown in the bottom panel and, the image from the endoscopic examination is projected in the upper right corner. The red cross marks the point of time corresponding to the projected image from the endoscopy. For the purpose of review of the test results, short movie clips were made using a screen capturing software [CaptureWizPro, Arvada, CO]. The duration of each component of the exam and documenting clip (“run”) was 6.25 seconds.

Endoscopy was performed using a rigid 45 Hopkins rod endoscope (Karl Storz, Tuttlingen, Germany) or flexible nasopharyngoscope (Pentax, Montvale, NJ). The endoscope was fitted with a single chip analog charge coupled device (CCD) video camera (Karl Storz, Tuttlingen, Germany). A full screen image of the endoscopy was projected on a video monitor

(SONY, Japan) and the video feed was also presented on the LCD display monitor that was connected to the combined sonotubometer-endoscope analyzer. Sonotubometry was performed as follows: a speaker was placed into the nostril contralateral to the ET to be studied. A microphone was placed in the ipsilateral external auditory canal (EAC) and was sealed against the EAC walls with appropriately sized tips otherwise used for tympanometry. The endoscope was passed through the nasal cavity ipsilateral to the ET studied. The parameters for the nasal speaker were set to a 7 kHz tone at 100 dB SPL for a duration of 6.0 seconds. The nasal probe tone signal was detected by the EAC microphone, amplified, passed through an RMS converter, onto a true log dB amplifier and then to a 12 bit analog to digital (A/D) converter. Video recording was done at 30 frames per second.

Subjects were examined in the office in the sitting position. The ipsilateral nasal cavity was anesthetized with topical spray Oxymetazoline HCl 0.05% mixed in equal parts with topical Tetracain 2% (mixed by the pharmacy at Tel Aviv Sourasky medical center). Next, the microphone was placed in the ipsilateral EAC and the speaker into the contralateral nostril. Using a feature of the ET Analyser, the completeness of the seal between the microphone and the EAC wall and between the nasal speaker and the nostril was verified to limit external feedback from the nasal speaker to the EAC microphone in order to reduce background noise. Once adequately anesthetized, the rigid endoscope was introduced into the ipsilateral nostril. In the event that the nasal cavity was too narrow to easily accommodate the rigid endoscope, the contralateral nostril was also anesthetized and the fiberoptic endoscope was subsequently introduced, either through the ipsilateral or contralateral nostril, whichever yielded the better view into the lumen of the ET along its long axis. The rigid endoscope was passed through the nasal cavity along the floor until a satisfactory view into the lumen of the ET was obtained and

aligned with its long axis. Care was taken to avoid any disturbance of the nasal mucosa as any bleeding could significantly compromise the video examination.

Each subject was asked to perform 3 sets of maneuvers. The first was repeated vocalization of the letter “k”, demonstrating the activity of the levator veli palatini (LVP) muscle. Isolated LVP activation was not expected to dilate the valve to the fully open position since that requires the subsequent contraction of the tensor veli palatini (TVP) muscle. The second recording documented efforts of the subject to swallow as an example of normal dynamics. Water was provided for an oral bolus as needed. Although the initiation of swallowing is under significant voluntary control, subjects have variable and even quite limited control of the subsequent amount of reflexive muscular effort applied to dilate the ET valve to the open position. During each 6.25 seconds long video clip, subjects could usually perform two swallowing efforts, at times three. Normal individuals do not dilate their ET to open with every swallow. Lastly, a forced yawn was recorded to study maximal muscular effort. Before the actual exam the subjects were instructed to experiment with a number of yawns, and to make a maximal effort to open the ET. Most commonly, a yawn gives the best chance of producing ET dilation and can yield a maximal dilatory effort. Again, ET dilation to the open position does not occur with every swallow, but individuals can be coached to maximize the voluntary effort. Subject 2, a scuba diver, had developed significant voluntarily control over the contractions of the levator veli palatini (LVP) and tensor veli palatini (TVP). In addition to the standard protocol his examination included documentation of the results of his efforts to contract the LVP and TVP individually aided by video endoscopic feedback. Dilation of the valve was observed on endoscopy by the coordinated actions of the LVP contraction holding the posterior cushion (torus tubaris) of the ET in a medialized position against which the TVP subsequently dilated the

antero-lateral wall to produce a rounding of the valve to the fully dilated position. Dilation of the valve to the open position was determined by the observation of a rise in the dB SPL in the microphone signal from the sonotubometer that coincided with the muscular effort.

Results

Quantitative results of the measurements of the maneuvers to open the ET are summarized in table 1. The data for each subject was averaged and represented as a single row in the table. This method of data representation was chosen, rather than presenting the result of every swallow and yawn, to allow comparison between subjects, who differed in the number of efforts recorded, and for the sake of brevity and clarity.

One subject was tested and excluded from the data analysis. This 34 years old male had undergone conchotomy for nasal obstruction several years before being evaluated. His examination resulted in the largest increase in sound intensity during swallowing (ranging from 23 to 26dB). It is possible that this unusually high recording resulted from the surgically expanded nasal cavity.

Six out of the remaining seventeen (35.3%) subjects did not open their ET during swallowing. Interestingly, all six were females. As the middle ears of these subjects were normally aerated, it is most likely that they did open their ETs on a regular basis, but failed to demonstrate a voluntary ability to initiate dilation with swallowing. For those eleven that did open the ET during swallows, opening was recorded with 3 out of 4 of the swallow efforts (range 10-100% of openings per swallows). Four subjects opened the ET with every swallow (i.e. 100% openings per swallows). The average duration of opening of the ET during swallowing as

reported from sonotubometry was 0.44 seconds, and the average increase in sound intensity reaching the EAC was 9.2 dB. Yawning resulted in higher instances of ET opening compared to swallowing; only four subjects (23.5%) could not open the ET during a forced yawn. The average opening time of the ET during yawning was 2.03sec and the intensity of sound recorded in the EAC increased by an average of 10.1dB. Hence, the voluntary yawn resulted in longer opening of the ET.

Comparison of the results from simultaneous recordings of the two techniques demonstrated a 100% correlation between sonotubometric detection of a significant rise in 5 dB SPL to indicate tubal opening and endoscopic observation of valve dilation to the open position. On the contrary, endoscopic observations of valve dilation were not consistently associated with confirmation of full dilation to open on the sonotubometry. We documented one case of an effort that appeared to dilate the valve open as seen on endoscopy, but lacking sonotubometric confirmation (Figure 2). The lumen of the ET was partially dilated by the posterior displacement of the posterior cushion. Although the nasopharyngeal orifice appeared to be open, no functional opening was recorded by the sonotubometer.

A negative sound pressure wave was recorded in a number of instances, immediately preceding a swallow related opening. In figure 3a recorded from subject 8, a bubble of nasal secretion is seen in the ET orifice; the sonotubometer recording reflects a closed ET. Upon swallowing (Figure 3b) the bubble seems to be inflated and the sonotubometer records a reduction in the sound intensity reaching the EAC. These findings are compatible with air being pushed from the ET into the nasopharynx.

Discussion

In the search for a better tool to measure the function of the ET, the value of simultaneous synchronous recording of endoscopy and sonotubometry was evaluated in this pilot study.

The most commonly used tool for real time evaluation of ET function is endoscopy. ET allows for detailed studying of the nasopharyngeal orifice in passive and dynamic states. However, endoscopic examination of the ET orifice during swallows or yawns can demonstrate dilation of the ET without being certain that full tubal opening was achieved. Hence, it may lead to a false assurance of a normally functioning ET orifice (i.e. false negative). Adding a functional measurement of ET activity with sonotubometry can eliminate this source of error. In this study, in one instance ET dilation efforts were noted on endoscopy but dilation to open failed to occur on sonotubometry. (Figure 2) It is unlikely that this observation was caused by a fixed obstruction in other parts of the ET (e.g. the isthmus), as the middle ear was normally aerated. Reasons for failure to observe sonotubometric opening despite dilation seen by endoscopy could be secretions temporarily within the lumen (Figure 3a), incomplete dilation of the valve rostrally or sufficiently small dilation that it is below the sensitivity of the sonotubometer. Such a small dilation might still provide a significant amount of air exchange to be physiologically beneficial. Ordinary ET endoscopy will generally see most of the valve and in some cases up to the isthmus, but it is not possible to see the full length of the lumen. Therefore, it cannot reliably confirm true dilation to the open position in all cases. It is possible to pass smaller endoscopes higher into the ET lumen, but the low resolution of such microendoscopes and contact of the lens to the mucosal walls has not provided practical benefits from this approach.³

Sonotubometry seems to have high specificity (a recording of ET opening most likely reflected a true opening), but lower sensitivity (the ET may open without a corresponding

recording by sonotubometry). Simultaneous synchronous endoscopy with sonotubometry may improve the sensitivity of both isolated exams. The accepted threshold for ET opening in sonotubometry is 5dB, assumed to strike a good balance between false negatives and positives.¹⁰ In a number of instances we recorded an increase in EAC sound pressure that did not reach this threshold, but was clearly a sign of true opening of the ET, as it nicely corresponded with a simultaneous opening of the orifice as seen by endoscopy. Sonotubometry by itself would have recorded a false negative measurement. However, we suggest that in such instances even a sub-threshold recording can still be considered as an indicator of ET opening, given the concurrent endoscopic dilation. As mentioned, secretions may result in a non-opening pattern sonotubometry, but can be recognized as a transient and easily reversible impediment by endoscopy. In all efforts documenting opening of the ET by sonotubometry, a corresponding opening was observed during endoscopy.

Sonotubometry requires proper EAC sealing. Imperfect sealing of the EAC meatus can cause a leakage of sound pressure that will decrease the intensity recorded by the microphone or allow sound to enter the EAC from outside the head (feedback). Feedback could cause false recordings of elevation in sound pressure. This problem can be addressed by careful fitting of the microphone into the EAC. The analyzer used in the current study was equipped with continuous leak monitoring capability. The examiner should both be alert for noticeable changes in the intensity of the tone emitted by the sonotubometer as it will normally be just barely audible.

The combined exam has provided additional information about the normal activity of the ET orifice. Subject 2, a scuba diver, has trained himself to open the ET by voluntarily contraction of the LVP and TVP, even without swallows or yawns. With video endoscopic

feedback, he quickly learned to independently contract the LVP, but could not contract the TVP without first contracting and sustaining LVP contraction. The combined recording illustrates that contraction of the TVP is the final and necessary stage in the dilatory process of the ET that results in opening of the tube. Contraction of the LVP elevates the palate and medially rotates the posterior cushion, which dilates the postero-medial wall of the ET, but does not cause tubal opening as is evident by the flat sonotubometer recording (Figure 1a). When the TVP contracted (Figure 1b), a corresponding elevation of approximately 8dB in the sonotubometer was recorded. The duration of the opening of the ET was dependent on the duration of contraction of the TVP. This adds additional evidence that TVP contraction is the final step for the opening of the ET. This conclusion is also supported by the fact that LVP contraction during pronunciation of the consonant “K” never resulted in the opening of the ET. The pivotal role of the TVP in opening the ET has been established by other techniques, including paralysis with botulinum toxin.¹¹⁻¹³ Interestingly, subject 2 opened the ET with every swallow and helps to substantiate a potential role for endoscopic video feedback as a means for training patients with impaired ET dilation.

The average opening time of the ET during swallows was 0.44 seconds; this is compatible with the 0.43 ± 0.138 seconds reported by Mondain et al.¹⁴ However, these authors defined opening of the ET in sonotubometry as an elevation of 6dB and used different sound stimulus characteristics that might influence these measurements. Yawns, in contrast to swallows, can produce a strong voluntary opening of the ET and can represent a maximal opening effort. As such, it is not surprising that with a maximal voluntary effort the ET can be maintained opened for longer durations compared with the largely reflexive sequence that occurs during swallows. However, the average increase in sound intensity during a yawn was not higher

than during swallow, potentially implying that the ET does not become more patent with the voluntary effort of the yawn compared to the swallow.

In one instance, an air bubble residing in the ET orifice was inflated by the contracture of the ET associated muscles (Figure 3a and 3b). Sonotubometry recorded a negative deflection wave. These findings may indicate that gas was being pushed from the lumen of the ET towards the nasopharynx, potentially serving one of the ET's functions of middle ear clearance. A detailed analysis of the anatomy of the orifice and the timing of muscle contraction¹⁵ and a clinical observation through perforated ear drums¹⁶ have supported such a notion.

In this study efforts to open the ET by swallowing and yawning were studied. Due to the equipment set-up studying spontaneous (non-swallow or yawn related) opening could not be evaluated; this would require subjecting an examinee to a long duration of instrumentation. As spontaneous opening has an important role in middle ear cleft homeostasis it would be beneficial to devise a method suitable for longer duration of surveillance. This preliminary study was limited by the small number of subjects, and its intention was to study the potential application of the technique of simultaneous recording of endoscopy and sonotubometry. There is a need for larger scale studies of normal subjects as well as patients with pathologies of the middle ear, nasopharynx or the ET (such as cleft palate).

In conclusion, simultaneous synchronous recording of endoscopy and sonotubometry can improve the accuracy of each of these tools separately as a technique for studying ET function. In addition, this preliminary study has confirmed the pivotal role of TVP contraction to ET opening.

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Abstract

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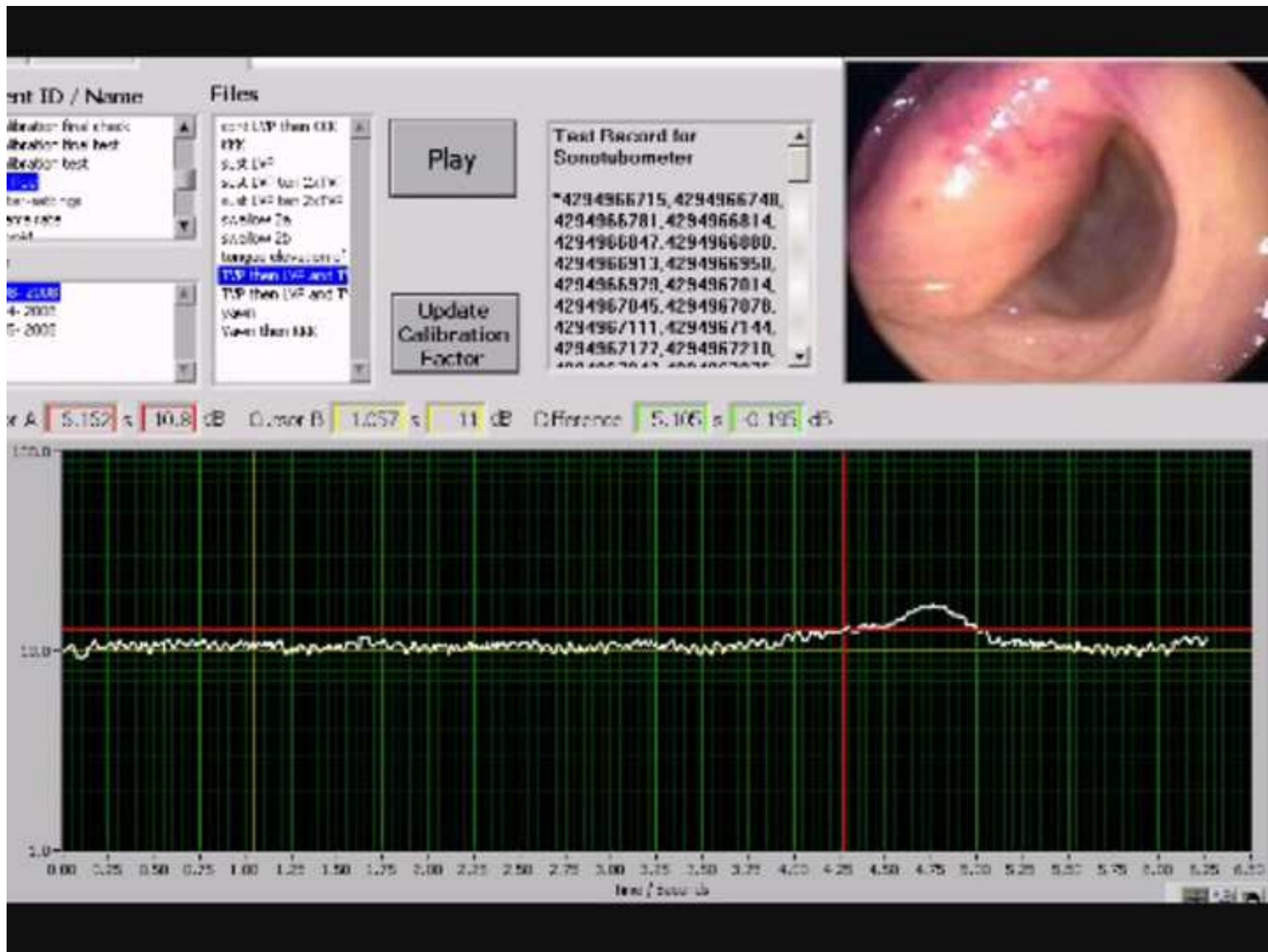
Figures' Legend

Figure 1 – Combined rigid endoscopic image (in the right upper corner of the figure) and sonotubometry (lower half of the image) recording a left Eustachian tube naso-pharyngeal orifice. All figures are screen images from the prototype device. The endoscopic image is projected on the right upper corner of the screen. In the lower part of the screen the sonotubometer results are shown. The white curved line is the sound pressure measurement in the external auditory canal, in a logarithmic scale (y-axis) vs. time (x-axis). The red cross on the sonotubometry recording marks the timing when the corresponding endoscopic picture was taken. A) Isolated contraction of the levator veli palatine does not result in opening of the Eustachian tube (as reflected by the stable recording of sonotubometry depicted with a white line). B) Contraction of the tensor veli palatini is seen as a concavity of the anterior (right side) wall of the lumen in the Eustachian tube orifice. The combined contraction of these two muscles results in opening of the Eustachian tube as measured by an elevation of approximately 8 dB in the sonotubometry recording. Contraction of the tensor veli palatini is essential for ET opening.

Figure 2 – Discordance between the endoscopic view and the recording of the sonotubometer. A rigid endoscopic view of the right Eustachian tube (ET) nasopharyngeal orifice seems to show an opening of the ET (white arrow); however sonotubometry did not record a compatible elevation in the sound recorded at the external auditory canal. This is an example of the improved sensitivity of the combined device for evaluating Eustachian tube opening compared with endoscopy alone (see legend of figure 1 for details of the image layout).

Figure 3 – Secretions in the right Eustachian tube orifice and the creation of pressure towards the nasopharynx in the orifice during initial stages of swallowing. A) Endoscopic view of the

nasopharyngeal orifice of the left Eustachian tube. A thin film of secretions covers the orifice. This finding may potentially dampen sound transmission from the nose to the external auditory canal causing a falsely negative sonotubometry recording. B) With a swallowing effort, evident in the elevation of the levator palatini muscle, an air bubble is being pushed from the orifice lumen towards the nasopharynx. This observation is compatible with the role of the Eustachian tube of clearing the middle ear to the nasopharynx (see legend of figure 1 for details of the image layout).



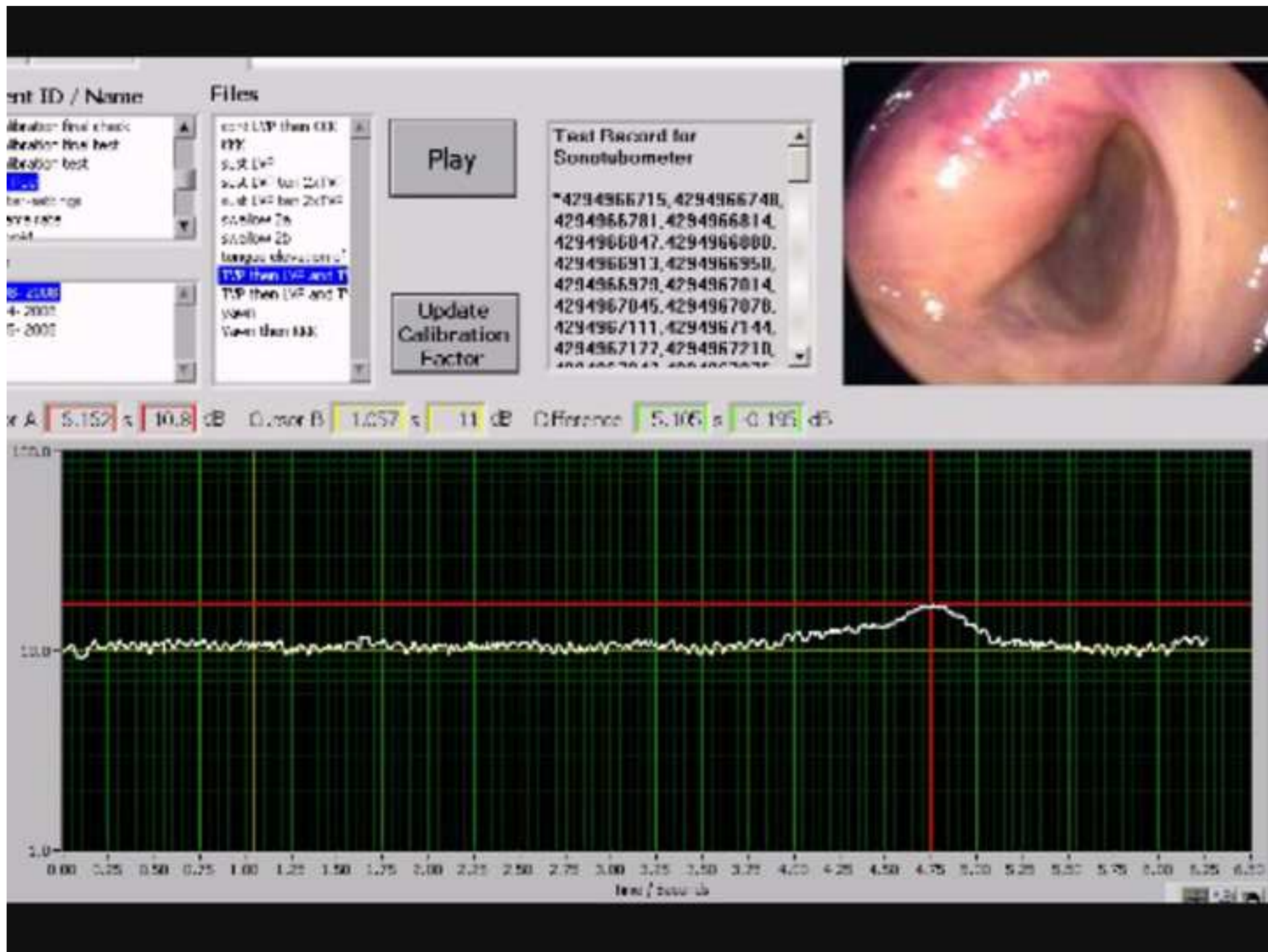


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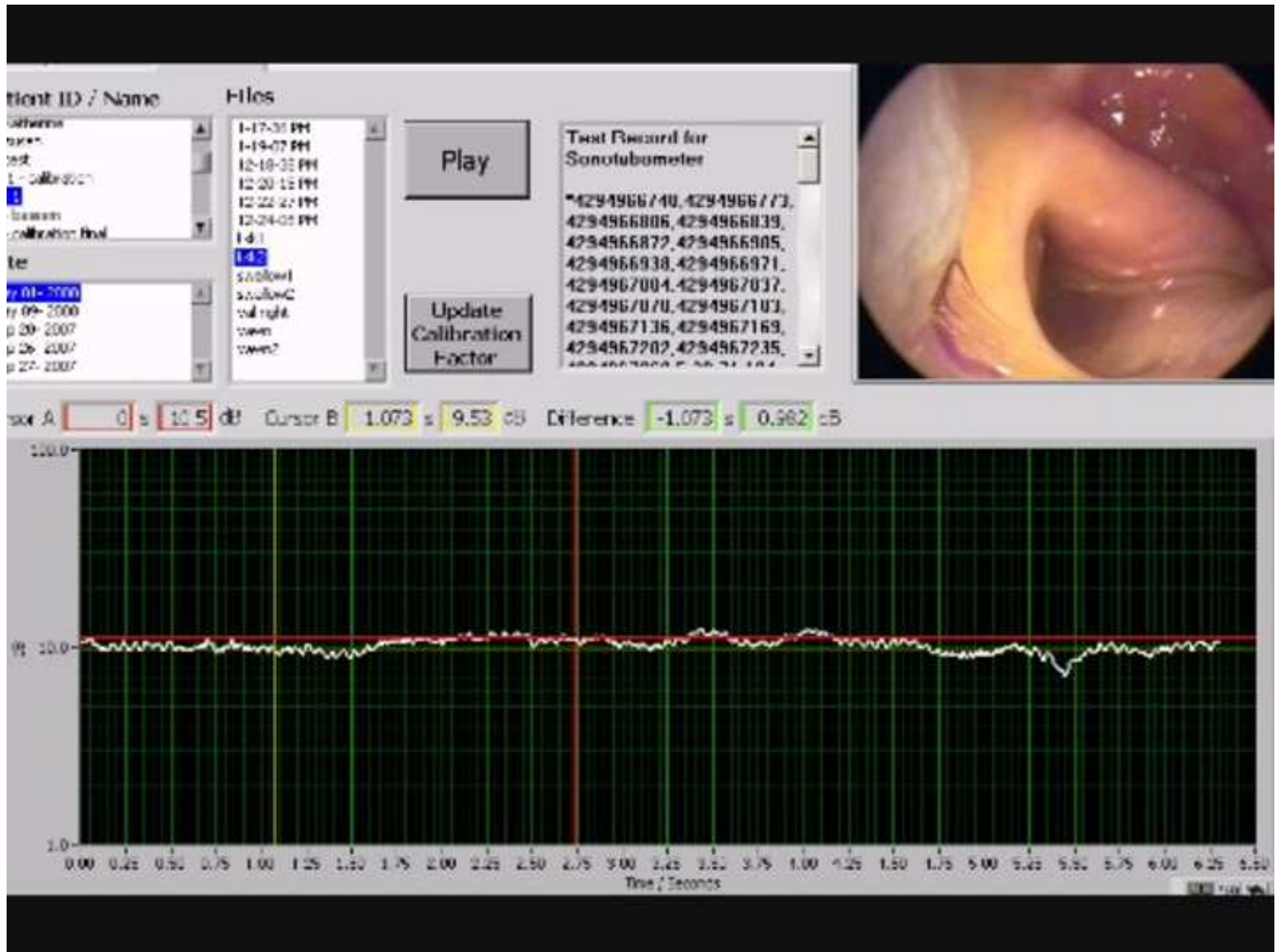


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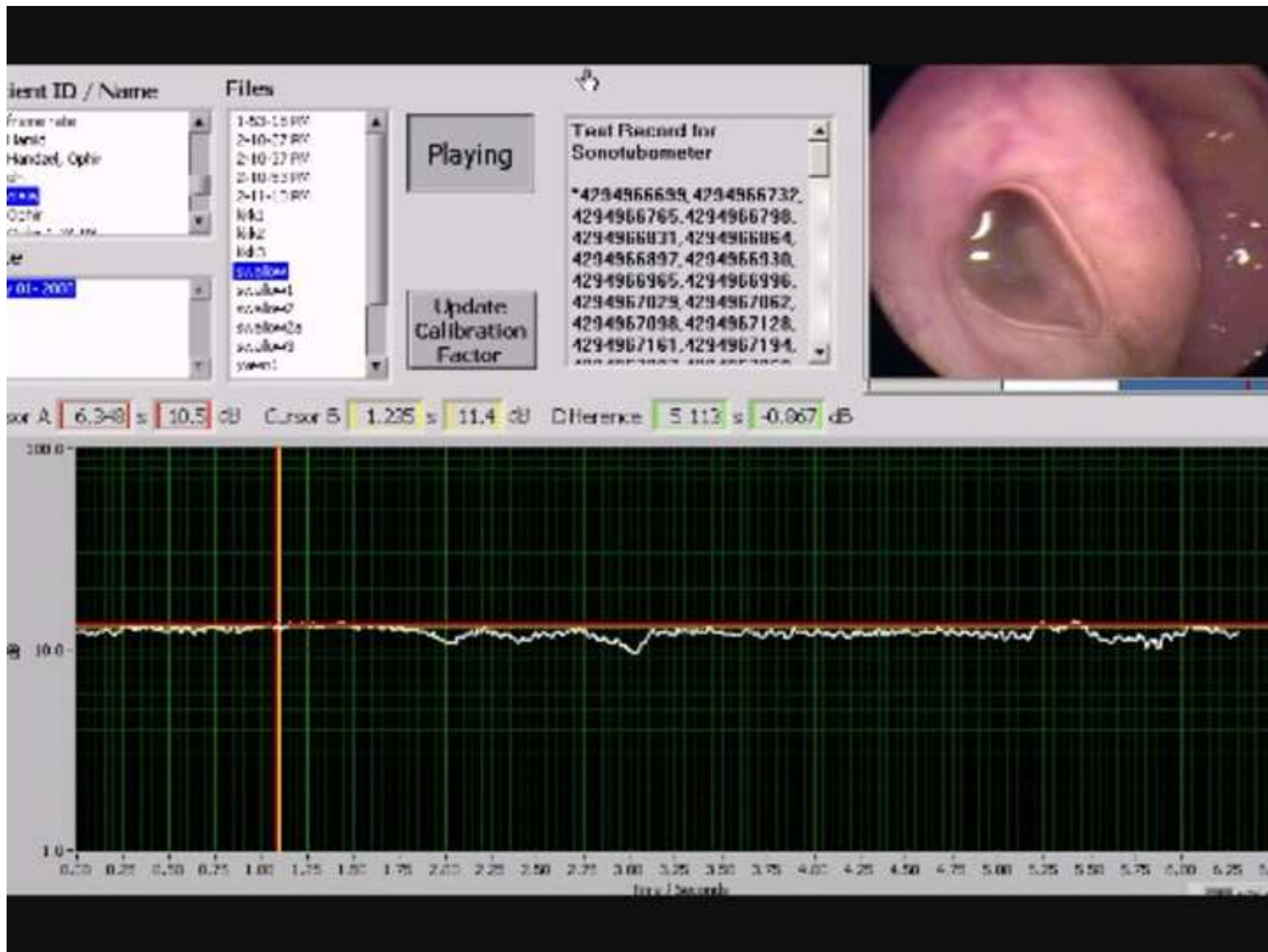


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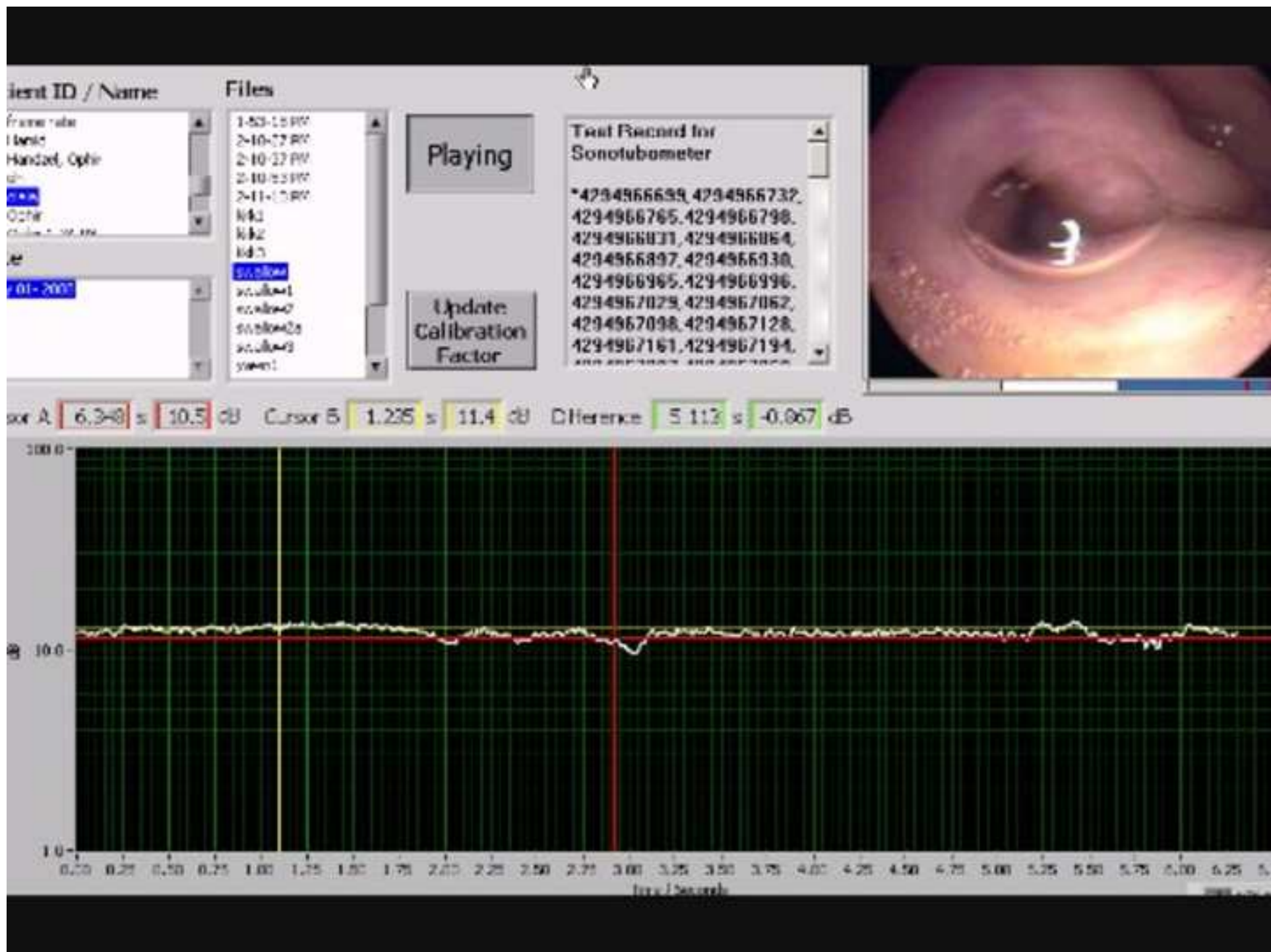


Table 1 – Summary of Eustachian tube opening with dilatory efforts

Subject	Swallow				Yawn			
	Fraction Open	Duration (sec)	Intensity (dB)	Number of efforts	Fraction Open	Duration (sec)	Intensity (dB)	Number of efforts
1	20%	0.2	7	5	0%			1
2	100%	1.06	12.8	6	100%	2	9.5	5
3	86%	0.28	11.5	7	100%	0.8	4	1
4	0%			7	100%	1.5	7	2
5	10%	0.35	5	10	100%	1.5	6.7	2
6	80%	0.27	15	5	50%	3	7	2
7	0%			4	0%			1
8	0%			5	0%			1
9	100%	0.48	6	6	100%	1.25	7	2
10	33%	0.5	9	6	100%	0.55	9.5	2
11	0%			4	100%	0.55	9.5	1
12	75%	0.3	7	4	100%	0.62	17.5	3
13	100%	0.49	15.3	4	100%	3.1	11.2	2
14	100%	0.35	5.8	2	n/a			
15	0%			5	0%			2
16	0%			3	100%	5.25	17.5	2
17	50%	0.63	7	4	100%	4.24	15	2
Average	44%	0.29	5.6		71.9	1.52	7.6	
Average(excluding non-openers)	68%	0.44	9.2		96%	2.03	10.1	

Laser Eustachian Tuboplasty: Two-Year Results

Dennis S. Poe, MD; J. Fredrik Grimmer, MD; Ralph Metson, MD

Objective/Hypothesis: Laser eustachian tuboplasty (LETP) combined with appropriate medical management will eliminate the chronic presence of middle ear effusions in selected patients. **Methods:** The study population consisted of 13 adults with otitis media with effusion (OME). Patients underwent slow-motion video endoscopy to identify the location and extent of surgical resection. A diode or argon laser was used to vaporize areas of hypertrophic mucosa and submucosa along the cartilaginous eustachian tube. Patients were evaluated at 6, 12, and 24 months. Successful outcome was defined as absence of OME. Patients with evidence of reflux disease or allergic rhinitis were treated with medical therapy before surgery and throughout the follow-up period as indicated. **Results:** LETP combined with medical management eliminated OME in 36% (4 of 11) of patients at 6 months, 40% (4 of 10) at 1 year, and 38% (3 of 8) at 2 years. Failure of LETP correlated with presence of laryngopharyngeal reflux ($P = .01$) or allergic disease ($P = .05$) for the results at 1 year but not at 2 years. **Conclusions:** LETP combined with appropriate medical management may be an effective treatment in select patients with chronic persistent eustachian tube dysfunction. A controlled trial with a larger number of subjects will be necessary to determine the efficacy of LETP and identify those factors predictive of successful outcome. **Key Words:** Eustachian tube, eustachian tube dysfunction, laser eustachian tuboplasty, otitis media with effusion, OME.

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INTRODUCTION

Eustachian tube (ET) dysfunction is a common problem of childhood, which may persist into adult life. The cause may be chronic infection, allergies, laryngopharyngeal reflux, primary mucosal disease, abnormalities of the dilation mechanism, and anatomic obstruction.^{1–8} When

tubal dysfunction is refractory to medical therapy, ventilation tube insertion into the tympanic membrane can be effective in aerating the middle ear. Patients with chronic, persistent ET dysfunction often require multiple sets of tubes. Long-acting tubes can also be inserted, although they are subject to crusting, infection, obstruction, and extrusion.

In previous studies,^{8,9} the authors have shown that the majority of patients with chronic, persistent ET dysfunction have identifiable bulky mucosal disease within the cartilaginous ET lumen that appears to interfere with the dilation process. These functionally “obstructive disorders” are in contrast to the much less common “dynamic disorders” in which normal-appearing ETs fail to properly dilate as a result of apparent abnormalities of muscular movement or coordination between muscles. Obstructive disorders are generally the result of degrees of mucosal inflammation and edema that may involve the entire nasopharynx or be isolated to the ET. Mucosal disease may be limited to the posterior cushion or may extend superiorly into the area we have termed “the valve.”^{9,10} The valve refers to the approximately 5-mm long segment of the tubal lumen, just inferior to the bony cartilaginous isthmus, in which the mucosal walls appose to close the tube in the resting position. Active dilation separates these mucosal walls under normal circumstances. Pathologic conditions that prevent dilation of the valve have been correlated with middle ear complications of otitis media with effusion (OME), atelectasis of the tympanic membrane, and cholesteatoma.⁸

Surgical correction of ET dysfunction has been attempted using various approaches to perform a eustachian tuboplasty by enlarging the osseous ET, especially the isthmus, which is the narrowest diameter segment of the ET.¹¹ None of these procedures have had any lasting success. Because it has become evident that the cartilaginous ET may be an important site of pathology, the authors have made an attempt to focus a surgical procedure on that portion for patients with refractory middle ear effusion.

Laser eustachian tuboplasty (LETP) was first performed by Kujawski in 1997¹² in patients with varying degrees of OME and/or atelectasis. We subsequently presented the preliminary results of a prospective pilot study evaluating the safety and efficacy of LETP in patients with refractory OME.¹³ We hypothesized that debulking of diseased mucosa with the tubal lumen’s posteromedial wall, in conjunction with appropriate medical management, could be effective in eliminating medically refractory OME. The procedure resulted in the absence of

From the Department of Otolaryngology (D.S.P., R.M.), Harvard Medical School, Boston, Massachusetts, U.S.A.; the Department of Otolaryngology (D.S.P.), Children’s Hospital, Boston, Massachusetts, U.S.A.; Department of Pediatric Otolaryngology-Head and Neck Surgery (J.F.G.), University of Utah, Salt Lake City, Utah, U.S.A.; and Primary Children’s Medical Center (J.F.G.), Salt Lake City, Utah, U.S.A.

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Send correspondence to Dr. Dennis S. Poe, Dept. ORL, Children’s Hospital LO 367, 300 Longwood Avenue, Boston, MA 02115. E-mail: dennis.poe@childrens.harvard.edu

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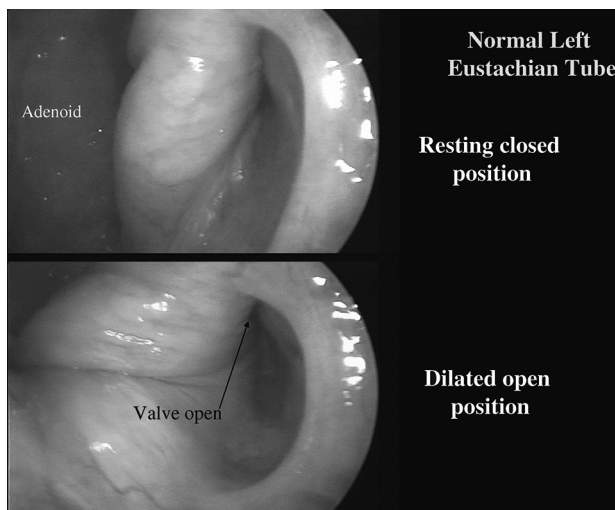


Fig. 1. Transnasal view of normal left eustachian tube nasopharyngeal orifice in closed and dilated positions. The patient was examined in the sitting position with a 0° 4-mm endoscope using slow-motion video endoscopy.

effusion in 7 of 10 (70%) patients at 6 months and 3 of 5 (60%) patients at 12 months. The purpose of the present study is to present the follow-up data from these and additional patients.

PATIENTS AND METHODS

Patient Selection

A prospective study of the results of a surgical intervention was undertaken at a tertiary medical center. The patients served as their own historical controls. The study population consisted of adult patients with at least a 5-year history of chronic otitis OME. Eligible patients must have undergone at least 2 prior tympanos-

tomy tube placements with recurrence of the effusion each time the tube was extruded.

Otitis media with effusion was documented by microotoscopy. Patients with cholesteatoma or atelectasis without effusion were not included in the study. All patients underwent a previously described transnasal endoscopic slow-motion video analysis of their ETs (Fig. 1) and were found to have disease within the cartilaginous portion consistent with an obstructive disorder.^{8,10} A tubal dysfunction MTV (*Mucosal disease, Tensor and levator veli palatini muscle strength, and Valve dilation*) score was determined for each patient.⁹

Medical histories included symptoms of seasonal allergies, food allergies, or reflux disease (Table I). Patients underwent endoscopic examination of their nasal cavity, nasopharynx, oropharynx, hypopharynx, and larynx looking for evidence of allergic disease or laryngopharyngeal reflux (LPR). All patients were treated for a minimum of 8 weeks with nasal corticosteroids. When allergic disease was encountered, oral antihistamines were administered for a minimum of 8 weeks. When evidence of laryngopharyngeal reflux was obtained, treatment with 20 mg per day of omeprazole was prescribed for at least 8 weeks. Failure to show improvement of OME after medical management was the final inclusion criterion.

Surgery was performed unilaterally. In the event of bilateral disease, the more severely affected ear was selected and tympanostomy tube or continued medical management was offered for the contralateral ear. Patients underwent preoperative evaluation by audiogram and tympanogram. The pure tone average (PTA) was calculated by averaging the air conduction decibel hearing level at 500, 1,000, 2,000, and 3,000 Hz. In the event that 3,000 Hz had not been obtained, the 2,000- and 4,000-Hz thresholds were averaged in accordance with the AAO-HNSF criteria.¹⁴ Preoperative tympanograms were not available for patient nos. 8 and 10. Audiograms were not available for patient no. 4.

A biopsy of the posterior eustachian tube cushion was performed immediately before LETP and 5 months after surgery in patient no. 15.

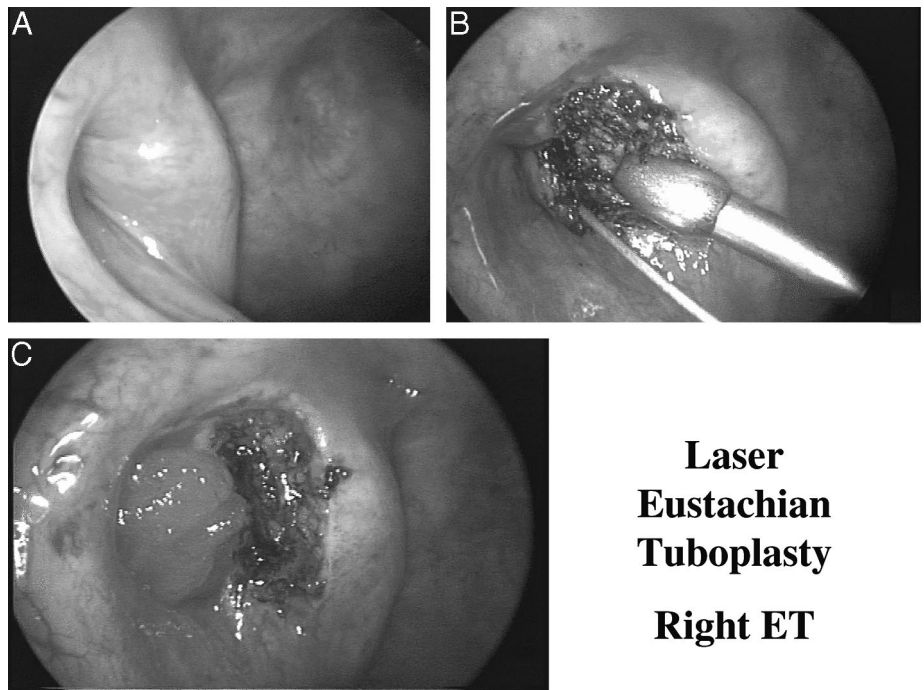
The study protocol was approved by the Institutional Review Board at the Massachusetts Eye and Ear Infirmary. All

TABLE I.
Preoperative and Postoperative Results for Laser Eustachian Tuboplasty.

Patient No.	Age	Sex	Laryngopharyngeal Reflux	Allergies	Preoperative		6-Month Follow Up		1-Year Follow Up		2-Year Follow Up	
					Examination	Tymp	Examination	Tymp	Examination	Tymp	Examination	Tymp
1	36	M	Y	Y	Atelec/OME	B	N/A	N/A	sl. Retrac	As	N/A	N/A
2	30	M	Y	N	OME	B	OME	B	TT	N/A	OME	N/A
3	44	M	Y	Y	Atelec/OME	C	sl. Retrac	C	Retrac	B	OME	B
4	62	F	Y	Y	OME	B	OME	B	Atelec	B	N/A	N/A
5	29	M	Y	N	OME	B	OME	B	OME	N/A	TT	N/A
6	48	M	Y	N	Atelec/OME	C	sl. Retrac	C	N/A	N/A	Tiny perf	N/A
7	50	M	N	Y	OME	C	OME	N/A	N/A	N/A	N/A	N/A
8	45	M	Y	Y	Atelec/OME	N/A	OME	B	OME	B	sl. Retrac	A
9	40	M	N	Y	OME	B	N/A	N/A	sl. Retrac	A	sl. Retrac	C
10	64	M	Y	Y	OME	N/A	OME	B	OME	B	TT	N/A
11	41	M	N	Y	OME	B	Retrac	C	N/A	N/A	sl. Retrac	A
12	56	M	N	Y	OME	B	OME	N/A	OME	B	N/A	N/A
13	33	M	Y	Y	OME	B	sl. Retrac	A	sl. Retrac	C	N/A	N/A

Atelec = atelectasis of the tympanic membrane (TM); N = no; N/A = not available; OME = otitis media with effusion; perf = perforated TM; Retrac = TM significantly medialized but not necessarily contacting the incus or promontory; there were no adherent retractions or pockets; sl. Retrac = slight retraction of the TM appearing nearly normal but mobile with negative pressure insufflation; TT = tympanostomy tube in the TM; Tymp = tympanogram: A (normal), As (normal pressure but shallow peak), B (flat), and C (negative pressure); Y = yes.

Fig. 2. Laser eustachian tuboplasty. (A) Intraoperative view of the right eustachian tube nasopharyngeal orifice as seen through a 0° endoscope passed through the ipsilateral nostril. The patient continues to have otitis media with effusion despite medical therapy and the placement of multiple tympanostomy tubes. The posterior cushion (Torus tubaris) has hypertrophic mucosa preventing adequate opening of the tubal valve region. (B) A 30° endoscopic view of laser vaporization of the hypertrophic mucosa and submucosa. The suction catheter is medially rotating the posterior cushion to dilate the tubal valve and allow for precise vaporization of valve mucosa. (C) A 30° endoscopic view of completed laser eustachian tuboplasty. A Merogel sponge with sulfacetamide and prednisolone topical ophthalmic solution has been packed into the tubal lumen.



Laser Eustachian Tuboplasty Right ET

patients were provided appropriate information regarding study design and signed informed consents.

Surgical Technique

The surgical technique has been described in detail in our previous work.¹³ To summarize briefly, patients were placed in the supine position, maintained with general anesthesia, and intubated. Ventilation of the ipsilateral middle ear was achieved by placing a 0.9-mm silicone mini-Baxter tympanostomy tube or by removing an obstructed permanent tympanostomy tube and thus creating a tympanic membrane perforation. In one case, myringotomy alone was performed. The surgery was typically performed with a 30° 4-mm-diameter nasal endoscope in the ipsilateral nasal cavity to visualize the tubal orifice. Surgical instruments were passed transorally with a tonsil mouth gag in place. Local infiltration with 1% lidocaine with 1:100,000 epinephrine was performed in the ET orifice. The orifice was further decongested with the topical application of 1:50,000 epinephrine on a cotton pledget. The medial cartilaginous lamina within the posterior cushion (torus tubarius) was identified and palpated as a landmark. A fiber-delivered laser was then passed into the nasopharynx, usually through the mouth but occasionally through the ipsilateral nasal cavity. A 980-nm contact-tip diode laser (Biolitec, East Longmeadow, MA) with settings of 7 W power, continuous pulse mode with 0.2 seconds on and 0.8 seconds off was used in the initial six cases. An argon laser (HGM;

Medical Laser Systems, Salt Lake City, UT) with settings of 3 W, 0.2-second pulse duration, continuous mode was used in 8 cases. Vaporization of mucosa and submucosa to expose the underlying cartilage was done to create a wedge-shaped defect on the intraluminal surface of the posterior cushion and posteromedial wall (Fig. 2). The resection was confined to the posteromedial wall taking great care to avoid any injury to the opposing anterolateral wall and the extent of the lesion never exceeded one-third of the lumen's circumference. The cartilaginous lamina was thinned only when it was unusually thick or stiff as seen on preoperative video endoscopy. The extent of surgical excision was determined by the degree of bulk seen at the preoperative slow-motion video analysis as described in previous studies.¹³ Mucosal biopsies of the ET were obtained at the time of LETP in 2 patients and 5 months postoperatively in one.

TABLE III.
Preoperative and Postoperative Hearing Results for Laser Eustachian Tuboplasty.

Patient No.	Preoperative PTA	6-Month PTA	1-Year PTA	2-Year PTA
1	21.3	N/A	11.3	N/A
2	20.6	43.8	17.5	31.3
3	23.8	18.8	18.8	32.5
4	N/A	N/A	N/A	N/A
5	40.0	N/A	N/A	26.2
6	30.0	35.0	N/A	26.3
7	57.5	N/A	N/A	N/A
8	28.8	55.0	55.0	30.0
9	51.3	N/A	12.5	15.0
10	47.5	38.8	32.5	21.3
11	31.3	16.3	N/A	17.5
12	42.5	N/A	47.5	N/A
13	37.5	N/A	8.8	N/A

PTA = pure tone average; N/A = not available.

TABLE II.

Overall Laser Eustachian Tuboplasty Results.

Follow Up (months)	Normal No.	Normal		Retracted TM	Retracted		Failure	Percent
		TM	Percent		TM	Percent		
6	11	0	0	4	36	7	64	
12	10	0	0	4	40	6	60	
24	8	0	0	3	38	5	62	

Failure = presence of otitis media with effusion, perforated; TM = tympanostomy tube, atelectasis.

Patients were followed prospectively. Audiograms, tympanograms, and microscopic examination of the ears were planned for 6 months, 1 year, and yearly intervals thereafter. Patients who were suspected of having LPR were continued on 20 mg omeprazole orally per day for at least 6 weeks after surgery. Failure of LETP was determined if the patient demonstrated OME on follow-up otomicroscopic examination. Statistical analysis was performed using the Student *t* test and χ^2 test.

RESULTS

Sixteen patients were entered into the study since June 25, 2001; however, three were excluded from the present report. One patient still had an extruding but patent tympanostomy tube in place at the time of surgery. A second had a long history of OME but it had converted to atelectasis without effusion just before surgery. The third patient had not yet reached 6-month follow up by the time of this report. Of the remaining 13 patients who met the criteria for inclusion into the study, 12 were male and one was female. Ages ranged from 29 to 64 years with an average of 44 years. Eight of the 13 patients were originally presented in the authors' preliminary LETP study¹³ and their follow-up data are included in this report. Patients were followed for an average of 26 months (range, 14–34 months).

The results are summarized in Tables I through III. In the preoperative assessment, LPR occurred in 9 of 13 (69%) and allergic disease in 10 of 13 (77%). OME with or without atelectasis of the tympanic membrane was identified in all patients preoperatively. LETP eliminated OME in 36% (4 of 11) of patients at 6 months, 40% (4 of 10) at 1 year, and 38% (3 of 8) at 2 years.

Two patients (nos. 1 and 13) did not return for 2-year follow up but reported by phone that they are doing well. Their phone follow up was not included in the 2-year data. Patient no. 6 was counted as a failure at 2 years as a result of the presence of a perforation, but most of the previous interval time, he had had an intact TM without effusion and was asymptomatic. Patient no. 10 was diagnosed with Samter's triad in the postoperative period.

The presence of comorbidities appeared to influence the surgical outcome of LETP at 1 year but not at 2 years. At 1 year, the difference between successful and failed LETP patients showed statistically significant correlation with the presence of LPR (0% vs. 40%, respectively, $P = .01$) or allergic disease (10% vs. 30%, respectively, $P = .05$). At 2 years, there was no significant difference between successful and failed LETP patients with the presence of either LPR (10% vs. 30%, respectively, $P = .10$) or allergic disease (10% vs. 20%, respectively, $P = .20$) by χ^2 analysis.

Successful LETP patients demonstrated a statistically significant difference in their mean pretreatment PTA (35.3 dB) and posttreatment PTA at 1 and 2 years (12.9 dB and 20.8 dB, respectively, $P = .028$). As expected, failed LETP patients did not show a statistically significant change in their PTA. Before treatment, there was also no statistically significant difference between the mean PTA in the failed and successful LETP groups at 1 year (33.4 vs. 37.3 dB, respectively, .xx) and 2 years (37.1 vs. 35.6 dB, respectively, .31). There was no statistically significant worsening of the PTAs.

On histologic examination of one subject, the LETP specimen showed severe inflammation with hemorrhagic

changes (Fig. 3). The pseudostratified columnar mucosa was hypertrophied and no cilia were recognizable. There was a severe infiltration of inflammatory cells into the submucosa and mucosa. The postoperative specimen showed only moderate inflammation and hypertrophy with return of a ciliated epithelial border. The inflammatory infiltrate did not penetrate into the mucosa. There was extensive fibrosis throughout the submucosal layer that was not present preoperatively. Grossly, the healed wounds showed a stellate puckered scar with a scaphoid loss of volume in the posteromedial wall adjacent to the valve (Fig. 4).

There were no significant complications. One patient developed a soft intranasal synechia between the inferior turbinate and septum that was lysed during the 1-month follow-up visit. The cause of this scar band was thought to be related to the laser fiber that was passed through the nasal cavity during the procedure. Another patient developed small synechiae between the posterior cushion and the adjacent nasopharyngeal mucosa noted at the 1-month postoperative visit. These bands thinned out over succeeding months and appeared to be of no clinical significance. Two additional patients developed a small red granuloma in the center of the resected area of mucosa. Both patients were treated with nasal corticosteroid spray for 6 weeks and the granulomas eventually subsided completely. There were no cases of epistaxis, nasal obstruction, or intraluminal adhesions or strictures.

DISCUSSION

Eustachian tube dysfunction remains without a clear definition and is assumed to be the absence of appropriate tubal function. The etiology of ET dysfunction appears to be multifactorial,^{1,5–8,15} but there is a final common pathway leading to middle ear disease once tubal ventilation of the middle ear is sufficiently compromised. The consequences of tubal dysfunction may be OME, atelectasis, tympanic membrane perforation, cholesteatoma, or complications of chronic ear disease.

In the past, the ET has often been regarded as a "black box" in which the organ either functions or not. It has become increasingly clear that there is a spectrum of dysfunction and that identification and treatment of the etiology of this dysfunction may provide clinical improvement. Tubal dysfunction appears to occur most commonly from functionally "obstructive disorders"⁸ in which the tube is not anatomically blocked, but there is sufficient bulky mucosal disease that dilation does not occur adequately to aerate the middle ear. The etiology of the mucosal disease remains uncertain, but there is increasing evidence that allergic disease,^{7,15} LPR,^{5,6} adenoid hypertrophy impinging on the posterior cushion,¹⁶ and anatomic factors,¹⁷ may play important roles. Additionally in children, exposure to tobacco smoke, wood and charcoal smoke, short-term breast feeding, and overcrowded living conditions¹⁸ correlate with a higher incidence of otitis media. Less common are purely muscular or "dynamic disorders"⁸ in which movement disorders have been identified in the tensor veli palatihi (TVP) or levator veli palatihi (LVP) muscles.

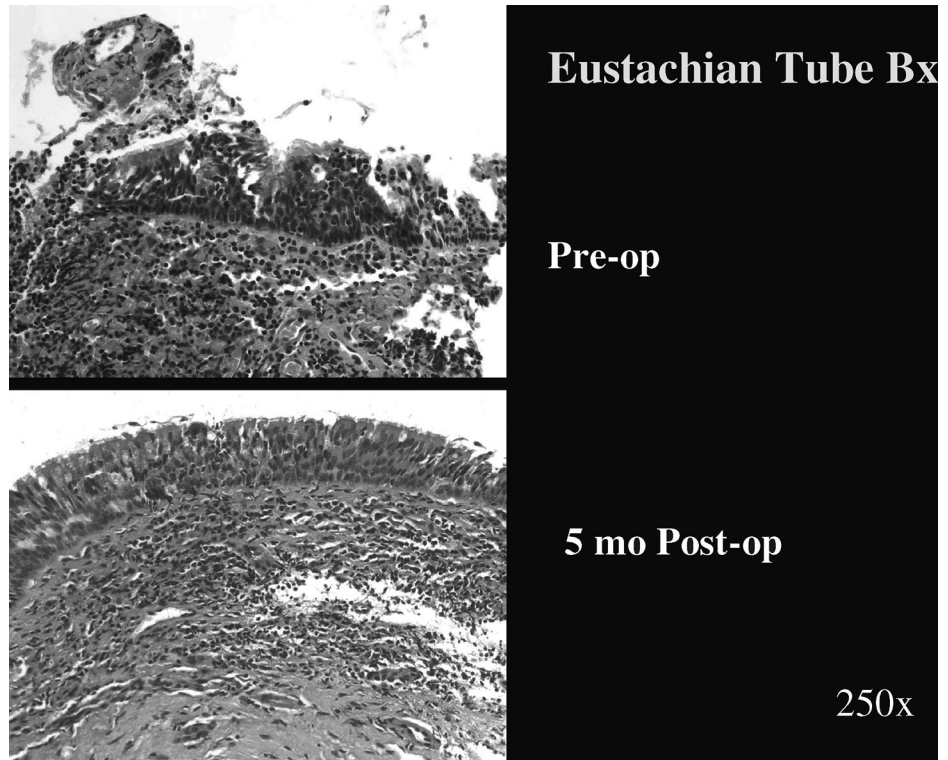


Fig. 3. Mucosal biopsies. (A) The pre-laser eustachian tuboplasty specimen shows severe inflammation with hemorrhagic changes. The mucosa is hyperthrophied and no cilia are recognizable. (B) The 5-month postoperative specimen shows only moderate mucosal inflammation and hypertrophy. The ciliated epithelium has returned.

Tympanostomy tubes have provided a very successful means for ventilating the middle ear in patients with ET dysfunction. The use of such tubes, however, has been associated with infection, crusting, obstruction, extrusion, and the development of perforation or cholesteatoma. For patients with long-term tubal dysfunction, repeated insertions are sometimes required and “permanent” tubes have

been developed, but they can have problems with crusting and extrusion as well.

This study has shown a possible correlation between failure of LETP with the presence of LPR or allergic disease. Patients with persistent ET dysfunction may benefit from a diligent evaluation to identify the underlying etiology of their problem and provide some options for effective

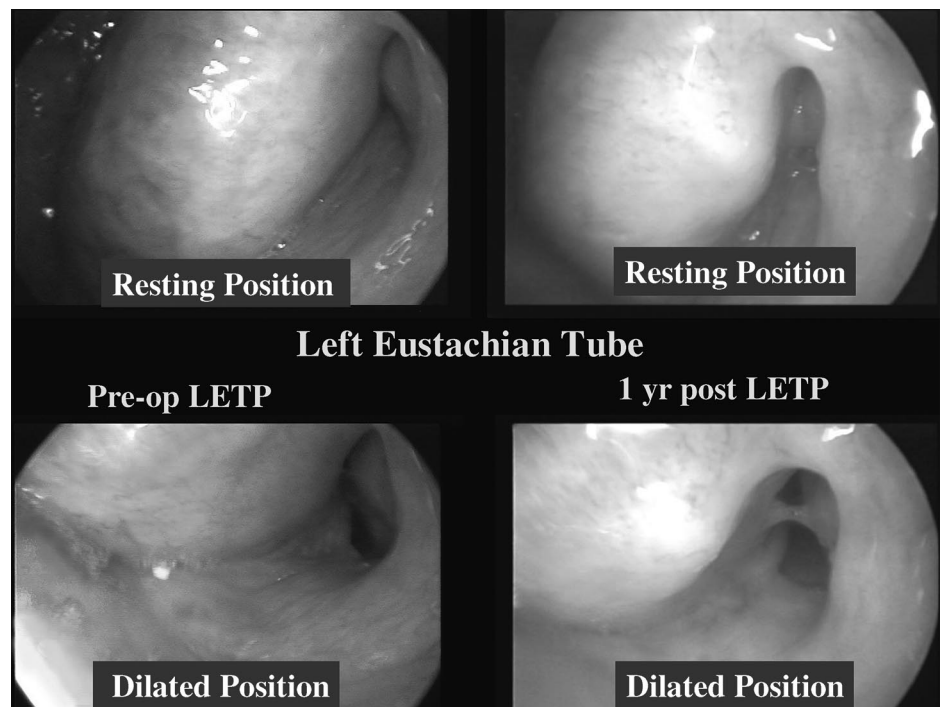


Fig. 4. Resting and dilated position of the eustachian orifice at (A) pre-laser eustachian tuboplasty (pre-LETP) and (B) 1 year post-LETP. After LETP, the eustachian tube demonstrates a persistent loss of volume in the posteromedial wall. The post-LETP dilated figure shows a strand of mucus bridging the otherwise open lumen. There are no adhesions.

tive medical treatment. A thorough history may disclose the possibility of environmental or food allergies, asthma, LPR, home/daycare/school/occupational exposures, sinus or pulmonary disease, and rheumatoid or autoimmune illnesses. Physical examination, including nasopharyngoscopy, may reveal evidence of inflammatory or anatomic lesions consistent with these disorders. When simple observation of the ET is insufficient to identify a possible cause for dysfunction, slow-motion video endoscopy may be performed for a detailed assessment of tubal dynamics.¹⁰ Tubal dysfunction may be identified as an obstructive or dynamic disorder.⁹

The possibility of primary mucosal disorders of the middle ear must also be considered. Wegener disease may cause a chronic draining ear with pale boggy mucosa that fails to respond to ordinary topical or oral antibiotic therapy. It may also be associated with pain and a sensorineural hearing loss component. Samter's triad may manifest in the ear as a chronic thick mucoid effusion that often occludes tympanostomy tubes and is oral or topical steroid-sensitive. There are a number of patients without Samter's who also present with thick mucoid effusions that frequently occlude tympanostomy tubes. It is possible that they may have an allergic or immune-mediated basis for the effusion and many do seem to respond to oral or topical steroids.

The purpose of the present study was to determine the safety and efficacy of combining LETP with ongoing medical management for OME. All enrolled patients represent failures of medical therapy alone to resolve OME. Candidates had demonstrated obstructive disorders of their ET on slow-motion video endoscopy. This pilot study used patients with long-term refractory OME as their own historical controls.

The results of this study appear to support the hypothesis that debulking of diseased mucosa within the tubal lumen's posteromedial wall in conjunction with appropriate medical management is effective in eliminating medically refractory OME in some patients. The results were not static and there was variation in tubal function that appeared to correlate with exacerbations or remissions of associated medical conditions, most notably LPR or allergic disease. When patients stopped following their dietary or medication recommendations, they often had deterioration of tubal function. Resumption of treatment was sometimes successful in relieving the effusion, whereas preoperatively, medical treatment alone had not been successful. Like in surgery for chronic sinusitis, relief may only be temporary if underlying etiologies are not adequately controlled. Formal testing and documentation of allergic disease and LPR was not performed in this study and is recommended for future study.

The histologic studies in this and other studies¹⁹ along with postoperative endoscopic examinations suggest that LETP results in a reduction of mucosal volume and creates submucosal scarring. It may be that the reduction of soft tissue volume along the posterior ET cushion facilitates the dilatory action of the TVP muscle. In some patients, however, the tissue vaporization stopped short of the valve itself raising the question of other possible beneficial effects from this procedure such as a reduction in

tissue inflammation or edema, replacement of irreversibly diseased mucosa with functional epithelium, or perhaps eradication of adherent bacterial biofilm.

Although there were no significant surgical complications in this study, it is of utmost importance to recognize that the authors had undertaken a thorough study of the surgical anatomy in the laboratory before performing LETP. In addition, great caution was exercised by excising only limited amounts of excision of mucosa and submucosa as much as deemed necessary based on the preoperative slow-motion video endoscopy. Furthermore, great care was taken to avoid any thermal or abrasive injury to the mucosa of the anterolateral wall of the ET. Given the small diameter of the ET, it would be relatively easy to injure the opposing wall mucosa and create strictures or adhesions that could exacerbate ET dysfunction.

The proximity of the internal carotid artery must be kept in mind at all times to avoid the catastrophic injuries and deaths that have been anecdotally reported in the past during patulous ET injection procedures.²⁰ An intimate knowledge of the relationship between the intervening cartilaginous skeleton of the ET and the carotid is necessary before embarking on surgery within the tubal lumen.

CONCLUSION

Evidence from the present study suggests that LETP is effective in the treatment of some patients with medically refractory OME who have had multiple tympanostomy tubes. Failure of LETP correlated with the presence of LPR or allergic disease in the 1-year results but not in the 2-year results. Additional studies are necessary to identify those individuals who are most suitable candidates for this procedure.


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Balloon Dilation of the Cartilaginous Eustachian Tube

Dennis S. Poe, MD^{1,2}, Juha Silvola, MD, PhD³, and Ilmari Pyykkö, MD, PhD¹

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Abstract

Objectives. (1) To translate techniques developed in a previous cadaver study of balloon dilation of the cartilaginous eustachian tube (ET) into clinical treatment for refractory dilatory dysfunction and (2) to study the safety/efficacy of the technique in a pilot clinical trial.

Study Design. Prospective with subjects as their own historical controls since June 2009.

Setting. Regional academic center.

Subjects and Methods. Eleven consecutive adult patients with longstanding otitis media with effusion (OME) who were unable to autoinsufflate their ET by Valsalva, swallow, or yawn and who had previous tympanostomies (average, 4.7). At the time of intervention, 5 of 11 had a tube; 2 of 11 had a tympanic membrane (TM) perforation. Four of 11 had intact TMs, 2 with OME and tympanogram type B and 2 with TM retraction and tympanogram types B and C. Balloon dilation of the cartilaginous ET was performed with sinus dilation instruments via transnasal endoscopic approach under general anesthesia in a day surgery setting. Inflation was to a maximum of 12 atm for 1 minute. Outcome measures: ability to Valsalva, rating of ET mucosal inflammation, tympanogram, and otomicroscopy findings.

Results. All cases successfully dilated. Eleven of 11 could self-insufflate by Valsalva ($P < .001$); tympanograms were A (4/11), C (1/11), or open (6/11). All atelectases resolved. Procedures were well tolerated, without pain or complications related to dilation.

Conclusion. Dilation of the cartilaginous ET appeared to be beneficial and without significant adverse effects in the treatment of ET dilatory dysfunction. Larger controlled trials with long-term results are now justified and needed.

Keywords

otitis media, OME, eustachian tube dysfunction, balloon dilation

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The cartilaginous portion of the eustachian tube (ET) is the most likely site of pathology that leads to tubal dilatory dysfunction.^{1–3} Normally, the middle 8- to 12-mm-long segment within the cartilaginous ET contains mucosal surfaces in apposition at rest that function as a valve. Dilatory dysfunction of the ET is most commonly due to mucosal inflammation that limits dilation of the valve, causing insufficient ventilation of the middle ear.⁴ Eustachian tuboplasty consisting of a partial resection of inflamed mucosa, submucosa, and cartilage, from the intraluminal posteromedial wall, where the soft tissue is thickest, has been beneficial in approximately 50% of cases with severely persistent otitis media with effusion (OME) with 2-year follow-up.⁵ In patients with OME and sinus disease, tuboplasty combined with endoscopic sinus surgery was effective in relieving tubal dysfunction symptoms in 70%.⁶ These early results support the concept that enlargement of the valve of the ET could facilitate the dilatory efforts of the tensor veli palatini (TVP) muscle and provide effective benefit for chronic OME.

Widening of the tubal valve by balloon dilation has been demonstrated in cadaver studies to have potential for clinical benefit and without any evidence of significant adverse effects.^{7,8} In 1 study, dilation was effective in significantly enlarging the cross-sectional area of the functional valve with an average increase volume of 357%.

This pilot study was done to test the effectiveness and safety of employing balloons for dilation of the cartilaginous ET in patients with chronic OME. It was considered an important first step toward developing a future clinical trial to test the hypothesis that balloon dilation could have a beneficial effect on chronic OME.

¹Department of Otolaryngology, University of Tampere Medical School, Tampere, Finland

²Department of Otolaryngology, Children's Hospital and Department of Otology and Laryngology, Harvard Medical School, Boston, Massachusetts, USA

³Department of Otolaryngology, Päijät-Häme Central Hospital, Lahti, Finland

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Corresponding Author:

Dennis Poe, MD, Department of Otolaryngology, Children's Hospital, LO 367, 333 Longwood Ave, Boston, MA 02115, USA
 Email: dennis.poe@childrens.harvard.edu

Methods

Hypothesis

Sinus balloon dilation catheters could be adapted to safely and effectively dilate the cartilaginous portion of the ET in patients with chronic OME.

Aims/End Points

1. To evaluate the effectiveness of using a balloon for dilation of the cartilaginous portion of the ET in patients with chronic OME
2. To evaluate the safety of the dilation procedure with an analysis of any potential adverse effects

Outcomes included the ability to self-insufflate air through the ET with a Valsalva maneuver, rating of mucosal inflammation at the tubal orifice as seen by endoscopy, otomicroscopic findings of OME/TM retraction/normal, and tympanogram curve types A/B/C.

Patient Selection

Patients with unilateral or bilateral persistent OME for ≥ 5 consecutive years, broken only by tympanostomy tubes or tympanic membrane (TM) perforation, were evaluated as candidates for ET surgery. None of the subjects could insufflate their ears with a Valsalva maneuver. Otomicroscopy and tympanometry were done bilaterally. Video rigid or fiberoptic endoscopy of the eustachian tube with slow-motion review demonstrated mucosal inflammation as the predominant finding, indicating dilatory dysfunction of the ET as opposed to dynamic (muscular) dysfunction. The techniques for endoscopic examination and a scoring system for rating mucosal inflammation have been previously reported.⁹ The mucosal inflammation score was modified to separate mild and moderate disease. The score consisted of 1 = normal mucosa; 2 = mild edema and/or erythema, with or without increased mucus; 3 = moderate edema and erythema with significant compromise of dilation of the lumen during swallows and yawns; and 4 = severe edema and erythema with inability to dilate the lumen open. Preoperative high-resolution computed tomography (CT) scans were obtained to rule out anatomical anomalies of the ET or cranial base and dehiscence of the internal carotid artery into the tubal lumen.

Candidates for surgery were offered the option of continuing their current management or undergoing a procedure consisting of unilateral balloon dilation of the cartilaginous ET. In the case of bilateral disease, the side with the worst ear pathology was selected.

Informed consent was obtained, and the protocol was approved by the Ethical Committee (equivalent to a US institutional review board) for the Päijät-Häme Central Hospital, Lahti, Finland (Balloon Dilation of the ET R09054). All cases were performed by the second author at that teaching hospital.

Surgical Technique

Patients were induced and maintained under general anesthesia with endotracheal intubation in the supine position.

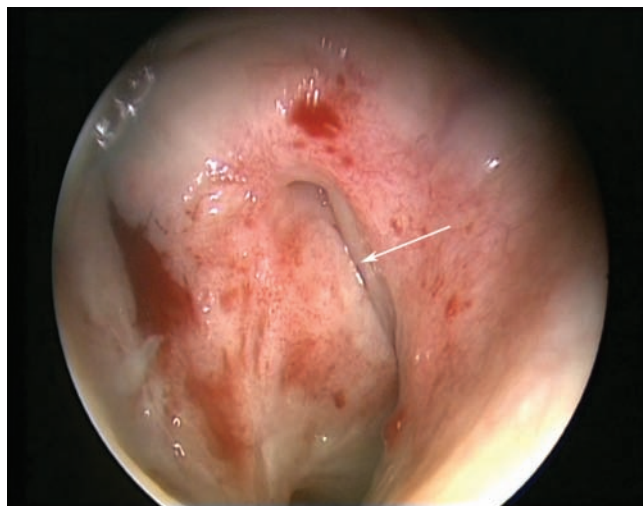


Figure 1. Intraoperative photo of left eustachian tube (ET) nasopharyngeal orifice in a patient with otitis media with effusion prior to balloon dilation. The lumen (arrow) is closed in the resting position, and the posterior cushion is edematous. Images were taken through a 30-degree 4-mm-diameter Hopkins rod endoscope.

Topical oxymetazoline hydrochloride decongestant was applied to the nasal cavities. A 30-degree Hopkins rod endoscope (Karl Storz, Culver City, California) was introduced through the ipsilateral or contralateral nasal cavity (**Figure 1**). Video images were displayed on a monitor (Karl Storz, Tuttlingen, Germany).

The sinus balloon dilation system (Acclarent, Inc, Menlo Park, California) was employed to dilate the cartilaginous portion of the ET. A curved guiding catheter with a tip angle of 70 degrees was passed through the nasal cavity with the tip placed just into the ET nasopharyngeal orifice (**Figure 2**). A 7 mm (diameter) \times 16 mm (length) Relieva Solo (Acclarent) sinus balloon catheter was passed through the guiding catheter and atraumatically into the ET orifice until reaching the first mild resistance as it approached the narrowest diameter at the bony-cartilaginous isthmus (**Figure 3**). The balloon typically protruded from the tubal orifice about 2 to 3 mm.

The balloon catheter lumen was left open to allow for air escape from the proximal (toward the middle ear) ET during inflation. The balloon was inflated with sterile water according to the manufacturer's recommendations to a target pressure of up to 12 atm for 1 minute (**Figure 4**), after which it was deflated and removed (**Figure 5**). In the event that a balloon began to slip out of the ET orifice into the nasopharynx during inflation, it was either maintained at the maximum pressure attained before beginning to slip or reinserted and the inflation repeated. Careful endoscopic inspection was made of the postdilation tubal lumen to assess the effects and to note whether there was any evidence of an adverse effect (**Figure 6**). The posterior cushion was manipulated and rotated medially, before the dilation and afterward, looking for any change in the flexibility or increase in angle of rotation.

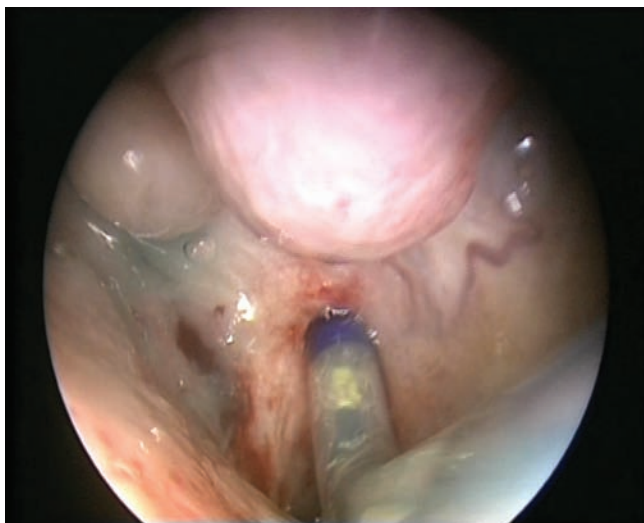


Figure 2. Guide catheter has been placed into the eustachian tube orifice.

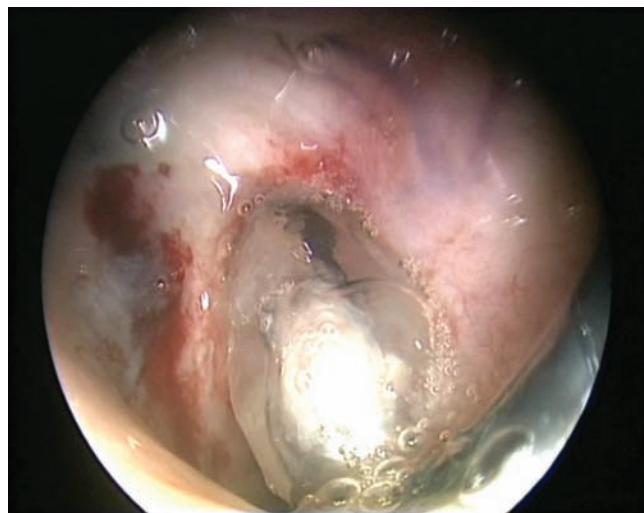


Figure 4. The balloon has been fully inflated to 12 atm for 1 minute. Approximately one-third of the balloon protrudes from the eustachian tube orifice.

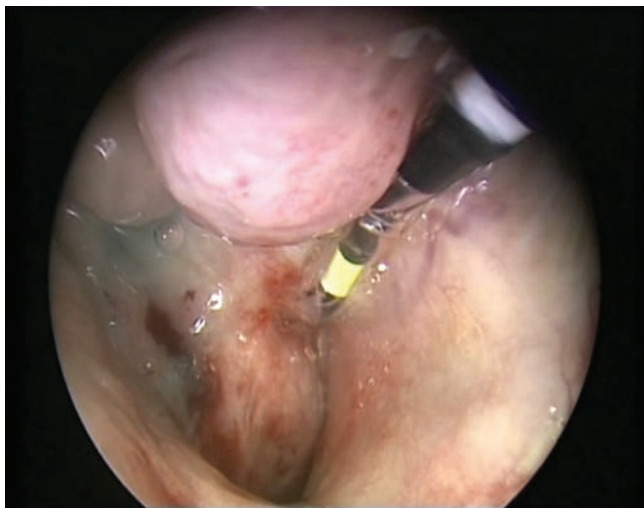


Figure 3. The balloon catheter has been inserted through the guide catheter and into position within the lumen of the eustachian tube until meeting slight resistance from the isthmus (bony-cartilaginous junction). The band on the catheter indicates the proximal end of the balloon.

The immediate effect on widening of the lumen of the ET was judged qualitatively from intraoperative videos reviewed following the surgery. The degree to which the functional valve was opened by the dilation and remained open was estimated by the increase in apparent depth of view into the lumen of the ET. As the mucosal surfaces are normally in apposition in the valve, the length of persistent opening of the valve could reflect the immediate result of the dilation. The effectiveness of the dilation was rated as none if there was no visible change, small if the apparent increase in distance seen was estimated at <4 mm, medium for ≥ 4 mm without seeing the isthmus, and patent if the valve was dilated open and the isthmus was visible.



Figure 5. The balloon remains in position but has been fully deflated.

All patients were treated on an outpatient basis. Follow-up exams were scheduled for 1 and 6 months postoperatively and were planned to include otomicroscopy, tympanogram, endoscopy of the ET, demonstration of an attempt to do a Valsalva maneuver, and a repeat rating of the mucosa of the ET lumen.

Statistical analysis was done using SPSS 17.0 statistical software package (SPSS, Inc, an IBM Company, Chicago, Illinois) with 2-tailed paired samples *t* tests performed using $P < .05$ for significance. The patients were used as their own historical controls, given their longstanding disease.

Results

Eleven patients (5 men, 6 women) aged 33 to 76 years (average, 51.8) having had previous tympanostomy tubes

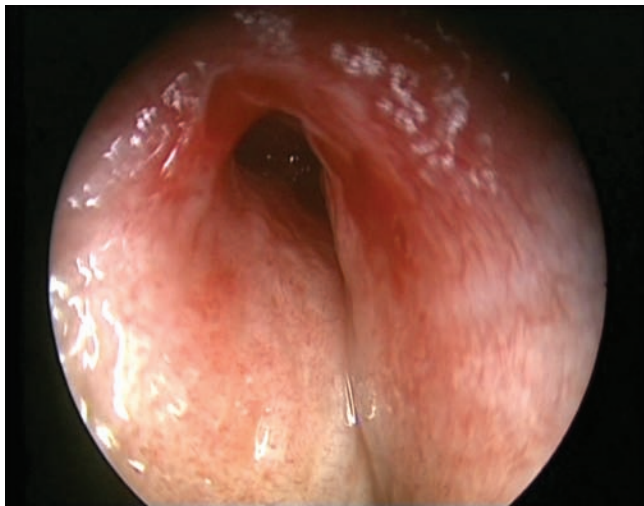


Figure 6. Postdilation, the entire length of the cartilaginous eustachian tube has been dilated by the balloon. The isthmus is not directly seen because of blood from a small mucosal laceration.

(average, 4.7) underwent unilateral balloon dilation of the cartilaginous portion of their ET since June 2009. Preoperative findings are summarized in **Table 1**.

Two patients had OME with type B tympanograms, 2 had generally retracted TMs with type B or C tympanograms, 5 had tympanostomy tubes in place, and 2 had TM perforations. ET mucosal inflammation scores were 2 in 4 of 11 (36.4%), 3 in 4 of 11 (36.4%), and 4 in 3 of 11 (27.2%), with a mean (SD) of 2.91 (0.83). None of the patients could insufflate air into their ears with a Valsalva maneuver. Middle ear mucosa seen through tympanostomy tubes was mildly inflamed with some mucus in 1 case, moderately inflamed (significant hypertrophy reducing the middle ear space) in 2, and severely inflamed (hypertrophy nearly filling the middle ear space) in 2 cases, including a small polyp in one of those. In the 2 cases with perforations, mucosal inflammation was mild in one and moderate in the other.

Adjunctive Procedures

At the time of surgery, tympanostomy tubes were placed in the 2 patients with OME, and tubes were removed from 3 patients with moderate to severe middle ear mucosal inflammation. Balloon dilation results are summarized in **Table 2**.

Dilation was done at 12 atm in 7 cases and 8 to 10 atm in the remainder. Reinsertion and repeat dilation due to slippage were done in 1 case. The balloon typically protruded out of the orifice by 25% to 30%. It was monitored during inflation and the guide catheter adjusted to hold it in position if it began to slip out more than 30%. The balloon began protruding in 1 case as the pressure reached 8 atm, and this pressure was maintained for the 1-minute duration, but the catheter slipped out at the end of the minute. Repeat dilation was not deemed to be necessary in this case.

Dilation of the ET occurred successfully in all cases. The dilation effectiveness was small in the 2 cases inflated to 8 atm, medium in the 2 cases dilated to 10 atm, and dilated to fully open in 5 of 6 (83.33%) cases inflated to 12 atm. The full dilation associated with 12 atm was significant ($P = .004$). The position of the posterior cushion was not altered, and there was no increase in flexibility to suggest cartilaginous fractures. There was no persistent bleeding.

Adverse Effects

A mucosal laceration within the lumen of the ET occurred in 5 of 11 (45.5%), and 4 of the 5 had been inflated to 12 atm. The lacerations were limited to the mucosa, were under 5 mm in length, and were considered clinically acceptable (minor adverse effect). Bleeding from the lacerations was very limited and of brief duration. All of the patients had a mild sore throat after surgery that resolved within 2 days. There were no major adverse effects.

Postoperative results are summarized in **Table 3**.

Follow-up duration ranged from 6 to 14 months (median 7.0). All patients could perform a Valsalva maneuver postoperatively ($P < .001$). At the time of the last follow-up visit, 7 of 11 (63.6%) could still consistently perform the maneuver, and 4 of 11 (36.4%) could perform it but inconsistently. Otomicroscopy demonstrated that 5 of 11 (45.4%) tympanic membranes now appeared normal, although 1 of these cases had a type C tympanogram but normal hearing. Mucosal inflammation scores of the ET lumen were 1 in 4 of 11 (36.4%), 2 in 4 of 11 (36.4%), and 3 in 2 of 11 (18.2%) with a mean (SD) of 1.73 (0.79). Improvement in mucosal inflammation scores was statistically significant ($P = .003$). All mucosal lacerations had healed without scarring. There was no evidence of injuries, synechial bands, narrowing of the lumen, or patulous ETs. There was no postoperative epistaxis.

Complications

A C6-7 contralateral radiculopathy occurred in 1 patient thought to be due to the neck extension required for endotracheal intubation. It fully recovered. There were no complications related to the balloon dilation. No patients developed patulous ET symptoms (including autophony), even transiently. There were no cases of reflux otitis.

Discussion

This study demonstrated that balloon dilation of the ET is technically feasible and can be performed without significant adverse effects. The 7-mm sinuplasty balloon fit reasonably well into the tubal lumen and dilated the functional valve effectively, tending to slip out in a minority of cases. In the majority, the balloon actually “locked” into position, fitting to the inside curvature of the medial cartilaginous lamina that is contained within the posterior cushion. Protrusion of the balloon up to 30% was common and of no concern. Slippage of the balloon out of the ET could be

Table 1. Preoperative Findings

Case No.	Age, y	Sex	No. of Tubes ^a	Preoperative Findings					
				Type of Effusion	Associated Diagnosis	Previous Adenoidectomy	TM Status ^b	Tympanogram	Mucosal Inflammation
1	55	M	5	Serous	Chronic rhinitis	No	Tube	Open	3
2	36	F	1	Mucoid	Atelectasis, OME	Yes	Tube	Open	3
3	76	M	3	Mucoid	Chronic rhinitis	No	Perforated	Open	3
4	33	F	4	Mucoid	Chronic rhinitis, polyps	Yes	Retracted	C	3
5	63	F	5	Mucoid	Chronic rhinosinusitis, asthma	No	Tube	Open	4
6	48	F	2	Serous	Isolated OME	Yes	Perforated	Open	2
7	48	M	5	Mucoid	Chronic rhinitis	No	Tube	Open	2
8	49	M	6	Mucoid	Chronic rhinitis, polyps	Yes	OME	B	4
9	49	F	6	Mucoid	Isolated OME	Yes	Tube	Open	4
10	71	M	5	Mucoid	Skull base fracture	No	Atelectasis	B	2
11	35	F	10	Mucoid	Isolated OME	No	OME	B	2

Abbreviations: F, female; M, male; OME, otitis media with effusion; TM, tympanic membrane.

^aNo. of tubes = number of previous tympanostomy tubes.

^bTM status = otomicroscopic exam of the tympanic membrane.

Table 2. Balloon Dilation Results

Case No.	Side	atm	Balloon Dilation			Comment
			Dilation Effectiveness	Mucosal Tear	Adjunctive Procedure	
1	R	12	Medium	Yes	Remove tube	
2	L	12	Patent	Yes	Remove tube	
3	L	10	Medium			
4	L	8	Small			Balloon slipped out by end of dilation
5	L	8	Small		Remove tube	Balloon protruded 30%
6	L	12	Patent			
7	L	12	Patent			Balloon protruded 30%
8	L	12	Medium		Insert tube	
9	L	10	Medium	Yes		Dilation repeated 1 ×
10	L	12	Patent	Yes		
11	L	12	Patent	Yes	Insert tube	

Abbreviations: atm, atmosphere; L, left; R, right.

Table 3. Postoperative Findings

Case No.	Follow-up, mo	Postoperative Findings			
		Valsalva	TM Status	Tympanogram	ET Mucosal Inflammation
1	14	Yes, inconsistent	Normal	C	3
2	14	Yes	Normal	A	1
3	11	Yes, inconsistent	Perforated	Open	2
4	10	Yes	Normal	A	3
5	11	Yes	Normal	A	1
6	6	Yes, inconsistent	Perforated	Open	1
7	7	Yes	Tube	Open	2
8	7	Yes	Tube	Open	2
9	7	Yes, inconsistent	Tube	Open	2
10	7	Yes	Normal	A	1
11	7	Yes	Tube	Open	1

Abbreviations: ET, eustachian tube; TM, tympanic membrane.

limited by bracing the shaft of the guiding catheter against the floor of the nose for stability.

Balloon dilation in this pilot study demonstrated evidence for effectiveness intraoperatively, with an immediate widening of the functional valve, and postoperatively, with persisting benefits that included improvement in the ability to insufflate the ET and ear with a Valsalva maneuver in 11 of 11 (100%), resolution of OME in all of the 5 of 11 (45.4%) patients with an intact TM, and a reduction in inflammation of the mucosa of the ET from a mean of 2.91 to 1.73. Dilation of the cartilaginous ET could widen the lumen, thereby reducing the work required for the muscles, especially the TVP muscle, to fully open the lumen on demand. It is known that balloon dilation of vascular stenoses creates tearing of the intima and sometimes the media,¹⁰ with healing occurring by scar filling in the gaps, thus maintaining the widened lumen.¹¹ Compression of irreversibly injured hypertrophic mucosa and submucosa may permit healing with thinner and healthier layers. Histology following laser eustachian tuboplasty showed return of normal ciliated epithelium and thinner submucosa.⁵

Balloon dilation appeared to most effectively dilate the mid-portion of the cartilaginous ET, which corresponds to the functional valve, and this is likely because of the combination of the tapered shape of the balloon at each end, the flexibility of the loose cartilage at the orifice, and the rigid circumferential cartilage at the isthmus. These results correlated well with a cadaver study.⁷

The targets of 12 atm inflation pressure for 1 minute duration were taken from previous sinus experience and from the preclinical cadaver trial because, to our knowledge, this was the first clinical trial of balloon dilation of the ET. There was a greater tendency for mucosal laceration with the 12 atm pressure, and this may actually be a desirable goal, given the experience with endovascular dilation.

There were no major adverse events or complications related to the balloon dilation. Pain was predominantly related to the endotracheal intubation, and there were only minimal complaints of pain localized to the nasopharynx or radiating to the ear.

The potential for complications is considerable, including fatal injuries to the internal carotid artery that were experienced with ET surgery in the past.¹² To perform the procedure safely, surgeons must become familiar with the surgical anatomy. *No attempt should be made to dilate the bony ET, as it is not usually the site of pathophysiology, and the carotid artery courses to share the inferomedial wall of the ET within the temporal bone.* From the nasopharyngeal orifice, the ET lumen takes a slight medial curve initially, then courses toward the temporal bone and becomes progressively narrow. Care should be taken to slowly advance the balloon catheter atraumatically to follow the lumen without laceration of the mucosa, which could cause bleeding or create a false passage toward the carotid injury. The balloon dilation procedure would not be recommended for a patient with carotid dehiscence, and a CT scan is currently recommended.

Additional risks of balloon dilation could be circumferential stricture, fracture of the medial cartilaginous lamina, injury to the TVP or levator veli palatini muscles, hemorrhage into the pterygoid space, instrumentation of the middle ear, and excessive widening to cause a patulous ET. Techniques to repair a persistently patulous ET are now available.¹³ Guidewires can pass into the middle ear and should be avoided.⁷ The isthmus should be about 20 mm from the ET nasopharyngeal orifice, and the middle ear orifice occurs at about 36 to 38 mm.^{7,14} The isthmus should be sufficiently narrow that the balloon catheter would not normally pass through, and advancement should cease when meeting gentle resistance. Entry into the middle ear could occur with a widely patent anomalous isthmus or by excessive force of introduction.

There were several weaknesses of this study. It used the patients as historical controls and suffers from that bias. Insufflation of the ET by the Valsalva maneuver is an imprecise measure of tubal function that does not necessarily predict sufficiency of middle ear aeration. However, it did reflect a significant change in this study. There was a lack of objective tests for ET function. Although such tests have not been shown to have clear clinical correlation,¹⁵ they would have provided additional basis for comparison of pre- and postoperative results. An ET mucosal rating scale was employed but is only now undergoing validation testing. Some of the patients still had tympanostomy tubes in place at the termination of this study, and it remains to be seen if they recur with OME in the future. A tube could have an influence on the outcomes, relieving negative pressure, draining effusion, and facilitating a Valsalva maneuver. As none of the patients could perform a Valsalva maneuver previously while they had tubes, the outcome of being able to perform a Valsalva maneuver represented a real change.

All of the patients expressed an initial improvement in their symptoms, either by relief of effusion or by ability to be able to perform a Valsalva maneuver, which they perceived as a significant benefit. A disease-specific instrument for quantifying quality of life for ET disorders is being developed but is not yet available.

The pathogenesis of OME in children is different from adults and is being investigated. At present, we have not considered performing this procedure in pediatric patients.

If balloon dilation of the ET were ultimately demonstrated to be effective with sustained benefits, it would be a useful and minimally invasive alternative to tympanostomy tubes in patients with chronic OME. Careful selection of patients with medically refractory dilatory dysfunction of the ET should be done. The procedure may also prove to be beneficial to patients with atelectasis or scuba or flight barotrauma. It remains to be determined whether the procedure should be performed in children.

Conclusion

This study demonstrated that balloon dilation of the cartilaginous portion of the ET was feasible and without significant adverse effects in a pilot clinical trial. There was a reduction

in the rate of OME and improvement in the ability to consistently perform a Valsalva maneuver (100% postoperatively, 63.6% at 6 months). Intraluminal mucosal inflammation was reduced. A controlled clinical trial study to determine the efficacy of balloon dilation of the ET in patients with medically refractory dilatory dysfunction of the ET is now indicated.

Author Contributions

Dennis S. Poe, principal author, study design, assisted in surgical cases and data review; **Juha Silvola**, study design, primary surgeon for all cases, assisted in data review; **Ilmari Pyykkö**, study design, review of manuscript.

Disclosures

Competing interests: Dennis Poe received a speaker honorarium from Acclarent Corp, July 2010, for Sinus Forum, Waldorf Astoria, New York.

Sponsorships: None.

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Disclaimer

Sinuplasty balloons are not approved by the Food and Drug Administration for off-label use in the eustachian tube.

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Diagnosis and Management of the Patulous Eustachian Tube

Dennis S. Poe

Department of Otolaryngology, Children's Hospital Boston; and Department of Otolaryngology and Laryngology, Harvard Medical School, Boston, Massachusetts, U.S.A.

Objective: The patulous eustachian tube (ET) seems to be caused by a longitudinal concave defect in the mucosal valve at the superior aspect of its anterolateral wall and causes troublesome autophony of one's own voice and breathing sounds. Patulous ET reconstruction was evaluated to analyze whether submucosal graft implantation to fill in the concavity within the patulous tubal valve may produce lasting relief of symptoms.

Study Design: Prospective trial.

Setting: Tertiary referral center, ambulatory surgery.

Patients: Fourteen ETs in 11 adults with 1 or more years of confirmed continuous patulous ET symptoms refractory to medical care.

Intervention: Endoluminal patulous ET reconstruction was performed in 14 separate cases using a combined endoscopic transnasal and transoral approach under general anesthesia. A submucosal flap was raised along the anterolateral wall of the tubal lumen up to the valve and mobilized superiorly off of the basisphenoid. The pocket was filled with autologous cartilage graft or Alloderm implant, restoring the normal convexity and competence to the mucosal lumen valve.

Main Outcome Measure: Autophony symptoms were scored as 1) complete relief; 2) significant improvement, satisfied;

3) significant improvement, dissatisfied; 4) unchanged; or 5) worse.

Results: All 14 cases reported immediate complete relief of autophony. Results with an average follow-up of 15.8 months are as follows: 1 (7%) case had complete relief; 5 (36%) had significant improvement, satisfied; 7 (50%) had significant improvement, dissatisfied; and 1 (7%) was unchanged. There were no complications. Correlation between patulous ET and other conditions was strongest with previous tubal dysfunction. Autophony of voice, but not breathing sounds, was also found to be experienced by 17 (94%) of 18 patients with superior semicircular canal dehiscence syndrome and could be easily mistaken for patulous ET autophony.

Conclusion: Patulous ET seems to be caused by a concave defect in the tubal valve's anterolateral wall. Submucosal graft implantation to restore the normal convexity to the valve wall seems to provide lasting relief of symptoms. Long-term study is needed. It is important to differentiate between the autophony of semicircular canal dehiscence syndrome and patulous ET. **Key Words:** Patulous—Eustachian tube—PETR—Superior semicircular canal dehiscence—SSCD. *Otol Neurotol* 28:668–677, 2007.

The eustachian tube (ET) has the function of aiding in the maintenance of middle ear gas exchange, clearing of middle ear secretions, and protection of the ear from reflux of material and sounds from the nasopharynx (1). The tube is ordinarily closed in the resting position and dilates to the open position typically with swallows, yawns, and with other voluntary or involuntary efforts (Figs. 1 and 2). Tubal opening typically lasts less than one-half second (2). Closure of the tube is maintained by a valve-like function of the opposing mucosal surfaces, submucosal tissue, fat, muscle, and cartilage. The valve measures approximately 5 mm in length and lies within

the cartilaginous portion of the ET located about 10 mm distal into the tube from the nasopharyngeal orifice's posterior cushion or torus tubarius (3). The patulous ET has been defined as an abnormal patency that results in autophony (4).

The symptoms of the patulous ET were first described by Jago in 1858 (5), and recognition of this clinical entity was reported by Schwartze in 1864 (6). Jago later described that he personally experienced autophony and patulous ET symptoms (7). Patients typically report a feeling that their affected ear is blocked, leading to confusion between the patulous ET and tubal obstruction or dysfunction. On further questioning, they often describe the sensation of talking into a wind tunnel or barrel and experience an echo or abnormally loud perception of their voice and nasal breathing. It can occur spontaneously or can be activated by exercise, prolonged talking, and using nasal or

Address correspondence and reprint requests to Dennis S. Poe, M.D., Department of Otolaryngology, Children's Hospital Boston, 300 Longwood Avenue, Boston, MA 02115; E-mail: dennis.poe@childrens.harvard.edu

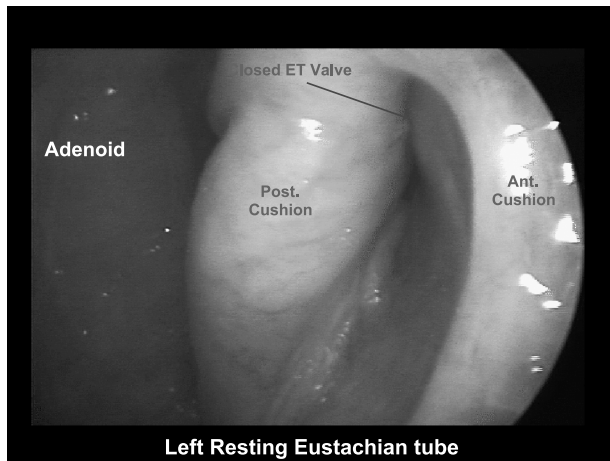


FIG. 1. Image showing normal ET in resting closed position.

oral decongestants. This autophony can be very disturbing to patients and even lead to major depression and suicide.

Most patients report that their autophony is intermittent, although in severe cases, the symptoms may persist for hours at a time. The autophony can generally be relieved, at least temporarily, by placing the head down into a dependent position or lying supine for some time. Sniffing inward against a closed nostril to generate negative middle ear pressure, ipsilateral internal jugular vein compression, and the presence of an upper respiratory tract infection or allergies are also known to provide some temporary relief from the condition.

Confirmation of a patulous ET on physical examination can only be done if the patient has active autophony during the examination. If the symptoms are absent, having the patient take a brisk walk or go up and down stairs for several minutes before the examination may activate them. Most commonly, the tympanic membrane and middle ear will seem normal. Evidence of tympanic membrane scarring, atrophy, and retraction are sometimes observed. The diagnosis can be confirmed by visualizing medial and lateral movements of the tympanic membrane coincident with regular or forced nasal breathing. These patulous excursions of the tympanic membrane are best observed with the operating microscope and with the patient in the sitting position. Lying supine may cause venous congestion to close the patulous tube (8), and the excursions may be missed with a handheld otoscope. Excursions may be enhanced with obstruction of the contralateral nostril (9). Nasopharyngeal endoscopy into the ET lumen will reveal a concave longitudinal defect in the superior aspect in the anterolateral wall of the tubal valve (Fig. 3A). This wall of the valve is normally convex and bulges into the posteromedial wall to close the valve in the resting position (10). Although autophony symptoms are active, impedance tympanometry may be successful in documenting fluctuations in the tracings synchronous with breathing and normal tracings with breath-holding (11). Tympanome-

try may also show middle ear negative pressure or hypermobility of the tympanic membrane (9).

The patulous ET is thought to be caused by the loss of tissue within the cartilaginous portion of ET. The condition has been commonly reported with weight loss, especially in chronic wasting illnesses (12,13). It has also been associated with pregnancy (14), use of high-dose oral contraceptives (4), and estrogen therapy for carcinoma of the prostate (15,16). Additional associations are conditions causing atrophy or scarring within the nasopharynx and musculature, including adenoidec-tomy, radiation therapy, poliomyelitis, multiple sclerosis, and other neuromuscular diseases, cerebrovascular accident, temporomandibular joint dysfunction, malocclusion, iatrogenic trauma, and craniofacial abnormalities (4,17,18). Patulous symptoms have been reported after protracted otitis media (19), especially in patients who have developed a habit of excessive nose blowing or Valsalva maneuvers. Up to one third of patulous ET patients have had no identifiable cause (9). Occasional association between patulous ET and palatal myoclonus has been noted (20).

Numerous medical and surgical treatments have been reported for patulous ET. Patients need reassurance that although the condition may be very disturbing, it is in no way dangerous or destructive. Weight gain has been suggested, but it is only recommended when the patient is undernourished and underweight. Discontinuation of decongestants and nasal steroid sprays may be indicated. Mucous-thickening agents (21), topical estrogen drops (11), and topical irritants to induce mucosal edema (22) may be effective, but usually only temporarily. Myringotomy with or without a ventilating tube has been reported to be helpful in 50% of cases (23,24), but it seems to be most effective in relieving the sensation of the tympanic membrane moving during breathing.

Surgical correction of the patulous ET has been attempted by cauterization of the ET orifice or lumen and removal of portions of the tubal cartilage. Peritubal injections of various materials have usually achieved

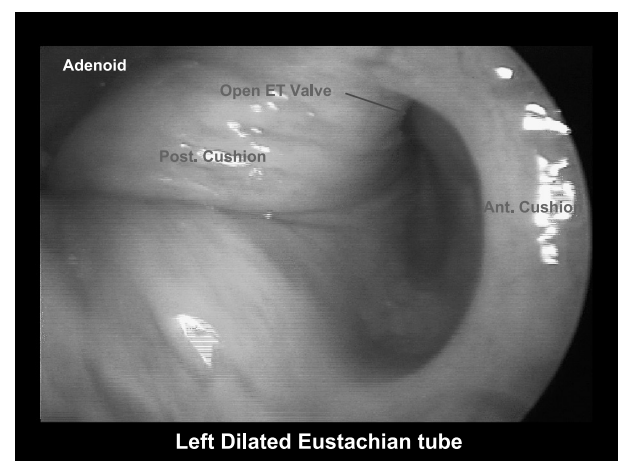


FIG. 2. Image showing normal ET in active open, dilated position.

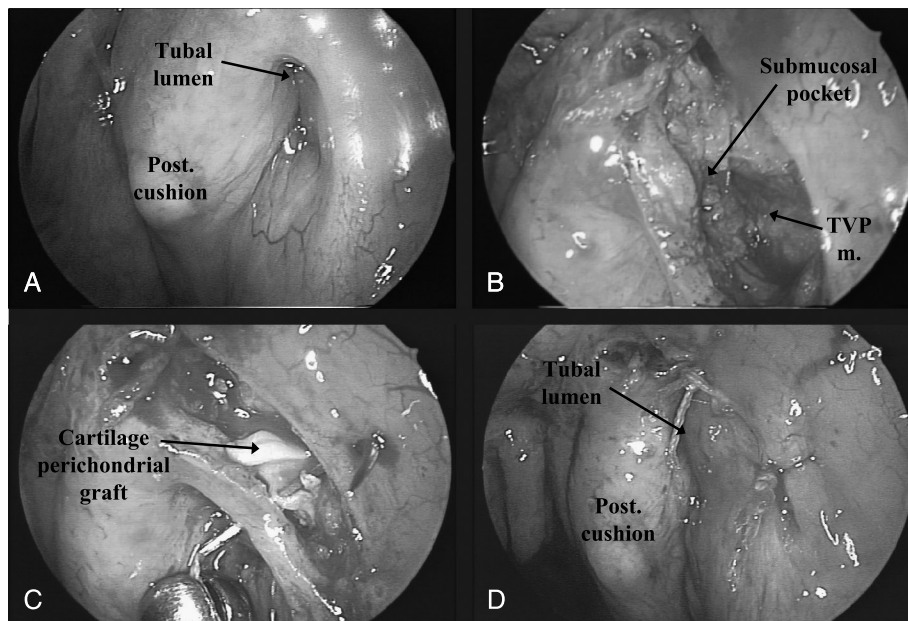


FIG. 3. Image showing PETER. *A*, Left preoperative patulous tube. *B*, Dissection of the submucosal pocket along the TVP muscle. *C*, Cartilage graft is inserted into the pocket. *D*, Completed operation with suture closure of wound.

only temporary success. Lasting relief of autophony has been achieved by complete obstruction of ET using a catheter and bone wax (25) or by cauterization of the lumen with insertion of a fat graft (9), but these procedures generally require long-term middle ear ventilation with a tube. Insertion of a cartilage graft into a submucosal intraluminal pocket to add bulk to the posteromedial wall (distal to the posterior cushion or torus tubarius) has had some early success (26).

This report tested a hypothesis that the endoscopically observed longitudinal defect in the anteromedial wall is responsible for the patulous ET, and that surgical closure of the defect would relieve the patulous symptoms in patients. A patulous ET reconstruction (PETER) technique is presented for augmentation of the specific concave or scaphoid defect within the tubal valve. Grafting material was introduced into a submucosal pocket within the tubal lumen to obliterate the space in the anterolateral wall in an attempt to restore it to the normal convex shape and reestablish the valve's competence without necessitating a ventilating tube or creating tubal dysfunction and otitis media. Autologous cartilage or AlloDerm implant (Life Cell Corp.; the Woodlands, TX, USA) were used for graft materials.

AlloDerm is human acellular dermis stripped of the epidermal layer and processed with salts and detergents to remove all cellular immunogenic components. The remaining graft material is an acellular matrix that retains a basement membrane and vascular channels. When implanted, the matrix serves as a scaffold for ingrowth of the host fibroblasts and vascular endothelial cells (27,28). AlloDerm has been successfully used in plastic and reconstructive surgery and more recently in otologi-

cal surgery for tympanoplasty (29) and neurotological surgery for dural and skull base reconstruction (30).

This report will also present a series of patients diagnosed with the superior semicircular canal dehiscence (SSCD) syndrome. Most of these patients experienced autophony of their voice that they self-described in terms identical to the patulous ET syndrome. Given the apparent similarity in presenting symptoms between these two very different conditions, an analysis of signs and symptoms in this series of SSCD patients was undertaken and compared with those of the patulous ET patients. Recommendations to differentiate between these two syndromes are made.

MATERIALS AND METHODS

A prospective trial of PETER was undertaken in adult patients with medically refractory patulous ET symptoms for 1 or more years. The hypothesis was that surgical obliteration of an endoscopically recognized concave defect in the tubal valve would relieve the patient's autophony. It was hoped that the relief is of lasting benefit. Candidates for the procedure were required to demonstrate persistent patulous ET signs and symptoms, despite appropriate medical therapy. Patulous excursions of the tympanic membrane and a visible characteristic patulous defect in the ET lumen had to be identified.

All candidates had failed medical therapy with mucous thickening agents, topical estrogen drops, or topical irritants. Most had undergone previous myringotomy with or without placement of a ventilating tube and even other ET procedures. An assessment for possible risk factors was done in the history and physical examination, looking for evidence of weight loss, rheumatologic or autoimmune conditions, laryngopharyngeal reflux (LPR), pregnancy, allergic rhinitis, ET dysfunction or

otitis media, habitual sniffing or Valsalva, and other possible factors.

All candidates underwent a thorough head and neck examination, including micro-otoscopy, flexible fiberoptic nasopharyngoscopy, and rigid nasal endoscopy with slow-motion video endoscopy of the ETs, the technique for which has been previously presented (10). All of these patients were examined while they had active autophony. In the event that a patient initially presented with absence of autophony, they were reexamined after taking a brisk walk or going up and down stairs for several minutes until their symptoms were activated. Micro-otoscopy was initially attempted in the supine position, but if the autophony was not present while supine, the patient was raised and examined in the sitting position. All patients exhibited patulous excursions of the tympanic membrane while the patient did quiet and forceful nasal breathing. The larynx was carefully inspected for any evidence of LPR. Slow-motion video endoscopy of the cartilaginous ET demonstrated a concave (scaphoid) defect in the superior aspect of the anterolateral wall in the tubal valve in all patients. Candidates for PETR were offered the options of ongoing conventional treatment, ET obliteration along with a ventilating tube, and the new unproven PETR procedure. Informed consent for PETR was obtained in all patients, including a discussion of neurological complications and deaths that had occurred in the past with ET surgery (4).

During this study, 18 patients with SSCD were identified, and their signs and symptoms were retrospectively analyzed because of the newly recognized similarity of autophony symptoms between patulous ET and SSCD. The diagnosis of SSCD was confirmed by an identifiable dehiscence in the superior or posterior semicircular canal on computed tomographic (CT) scan, and/or identification of abnormally low thresholds on Vestibular-evoked Myogenic Potential (VEMP) testing (31–35). When CT scans were obtained at our institution, a noncontrasted temporal bone protocol was used with 0.5-mm collimation reformatting images in axial, coronal, and modified Poschel's and Stenvers' projections (34).

PETR was performed on 14 ETs of 11 patients. Bilateral cases were done as separate procedures.

The patient's self-reporting of presence or absence of autophony was used as the outcome measure. Patients were interviewed postoperatively to assess their amount of autophony and symptoms were scored as 1) complete relief; 2) significant improvement, satisfied; 3) significant improvement, dissatisfied; 4) unchanged; or 5) worse. "Complete relief" required that the patient no longer experienced any autophony at all. "Significant improvement, satisfied" meant that patients no longer experienced autophony under normal circumstances, but could experience it with prolonged exercise or talking. The symptoms were easy to control by placing the head in a dependent position for a short time or by sniffing inward. The patients no longer felt the desire for further medical or surgical intervention. "Significant improvement, dissatisfied" was reported when the patients felt that they had gained significant benefit from the operation but continued to have sufficient autophony that further medical or surgical intervention was desired. A second procedure was done in one patient, making an injection of hydroxylapatite microspheres into the ET valve.

Surgical Technique

PETR was performed as an outpatient procedure under general anesthesia using a combined endoscopic transnasal and

transoral approach. The patient was placed in the supine position, and adequate general anesthesia was administered. The oral endotracheal tube was taped midline to the lower lip. Patients intending to fly home postoperatively initially had placement of a soft silicone mini-Baxter button, a 0.91-mm-diameter ventilating tube in the ipsilateral tympanic membrane (Gyrus Co.; Memphis, TN, USA). A nasal septal cartilage graft was harvested in the first patient. Alloderm implant was used as the graft material in the subsequent 12 patients. A tragal cartilage graft was used in the last patient. If cartilage grafts were to be used, these were harvested first through standard techniques. The nasal cartilage graft did not contain any perichondrium. The tragal composite graft was harvested including the posterior surface perichondrium. Topical nasal decongestant spray was applied to both nostrils. A 4-mm-diameter, 45-degree, rigid Hopkins rod nasal endoscope with video monitoring (Karl Storz, Inc.; Culver City, CA, USA) was used to visualize the ET from the nasopharynx. A tonsil mouth gag was placed, and the mouth was partially opened sufficiently to view the oropharynx. Using a 45-degree angled nasal sinus needle, lidocaine 1% with epinephrine 1:100,000 was infiltrated into the anterior and superior aspects of the anterolateral wall (anterior cushion), and topical cocaine 4% solution was placed in the ipsilateral nasal cavity for hemostasis. A red rubber catheter was placed in the contralateral nasal cavity to retract the soft palate, and a nasopharyngeal suction catheter was placed alongside it into the nasopharynx for smoke evacuation of laser plume. The cocaine pledget was subsequently removed, and the endoscope was reintroduced into the nasopharynx and held in position with a mouth gag-mounted endoscope holder (Karl Storz, Inc.; Culver City, CA, USA) assisted by manual support. An argon ion laser (HGM Medical Lasers; Salt Lake City, UT, USA) with settings of 3.5 W and 500 ms or a diode pumped KTP laser (Iridex Corporation; Mountain View, CA, USA) with settings of 1,500 mW and 500 ms were used to make the laser incision and dissection. The endoscope was left in place throughout the procedure to minimize the possibility for nasal trauma and resultant bleeding that would obscure the ET orifice. The endoscope lens was periodically defogged by irrigation with saline introduced through the ipsilateral naris and cleaned with a curved olive-tip maxillary antral suction from within the nasopharynx. All instruments were passed through the oropharynx to reach the ET. Standard otologic fiberoptic 200- μ m-diameter laser probes were used, and the probes were fashioned into a curved shape to reach the tubal orifice. While visualizing the tubal orifice, a laser incision was made from the 11-o'clock to the 5-o'clock position on the anterior cushion. The incision was carried down until the tensor veli palatini (TVP) muscle was visualized, and this plane was followed superiorly and distally into the level of the tubal valve using a combination of sharp and blunt dissection with curved instruments (Fig. 3B). Hemostasis was achieved via watchful waiting, laser cauterization, or monopolar electrocauterization with curved probes (Karl Storz, Inc.; Culver City, CA, USA). This submucosal flap was developed along the anterolateral wall of the tubal lumen into the valve and mobilized superiorly off of the basisphenoid bone. In earlier cases, the flap was separated off of the cartilage superiorly, but in later cases, the cartilage itself, with its attached mucosa, was delivered off of the basisphenoid bone to inferiorly depress the tubal roof and reduce its lumen. In the event that the cartilage was very thick, the inferior cartilage-mucosa flap was mobilized by filleting the cartilage superiorly with sharp or laser dissection. The resultant submucosal-subcartilaginous

pocket was filled with autologous cartilage graft or Alloderm implant measuring between 1 × 1 cm to 1 × 2 cm. Sufficient graft material was placed into the pocket to overcorrect the concave anterolateral wall defect, anticipating a 50 to 60% loss of graft volume postoperatively. The mucosal wound was closed with three interrupted 4-0 Vicryl (Ethicon, Inc.; Somerville, NJ, USA) sutures passed and tied through the oropharynx. At least one of the sutures was passed through the underlying graft (Fig. 3D). Patients were subsequently discharged after satisfactory recovery from general anesthesia. Follow-up examinations were done when possible, and phone follow-up was done when necessary. Of the patients who flew home, the ventilating tube was removed by a local otolaryngologist a few days postoperatively.

The first patient opted to undergo a second procedure 10 months after the cartilage graft PETR. The patient was administered general anesthesia, and an identical operating setup was used. Radiesse (BioForm Medical Co.; Franksville, WI, USA) injectable calcium hydroxyapatite (HA) was used as an implant. It is composed of 25- μ m-diameter microspheres of HA in an aqueous gel carrier and is U.S. Food and Drug Administration–approved for craniofacial and oral-maxillofacial defect reconstruction as well as vocal cord implantation. While visualizing the ET lumen, the Radiesse was injected through a 20-gauge nasal sinus 45-degree angled needle. A series of 3 injections were made longitudinally into the submucosal layer of each side, including the remaining concave defect in the anterolateral wall and also in the opposing posteromedial wall. A total of 0.9 mL was injected.

RESULTS

PETR was performed in 14 ETs of 11 patients. There were 5 males and 6 females. Seven patients had bilateral patulous ETs and 4 were unilateral. Of the 14 patients, 7 were on the left side and 7 were on the right. The duration of preoperative autophony symptoms ranged from 1 to 38 years, with an average of 8.5 years and a median of 6 years. Preoperative risk factors based on history and physical examination are presented in Table 1. All patients had failed medical therapy. Eight (73%) of 11 had a myringotomy or ventilating tube trial. Two patients had undergone previous ET procedures at other centers without success. One patient had botuli-

TABLE 1. Risk factors in patulous eustachian tube reconstruction patients

Risk factor	No.	Percentage
Eustachian tube dysfunction/otitis media	5	45
Rheumatoid/autoimmune	3	27
Laryngopharyngeal reflux	3	27
Allergic rhinitis	3	27
Weight loss	2	18
Sniff/Valsalva habit	2	18
Palatal myoclonus	2	18
Pregnancy	1	9
Cocaine abuse	1	9
Lactose intolerance	1	9

n = 11 patients.

TABLE 2. Outcome scores for patulous eustachian tube reconstruction

Initial outcomes Autophony score	Primary procedure only			Final outcomes after hydroxyapatite injection		
	No.	%	Complications	No.	%	Complications
1	1	7	0	2	14	0
2	5	36	0	5	36	0
3	7	50	0	6	43	0
4	1	7	0	1	7	0
5	0	0	0	0	0	0
No. satisfied (overall)	6	43		7	50	

n = 14 patients.

Autophony scores: 1 = complete relief; 2 = significant improvement, satisfied; 3 = significant improvement, dissatisfied; 4 = unchanged; 5 = worse.

num toxin (Botox) tubal injection and then cartilage implantation into the posterior cushion, and the other received tubal injection of collagen.

The initial procedure took approximately 3½ hours to complete, and the most recent procedures have taken between 1½ and 2 hours. Nasal septal cartilage was used in the first patient, but bleeding from the septum drained over the ET orifice, slowing the procedure, and prompted the subsequent use of Alloderm implant. Over time, a progressively larger submucosal and subcartilaginous pocket was used to accommodate larger and deeper placement of the implant or grafts in an attempt to improve the outcomes. The use of tragal cartilage in the last patient was intended to minimize the loss of graft volume in the healing period.

Outcomes for relief of autophony after PETR are presented in Table 2. There were no complications. No one experienced persistent otitis media with effusion (OME), and only one patient had OME for 2 weeks. Patients experienced 2 to 3 days of oropharyngeal and nasopharyngeal pain that was well controlled by oral analgesics. All patients experienced immediate and complete relief of their autophony postoperatively. They were limited to light activities for 2 weeks postoperatively. Follow-up duration ranged from 3 to 30 months, with an average of 15.8 months. The patient who had a secondary HA injection has had complete relief of autophony for 22 months. In the 2 patients with palatal myoclonus, those symptoms remained unchanged postoperatively.

Results from a retrospective analysis of 18 adult patients diagnosed with dehiscence of the superior or posterior semicircular canal are tabulated in Table 3. The CT scan confirmed the dehiscence of the superior semicircular canal in 15 (83%) of the patients and a dehiscence of the posterior semicircular canal in one (5.6%). The CT scan was equivocal in one patient, and no dehiscence was demonstrated in one patient. The VEMP, however, was strongly abnormal in both of these patients. The VEMP was performed in 12 of

TABLE 3. Signs and symptoms of superior or posterior canal dehiscence syndrome patients

	No.	Percentage
Symptoms		
Autophony of own voice	17	94
Autophony of bone conducted sounds ^a	9	50
Symptom relief with strain/supine	9	50
Tullio symptom	9	50
Vertigo/disequilibrium	7	39
Vertigo with strain/Valsalva	7	39
Hyperacusis	2	11
Auditory distortion	1	6
Autophony of nasal breathing	0	0
Signs		
Conductive hearing loss	13	72
Objective positive fistula test	6	33
Tullio sign (torsional nystagmus)	2	11

n = 18 patients.

^aPatients report hearing amplified perception of sounds presumably transmitted through bone conduction. Examples are unusually loud perception of chewing, pulsatile tinnitus, an elbow hitting a table, and footsteps striking the ground during normal walking.

18 patients, and all 12 were abnormal and consistent with the dehiscence syndrome.

DISCUSSION

Patients with patulous ET may present with a wide spectrum in severity of symptoms ranging from asymptomatic (4) to severe disturbance in quality-of-life and suicidal tendencies. Most patients can be helped simply with reassurance. Symptoms can often be relieved by a swallow or yawn. Placing one's head between their legs or lying supine for a few minutes is very effective for most patients. Good hydration, nasal saline spray, and discontinuation of unnecessary decongestants or nasal steroid sprays may be helpful. When the symptoms recur too frequently or become excessively persistent, patients typically request additional medical intervention. Most of these interventions are only of temporary benefit. Premarin nasal solution, prepared as 25 mg of intravenous Premarin in 30 mL of isotonic sodium chloride solution, is taken as 3 nasal drops 3 times daily (9). It may have side effects of epistaxis or nasal irritation. SSKI, an expectorant, has been used to thicken mucus secretions and is dispensed as 1 g/mL of saturated potassium iodide oral solution in a 30-mL dropper bottle. Seven to 10 drops in 8 ounces of juice or water are taken orally 3 times daily (9,21).

Numerous methods for causing irritation and inflammation of the tubal orifice have been described, but results are generally very temporary, and no long-term successes have been reported (11). Salicylic and boric acid in a 1:4 ratio has been instilled as a solution through an ET catheter (22) or insufflated as a powder into the nasopharynx (9) for temporary relief.

Myringotomy with a ventilating tube has been reported to provide some improvement in approximately 50% of patients (13,21,24). In the author's experience, it is

unusual for patients to experience relief from their autophony with a ventilating tube, but they do find significant relief from the variations in the middle ear pressure and tympanic membrane movements that can be quite distracting while talking and breathing.

Monopolar electrocauterization of the tubal orifice (35) and the tubal lumen (36) has met with some successes, but injuries to the middle cranial fossa dura and the mandibular division of the trigeminal nerve have been reported (4). Application of 20% silver nitrate solution into the tubal lumen has achieved temporary successes, but repeated applications were usually required.

Surgical closure of the tubal orifice was attempted by Simonton (36), making a superior incision to separate the medial and lateral cartilaginous laminae and remove a portion of the medial lamina. Complete occlusion of the ET with middle ear effusion was sometimes achieved, but many patients had no improvement. Doherty and Slattery (9) reported lasting success in three patients using monopolar electrocautery in the proximal tubal lumen and occlusion with an autologous fat graft. These patients required ventilating tubes.

Surgery on the tensor veli palatini muscle has been performed. Stroud et al. (37) transposed the muscle tendon off of the hamulus in 10 patients and reported improvement in 90% after 6 months' follow-up. Virtanen and Palva (38) fractured or removed the hamulus with 70% complete success. When these procedures were performed in monkeys by Cantekin et al. (11), they were initially effective, but the success abated over time.

Various substances have been injected into the ET with mixed results. Zollner (39) was the first to attempt infiltration in 1937 using paraffin around the tubal orifice and achieving temporary improvements. Ogawara et al. (40,41) injected a mixture of absorbable Gelfoam (Upjohn Co.; Kalamazoo, MI, USA) and glycerin in saline with initially good results but a high rate of recurrence after 1 month. O'Connor and Shea (4) injected polytetrafluoroethylene (Teflon paste) into both sides of the tubal orifice with temporary success. Brookler and Pulec (42) injected Teflon into dogs to analyze the optimal location for the paste to maximally increase resistance to applied opening pressures without causing OME. They found that injection in the anterolateral wall, just anterior to the tensor veli palatini muscle gave the optimal results. Injection of 0.5 ml posterior to the torus tubarius (posterior cushion) in the posteromedial wall consistently produced a serous effusion without any measurable increase in opening pressures. Pulec (43) was subsequently successful in 19 of 26 patients injected with Teflon paste into the orifice of the anterolateral wall. He acknowledged that patients often required repeated injections, but most had long-lasting benefit, and there had been no complications in his experience (J. L. Pulec, personal communication, October 2003). Unfortunately, several cases of cerebral thrombosis and death have been reported with Teflon injection in the ET, and the practice was discontinued (4). The material was possibly injected directly into the

internal carotid artery, which runs immediately posterior to the posteromedial wall at the level of Rosenmüller fossa.

The patulous ET seems to be caused by loss of tissue in the superior aspect of the anterolateral wall within the tubal valve. This tissue loss can be cartilage and/or soft tissue, and the exact mechanism for the loss is unclear. Chronic inflammation with tissue atrophy is suspected in many patients. This is supported by the associated potential risk factors presented in Table 1. Chronic tubal dysfunction with a long history of otitis media was the most prevalent possible risk factor and then rheumatoid or autoimmune connective tissue disorders, LPR, and allergic rhinitis. Weight loss and pregnancy were minor risk factors in this series. These results are consistent with the potential risk factors identified in the patulous ET patients who were evaluated and treated without surgery.

Identifying the patulous defect within the tubal valve allows for more precise surgical correction with the goal of restoring the tubal valve's competence and avoidance of overcorrection and OME. The author initially tried submucosal injections of autologous fat, collagen, and injectable HA. Injections of as little as 0.3 mL were immediately effective in all patients, but most experienced the recurrence of symptoms within 1 month. This helped to confirm that the endoscopically observed defect in the anterolateral wall was most likely the cause of the incompetence in the tubal valve. The next challenge was to find a suitable filler material that would provide lasting benefit. The work of Brookler and Pulec (42) seems to

support this hypothesis when they found that even small amounts of injected Teflon into the tubal valve region uniformly caused persistent OME. The goal of trying to place enough material to raise the opening pressure resistance for the whole length of the tube is probably unnecessary and requires an excessive volume of material.

Injectable HA provided a convenient opportunity for subsequent CT scan evaluation. It was found that when the material was injected into the posteromedial wall, it remained in place, but when injected into the patulous defect of the anterolateral wall, it gained access to the tensor veli palatini muscle fascial plane and dissected superiorly to the basisphenoid and inferiorly into the lateral hypopharynx (Fig. 4). This excessively wide distribution of material probably accounted for the short-lived results in most patients and necessitated installation of more volume than desired. It was difficult to obliterate the patulous defect by injecting the posteromedial wall, and there remains the danger that should the needle penetrate the medial cartilaginous lamina, the internal carotid artery lying immediately posterior to the cartilage would be in jeopardy. The author no longer recommends ET injections as a primary method for closure of a patulous defect.

The first patient in this PETR series underwent a small injection of Radiesse HA with long-term complete relief. Injection of material as a secondary procedure once the tensor veli palatini muscle fascial plane has been operated on and scarred may be a useful technique when a small amount of incompetence of the valve persists after PETR.

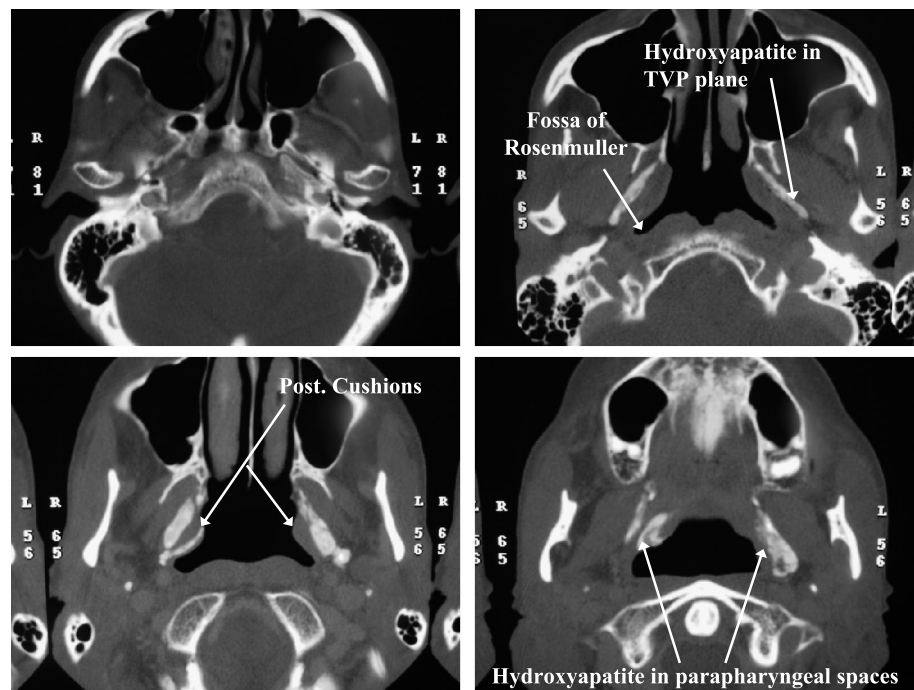


FIG. 4. Axial CT of the temporal bone demonstrating bone density injected with HA in the TVP fascial plane extending from the basisphenoid to the parapharyngeal space in the hypopharynx (arrows).

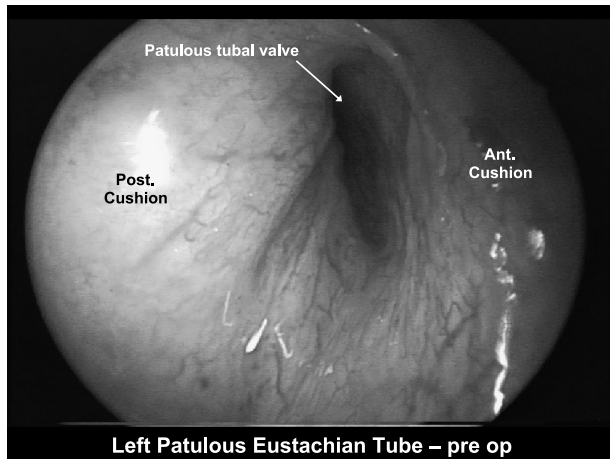


FIG. 5. Image showing preoperative left PETER. Patulous ET with characteristic concave defect in anterolateral wall.

The first patient in this PETER series had a septal cartilage graft for the initial procedure. Oozing from the septal incision drained over the tubal orifice and made the subsequent PETER procedure more difficult. The submucosal pocket was probably too small and made it difficult to secure the cartilage graft into position. It was found that the subsequent Alloderm grafts were easier to handle, but because of the 57% rate of dissatisfied or unchanged results, cartilage grafts from the tragus are now being used. Alloderm proved to be initially effective, but recurrence of symptoms in some patients began as early as 1 month postoperatively, presumably because of resorption of the graft. Postoperative endoscopic examination of the ET in satisfied patients demonstrated an appropriate convex bulge to the wall that nicely contacted the posteromedial wall (Figs. 5 and 6). Even in patients with recurrence of symptoms, the preoperative concave defect in the anterolateral wall remained nicely convex, except for a very small residual defect.

In performing the PETER procedure, it is important to dissect along the TVP muscle plane all the way superiorly to the valve area and dissect a cartilage-mucosal flap off of the basisphenoid to appropriately position the graft and have it remain in place deep to the valve. With a sufficiently broad and deep pocket, it is much easier to wedge the cartilage graft into position and have it stay in place even before it is sutured. It is anticipated that the resorption of cartilage is significantly less than with Alloderm. There were no complications with the PETER procedure. Closure of the patulous defect within the tubal valve does seem to support the original hypothesis. Further experience and long-term follow-up are important to analyze if the results are lasting.

The PETER procedure is currently performed principally with nasal sinus instruments, especially long curved frontal sinus instruments that can readily reach the ET when passed through the oral cavity. There is a need for dedicated instrumentation that will facilitate PETER in the future.

Caution is advised when beginning to attempt the PETER procedure because it is technically challenging to operate in the nasopharynx, and surgeons are generally less familiar with the surgical anatomy of the region. It is extremely important to be thoroughly familiar with the location of the internal carotid artery and its relationship with the ET to avoid the disastrous consequences of tubal surgery in earlier years. The surgeon should keep the dissection along the tensor veli palatini muscle and the basisphenoid bone. The internal carotid artery runs just deep and posterior to the medial cartilaginous lamina in the posteromedial wall. Maintaining awareness of the location of the cartilage and staying anterior to it at all times will help protect the carotid artery.

Making the diagnosis of patulous ET is not always straightforward, especially because the patients uniformly complain of "blockage" in their ears. The condition is often confused with ET dysfunction and negative middle ear pressure. Patulous ET is probably underdiagnosed. In addition, there has been confusion in diagnosis because of a great similarity with the autophony observed in the superior semicircular canal dehiscence (SSCD) syndrome. Amplification of somatosounds that are carried through bone conduction seems to occur nearly uniformly in this syndrome. Ninety-four percent of the patients with the syndrome in the author's series had a significant complaint of autophony of their voices. None of them experienced autophony of their breathing, with the exception of one patient who had both SSCD and a patulous ET. This patient had chronic baseline autophony of his voice but not breathing. During exercise or prolonged talking, he could develop true patulous ET symptoms with a much more dramatic autophony of his voice and breathing sounds that was clearly different from the SSCD autophony. SSCD patients also frequently hear other bone-conducted noises, such as their footsteps hitting the ground (50%), and have measurable conductive hearing loss (72%).

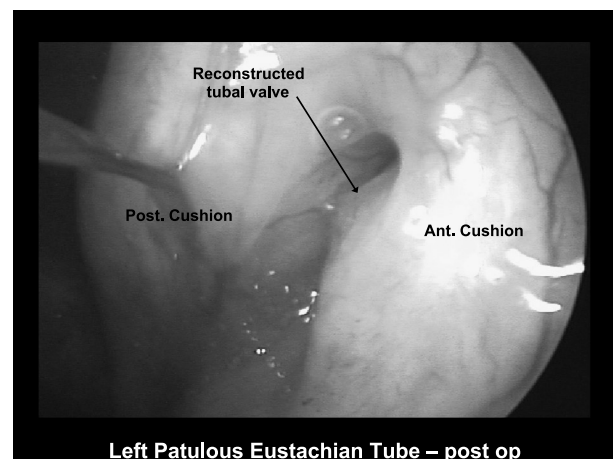


FIG. 6. Image showing PETER of same patient as in Figure 5 at 1 year postoperative.

The apparent conductive hearing loss in SSCD has been theorized by Minor et al. (31) and Mikulec et al. (44) to be a "pseudoconductive hearing loss" because of the effect of a "third window" in the labyrinth. There is a better than normal conduction of bone-transmitted sounds creating autophony of one's own voice but not of breathing sounds that are transmitted through the air.

Most patients did not complain of vertigo, and only 50% had signs or symptoms of Tullio phenomenon. For these reasons, the diagnosis of SSCD has probably been missed in many patients or erroneously diagnosed as a patulous ET on the basis of their autophony.

It was observed that 50% of the 18 SSCD patients experienced relief of their autophony with the head in a dependent position or when supine. One patient had autophony and an objective torsional nystagmus with a fistula test challenge when sitting, but it completely ablated with his head between his legs. It is postulated that increased intracranial pressure or increased intralabyrinthine pressure may reduce the "third window effect," perhaps by stiffening the dehiscent window. This ablation of symptoms with the head in a dependent position also increases the possibility for confusion with patulous ET autophony that characteristically is relieved similarly in head-dependent or supine positions.

It is proposed that SSCD syndrome be called Minor's syndrome. It should be suspected when a patient presents with complaints of chronic persistent autophony of their voice but not breathing sounds. The autophony tends to be unremitting from the time of onset, except for some very occasional hours or days of relief. There may or may not be accompanying vertigo or dysequilibrium, vertigo with pressure changes in the ear or with Valsalva and straining, or Tullio phenomenon. Torsional nystagmus may be observed with a loud tuning fork or Barany masker in the ipsilateral ear. An objectively positive fistula test may be present. There may be a conductive hearing loss, yet intact stapedial reflexes. Importantly, the patient will show no evidence of patulous excursions of the tympanic membrane under micro-otoscopy, despite experiencing active autophony during the examination. Ultimately, the diagnosis of SSCD is best made with a combination of high-resolution CT scan and VEMP. The CT is optimally done with reconstructed Poschel's and Stenvers' views to visualize the superior semicircular canal in its own cross-sectional and longitudinal planes (44). The VEMP will show abnormally low thresholds to elicit the responses, that is, the spinovestibular reflex is triggered at lower than expected levels of auditory stimulation. Ordinarily, VEMP thresholds are anticipated to be at higher than normal levels in the presence of conductive hearing loss.

Patulous ET should be suspected when patients complain of loud autophony of their voice and equally loud autophony of their breathing sounds. The author has occasionally experienced a patulous ET with heavy exercise and prolonged speaking. To appreciate the loudness of the autophony, it can be accurately simulated by speaking and breathing into the diaphragm of

one's own stethoscope held close to the mouth. Patients will often say that the autophony is constant, but on careful questioning, they will admit to relief, even briefly, throughout the day with sniffing, head down, or supine position. They should not have vertigo or dysequilibrium complaints as a result of a patulous ET. Past descriptions of a relationship between patulous ET and vertigo (15,23) may have been caused by misdiagnosis of SSCD patients before the condition had been described by Minor et al. (31). Most importantly, the patient should be examined while they have active autophony, and there should be patulous excursions of the tympanic membrane with normal or forced nasal breathing, especially if the contralateral nostril is closed. It may be necessary to examine the patient in the sitting position with micro-otoscopy to appreciate the movements. Nasopharyngeal endoscopy should demonstrate a longitudinal patulous concave or scaphoid defect in the valve area of the anterolateral wall within the tubal lumen. This is best visualized during forced yawns, which maximally dilates the lumen. The endoscopy is not pathognomonic because it is not always possible to visualize all the way up distally into the tubal valve. Because the autophony often occurs intermittently, tympanometry may miss the patulous sawtooth excursions overlying the impedance tracing that might be expected.

One patient who received the PETR procedure also had severe palatal and tensor tympani muscle myoclonus. The tympanic membrane moved with strong nasal breathing and with strong facial muscle contractions and could easily be misinterpreted as patulous excursions from air exchange. She had successful relief of her autophony but continued to show tensor muscle movements of the tympanic membrane on postoperative Day 1. PETR was not effective in relieving myoclonus.

CONCLUSION

It was hypothesized that the patulous ET was caused by a loss of tissue volume within the anterolateral wall of the tubal lumen in a region referred to as the valve, where the mucosal surfaces are in opposition in the closed resting position. Incompetence of this valve was thought to cause reflux of air and somatosounds from the nasopharynx that result in a spectrum of symptoms from asymptomatic to profoundly disturbing. It was hypothesized that filling in the specific concave defect within the valve would resolve the patulous ET symptoms, and the results seem to support this hypothesis. It remains to be observed whether improvements in graft technique and materials, such as with the current use of cartilage, will result in improvements in outcomes with a higher complete relief of vertigo that is enduring long-term.

When reassurance and medical treatments are not adequately effective for symptomatic patients, they may be offered a tubal obliteration procedure that will require a ventilating tube and subsequent monitoring or a PETR procedure that will likely preserve tubal

function. This pilot study of PETR found the operation to be effective in 43% of patients with the primary procedure and overall in 50% after one patient had a secondary tubal injection of HA. There were no complications. Long-term evaluation of the PETR procedure in larger numbers is needed to analyze whether the operation is ultimately effective. A secondary touch-up procedure with HA may be effective in correcting small defects, and this will need to be studied further. Dedicated instruments for PETR are being designed in the hopes of facilitating the operation.

Minor's syndrome of superior semicircular canal dehiscence has many symptoms that are similar to patulous ET symptoms, and careful assessment of these patients is needed to differentiate between these conditions.

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Balloon dilation of the cartilaginous portion of the eustachian tube: initial safety and feasibility analysis in a cadaver model^{☆,☆☆}

Dennis S. Poe, MD^{a,b,*}, Bassem Matta Nashed Hanna, MB, BCh, M Sc^{a,c}

^aDepartment of Otolaryngology, Children's Hospital and Harvard Medical School, Boston, MA, USA

^bTampere University Medical School, Finland

^cDepartment of Otolaryngology, Cairo University, Egypt

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Abstract

Background: Balloon catheter dilation of diseased sinus ostia has recently demonstrated efficacy and safety in the treatment of chronic sinus disease with 2 years of follow-up. Similar to sinus surgery, initial studies of partial resection of inflamed mucosa from within the cartilaginous eustachian tube (ET) have demonstrated efficacy and safety in the treatment of medically refractory otitis media with effusion. Therefore, balloon dilation of the cartilaginous ET was investigated as a possible treatment modality for otitis media.

Methods: A protocol for sinus balloon catheter dilation was evaluated in each of the cartilaginous ETs in 8 fresh human cadaver heads. Computed tomographic scans and detailed endoscopic inspections with video or photographic documentation were performed pre- and posttreatment, and gross anatomical dissections were done to analyze the effects of treatment and to look for evidence of undesired injury.

Results: Catheters successfully dilated all cartilaginous ETs without any significant injuries. There were no bony or cartilaginous fractures, and 3 specimens showed minor mucosal tears in the anterolateral or inferior walls. Volumetric measurements of the cartilaginous ET lumens showed a change from an average of 0.16 to 0.49 cm³ (SD, 0.12), representing an average increase of 357% (range, 20–965%).

Conclusions: Balloon catheter dilation of the nasopharyngeal orifice of the ET was shown to be feasible and without evidence of untoward injury. A significant increase in volume of the cartilaginous ET was achieved. A clinical study is now indicated to determine whether balloon dilation will demonstrate lasting benefits and safety in the treatment of otitis media.

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1. Introduction

Advances in technology, combined with expanding knowledge of pathophysiology, are facilitating the development of minimally invasive interventions that are increasingly

important and efficacious means of therapy that in most cases also reduce morbidity and expenses. Balloon dilation of stenotic or occluded lumina, although simplistic in concept, has contributed to remarkable advances in the fields of urologic, gastrointestinal, neurologic, vascular, and cardiac procedures with effective and remarkably durable results [1–3].

Balloon dilation of sinus ostia and recesses was introduced in 2005 with the hypothesis that it could provide lasting patency of ostia along with the advantages of minimizing tissue trauma, bleeding, and scarring [4]. Using the balloon dilating catheter (Acclarent, Inc, Menlo Park, CA), 1-year patency rates of 91.6% [5] and 2-year patient satisfaction results of 85%, with significant symptom improvement (Sino-Nasal Outcome Test 20 scores reduced

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* Corresponding author. Department of Otolaryngology, Children's Hospital, 300 Longwood Ave LO 367, Boston, MA 02115, USA. Tel.: +1 617 355 3794.

E-mail address: dennis.poe@childrens.harvard.edu (D.S. Poe).

from 2.17–0.87) and objective reduction of disease (Lund-MacKay score reduced from 9.66–2.69), have been reported. Revision sinus surgery rates for patients were 9.2% [6]. As of 2008, the rate of major complications in patients treated with balloon sinuplasty technology, with or without accompanying endoscopic sinus surgery, was 0.01% [7].

It is possible that balloon dilation of the cartilaginous portion of the eustachian tube (ET) could produce similar benefits in the treatment of chronic otitis media with effusion (OME). Under normal circumstances, there is a roughly 8- to 12-mm segment in the middle of the cartilaginous ET that is closed at rest, with mucosal surfaces in apposition, and therefore functioning as a valve. The cartilaginous ET dilates to the open position on demand, particularly with swallows and yawns, because of the action of, first, the levator veli palatini (LVP) muscle, which rotates and maintains the posterior cushion (torus tubarius) medially, followed by tensor veli palatini (TVP) contraction that distracts the anterolateral wall laterally to open the valve for approximately 0.4 seconds [8]. Tubal dilatory dysfunction is most commonly due to mucosal inflammation with swelling that limits or prevents dilation of the valve, causing insufficient ventilation of the middle ear [9]. Partial resection of inflamed luminal mucosa, submucosa, and occasionally bulges in the cartilage, from the posteromedial wall, where the soft tissue is thickest, has been beneficial in approximately 50% of cases with severely persistent OME with 2-year follow-up [10]. In patients with OME and sinus disease, this eustachian tuboplasty technique, combined with endoscopic sinus surgery, was effective in relieving symptoms in 70% [11]. These early results support the concept that enlargement of the valve of the ET may facilitate the dilatory efforts of the TVP muscle and provide effective benefit for chronic OME.

Widening of the tubal valve could be accomplished by balloon dilation. It would be expected to deflect the posterior cushion medially, stretching the cartilaginous “hinge” between the mobile medial cartilaginous lamina, within the posterior cushion, and the roof of the ET, which is firmly fixed to the basisphenoid bone. The balloon would circumferentially compress and stretch the mucosa and submucosa. No attempt would be made to dilate the bony-cartilaginous isthmus because it is usually patent, even when OME is present [8]. Furthermore, the dense temporal bone most likely would not be affected by the balloon; and the internal carotid artery comes to within a millimeter of the mucosa or can even be dehiscent within the bony portion of the ET. The purpose of this study was to investigate the feasibility and safety of performing balloon dilation of the cartilaginous ET before consideration of a human trial.

2. Methods

2.1. Hypothesis/research questions

Sinus balloon dilation catheters could be adapted to safely and effectively dilate the cartilaginous portion of the ET.

2.2. Aims/end points

Sinus balloon catheter technology was applied to human cadaver heads in a prospective acute procedural study with the following aims:

1. To evaluate the feasibility of using the system for dilation of the cartilaginous portion of the ET.
2. To evaluate the safety of the dilation procedure with an analysis of any potential adverse effects.

The primary end point of the study was the success or failure of tubal dilation and the occurrence of any adverse effects from the process.

2.3. Procedure design

Initial feasibility analyses were performed on embalmed human cadaver half heads, sagittally split in the midline, and computed tomography (CT) scans of patients with normal ears, patients with OME, and a fresh cadaver one-half head. From this work, a dilatory procedure was conceived using existing sinus balloon technology through a transnasal approach in which the catheter would be advanced into position over a guide wire. The trial procedures would be done first on one-half head specimens to facilitate post-procedure CT imaging and dissections. The procedure would then be evaluated in whole cadaver heads.

2.4. Procedure methods and study

Six frozen unembalmed adult human cadaver heads were divided in the midline sagittal plane and thawed for the procedure. Initial screening CT scans confirmed the absence of any ear or nasal pathology. Baseline CT scans (CereTom OTOScan; NeuroLogica Corporation, Danvers, MA) were obtained of each one-half head, placing it in the supine position and acquiring images in the axial plane with 0.625-mm slice thickness. Baseline endoscopic photographs of the nasopharyngeal orifice of the ET were obtained. Endoscopic visualization was performed with 0°- and 30°-angled, 4-mm-diameter Hopkins rod endoscopes fitted with a 3-chip CCD video camera (Karl Storz, Tuttlingen, Germany) and observed on a monitor with video and photographic capture capability. Instruments were introduced through the nasal cavity to simulate an actual surgical procedure to the maximum extent possible.

The sinus balloon dilation system (Acclarent, Inc) was used to dilate the cartilaginous portion of each ET. A curved guiding catheter with a tip angle of 70° was passed through the nasal cavity, and the tip was placed into the ET nasopharyngeal orifice. A Relieva Vigor sinus guide wire was inserted through the catheter into the ET lumen; and once engaged within the ET, it was advanced slowly under fluoroscopic guidance using a C-arm (GE OEC 9800, Fairfield, CT) through the bony isthmus approximately 5 mm into the temporal bone portion of the ET. The guiding catheter was removed, and another CT scan was performed

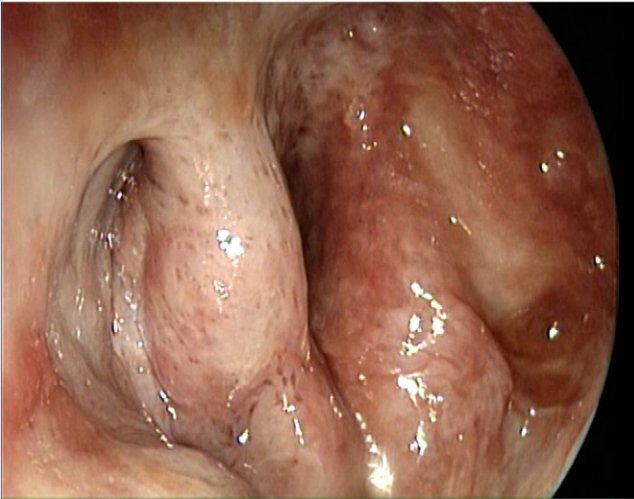


Fig. 1. Right ET nasopharyngeal orifice in fresh cadaver head viewed through a 30°, 4-mm-diameter Hopkins rod endoscope. Predilation.

with the wire in place to aid with identification of the cartilaginous tubal lumen and postprocedure image reconstruction. A 6- or 7-mm-diameter \times 16-mm-length Relieva Solo sinus balloon catheter was slipped over the guide wire into the ET orifice until it reached resistance near the bony-cartilaginous isthmus. The balloon typically protruded from the tubal orifice about 2 to 3 mm. The guide wire was then removed. Once in position, the balloon was inflated to 12 atm for 1 minute, after which it was deflated and removed. In the event that a 7-mm balloon slipped out of the ET orifice into the nasopharynx during inflation, it was replaced with a 6-mm balloon; and the inflation was repeated. Careful endoscopic inspection of the postdilation tubal lumen for any evidence of injury was done with photographic documentation immediately after the procedure, and a CT scan was subsequently performed. The one-half head was then placed

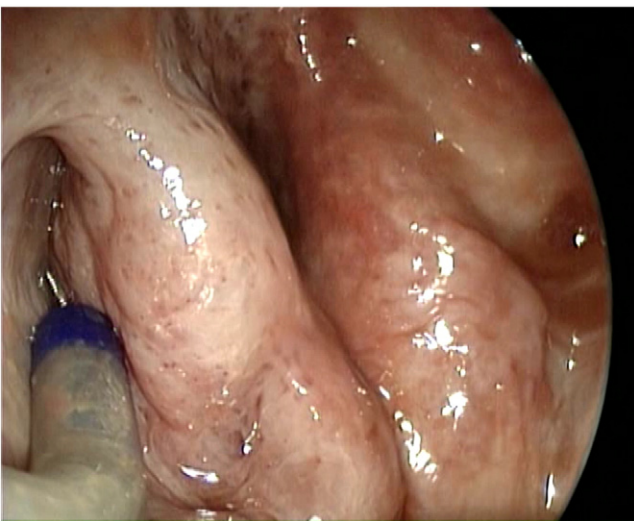


Fig. 2. Guide catheter has been placed into the ET orifice, and the balloon and guide wires are protruding from the catheter into the tubal lumen.

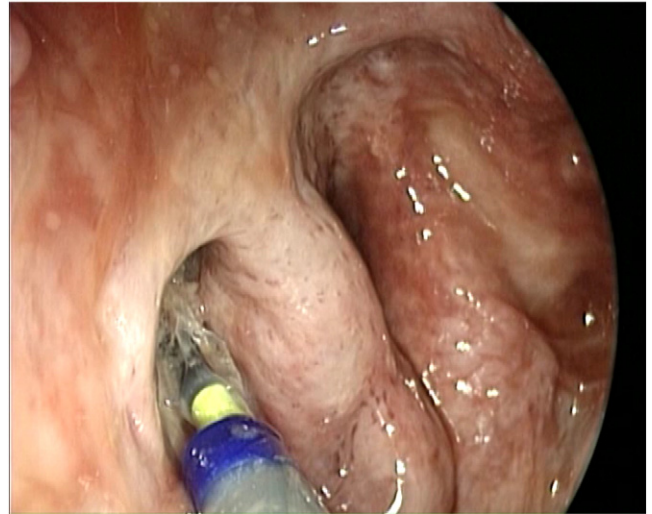


Fig. 3. The balloon has been fully inserted until meeting slight resistance from the bony-cartilaginous junction.

in a lateral decubitus position with the ET orifice facing upward; and the orifice was filled with Omnipaque contrast solution, 300 mg I⁻ per milliliter (GE Healthcare, Princeton, NJ), to accurately visualize and quantify the final dilation dimensions and volumes. A final CT scan was obtained in this position.

Each specimen was carefully evaluated for any adverse effects from the dilation. Inspection of the lumen was done with the endoscope; and a complete survey of the mucosa was done, looking for any evidence of injuries. The posterior cushion was manipulated and rotated medially, looking for any unusual flexibility or increase in range of mobility. A careful and systematic gross dissection was performed making a circumferential mucosal incision around the tubal orifice and making a longitudinal cut along the inferior free

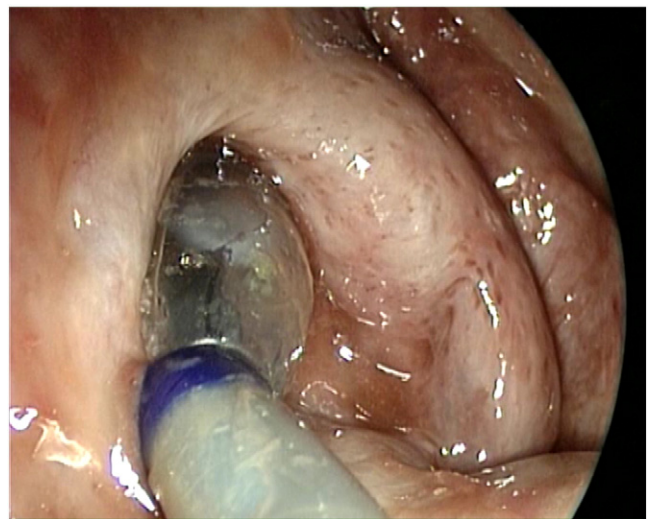


Fig. 4. The balloon has been fully inflated in position. Approximately one third of the balloon protrudes from the ET orifice. The guide catheter is left in position to help stabilize the inflated balloon.

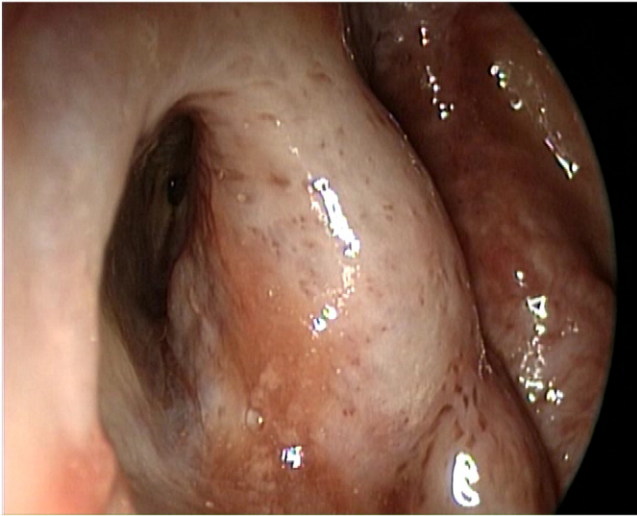


Fig. 5. The entire length of the cartilaginous ET has been dilated by the balloon.

margin of the medial cartilaginous lamina. Submucosal flaps were elevated extra- and intraluminally to reveal the entire medial and lateral cartilaginous laminae up to the bony-cartilaginous junction. Integrity of the cartilage and soft tissues was noted. Inspection was made of the TVP and LVP muscles, Ostmann fat pad, and pterygoid fossa.

A final feasibility trial of balloon dilation of the cartilaginous ET was performed in 2 unembalmed whole cadaver heads under endoscopic guidance. The dilation procedure was executed on each of the 4 ETs using a protocol modified from that in the one-half heads and without CT scans or postdilation dissections. It was found that it was easiest to place the guide wire into the balloon catheter, such that the wire protruded 5 mm from the distal tip of the catheter, and to introduce them together through the guide catheter. Once in position, the guide wire was removed; and the guide catheter was maintained in position to stabilize the balloon. After dilation, close endoscopic inspection was done to assess for any evidence of adverse

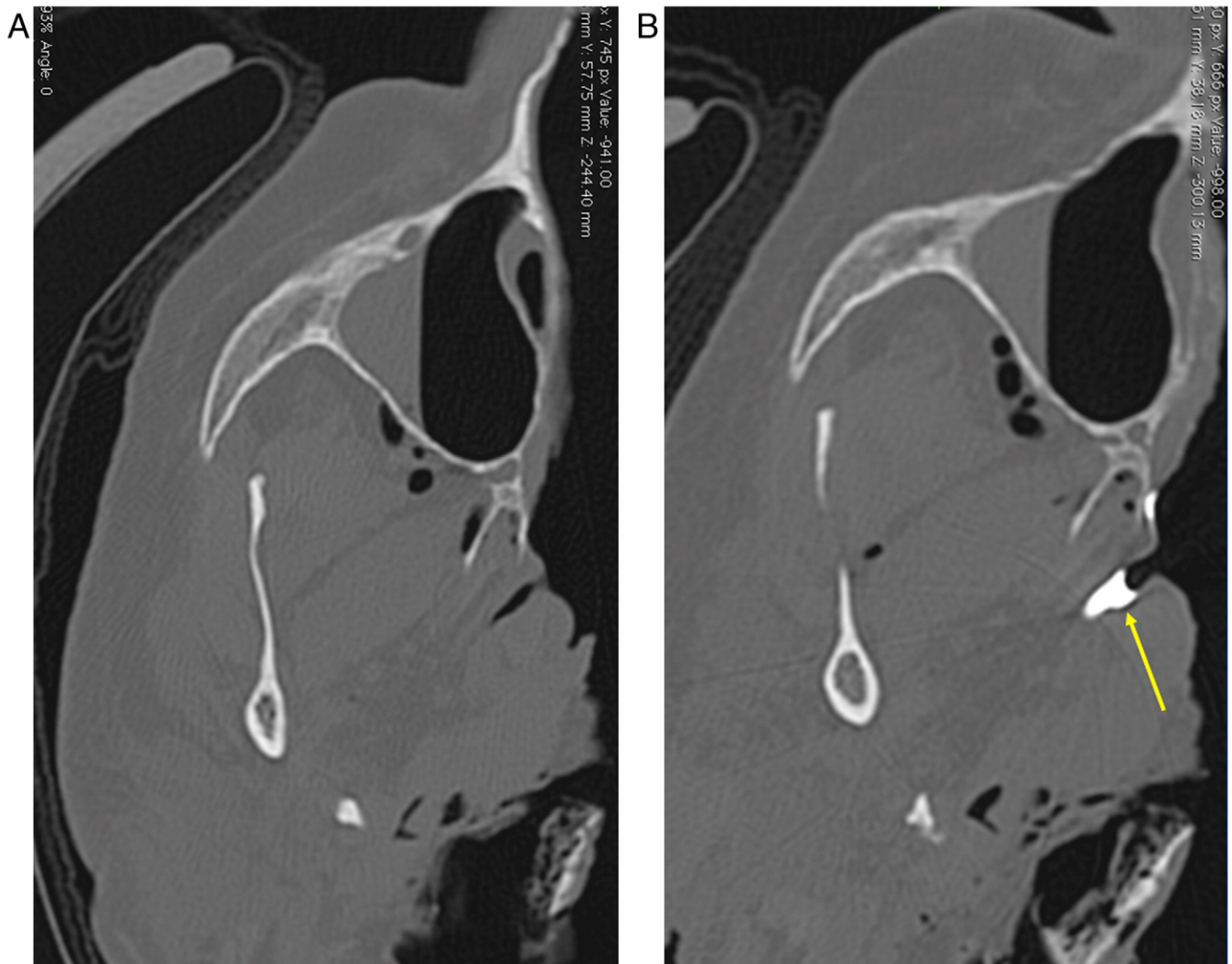


Fig. 6. (A) Axial CT scan through a right cadaver half head; predilation. (B) Axial CT scan through a right cadaver half head; postdilation, with contrast placed into the ET lumen.

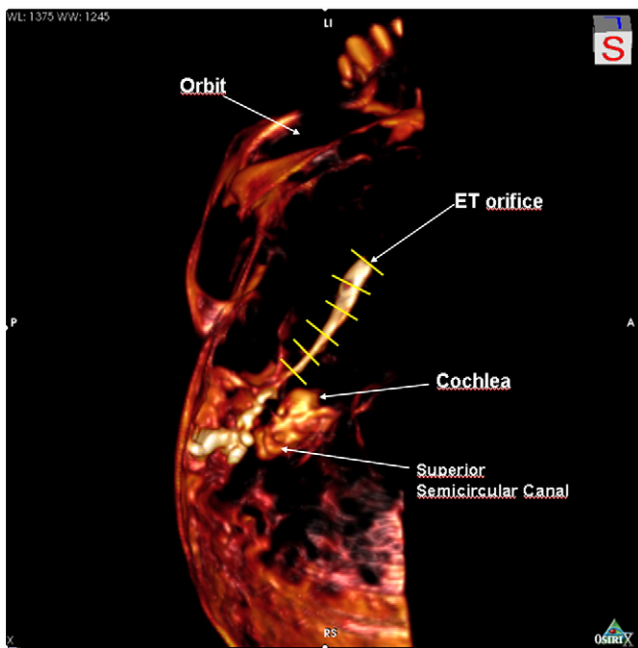


Fig. 7. 3-Dimensional volume reconstruction from CT scans postdilation, viewed inferiorly. Eustachian tube has been filled with contrast that has passed into the middle ear and mastoid. Cross-sectional slices constructed perpendicularly to the longitudinal axis of the ET were used to orient the CT reconstructed images from which luminal cross-sectional areas were measured.

effects, including a visual survey of the mucosa and palpation of the posterior cushion to inspect for excessive mobility (Figs. 1–5).

Postprocedure CT scans from the one-half heads were reviewed in extensive detail for any evidence of bony

fractures in the temporal bone, basisphenoid, or pterygoid plates. For the cartilaginous portion of the ET, lengths, cross-sectional areas with respective major and minor axis diameters at approximately 4-mm intervals, and volumes were computed using OsiriX software (OsiriX Foundation, Geneva, Switzerland) (Fig. 6). In predilation scans, the ET was identified based on the location of the guide wire, which was left in place for the initial set of predilation scans. Once the location had been determined, measurements were completed on an identical set of predilation scans taken with the wire removed. For the postdilation scans, the ET was identified based on the radiopaque contrast that had been poured into ET orifice. Measurements were completed on the postdilation scans with the contrast present. For both the pre- and postdilation scans, the midpoint of the ET was identified on each axial slice and tagged in OsiriX. The ET lengths were determined from the anterior-inferior–most point of the posterior cushion (torus tubarius) to the bony isthmus as the ET entered the temporal bone. A curvilinear line representing the longitudinal axis of the ET was created by following the identified midpoints from the orifice to the bony-cartilaginous junction. The curvilinear lines became the basis to create 2-dimensional curved multiplanar reconstructions containing the line, from which the length of the longitudinal axis could be measured, and perpendicular to the line, from which cross-sectional areas and major/minor axes were measured (Figs. 7 and 8). Volumes were calculated by manually outlining a region of interest on each axial slice and using the volume estimation function to interpolate between slices.

Statistical analysis was done with SPSS 16.0 statistical software (Espoo, Finland) with 2-tailed paired-samples tests performed using $P < .05$ for significance.

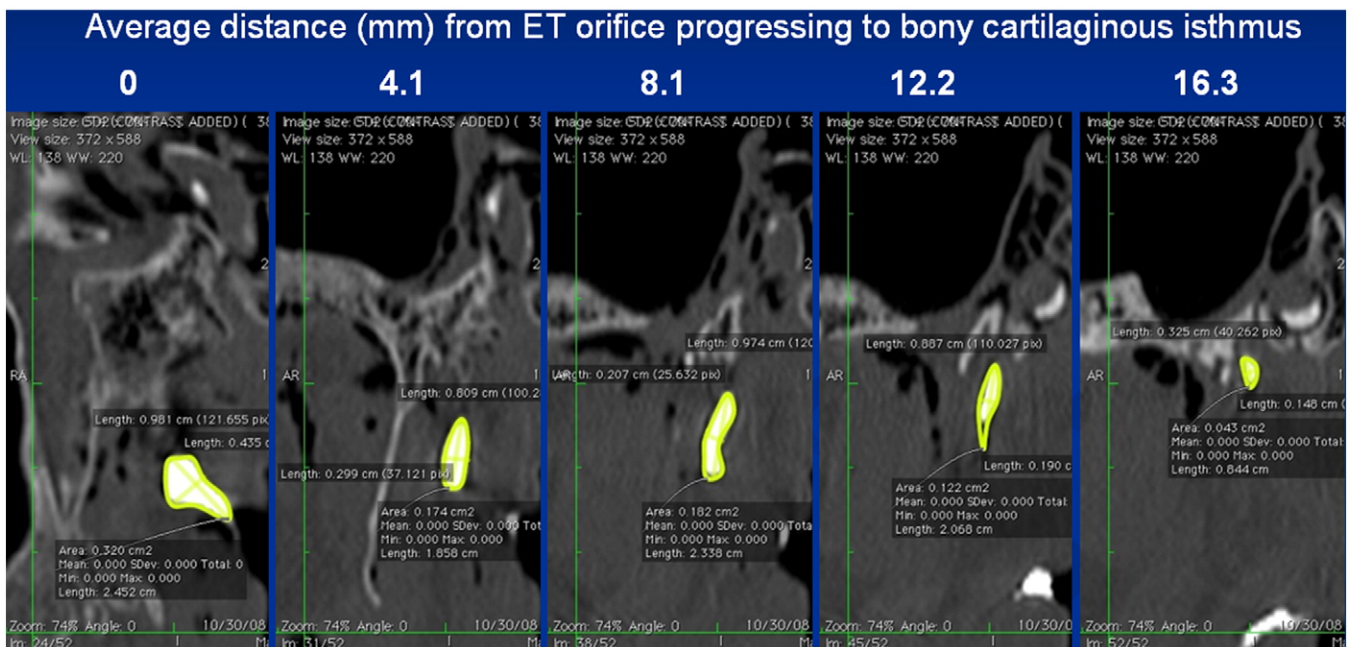


Fig. 8. Computed tomographic reconstructions as described in Fig. 7 yielding cross-sectional slices of postdilated ET. Contrast has been placed into the lumen.

Table 1
Eustachian tube balloon dilation results and intraluminal volumes

Specimen	Balloon(s) diameter (mm)	Final balloon protrusion (mm)	Mucosal tear (mm, location)	Volumes		
				Predilation (cm ³)	Postdilation (cm ³)	% Increase
1L	7, 6	6	0	0.0576	0.3627	530
1R	6	8	<1, inf	0.1463	0.4297	194
2L	6	<5	0	0.2758	0.6631	140
2R	6	5	0	0.2442	0.5343	119
3L	6, 7, 7	5	6 × 2, lat	0.0831	0.6828	722
3R	7	5	3 × 2, lat	0.1129	0.5767	411
4L	7	<5	0	0.1116	0.3922	251
4R	7	5	0	0.0846	0.3922	364
5L	7	<5	0	0.2414	0.6498	169
5R	7	<5	0	0.4099	0.4915	20
6L	7	5	0	0.0361	0.3845	965
6R	7, 7, 7	<5	0	0.0745	0.3730	401
			Average	0.1565	0.4944	357
			SD	0.1124	0.1227	

Final balloon protrusion = distance balloon protruded from ET orifice when inflated. Specimen 1R had a partial-thickness mucosa laceration in the inferior wall, superiorly. Specimens 3R and L had oval full-thickness lacerations in the lateral wall, superiorly.

3. Results

Successful balloon dilation was achieved in all ETs without any major adverse effects (Table 1). The guide catheter, guide wires, and balloon catheters were all inserted into the ET without difficulty. Dilation of the 12 ETs in the one-half heads was accomplished with a 7-mm-diameter balloon in 8 (66.7%) and with a 6-mm balloon in 4 (33.3%). In most cases, the inflated balloon locked securely into position, leaving approximately one third of the 16-mm length protruding distally (inferiorly) out of the orifice, but stable. In one specimen (1L), the ET was dilated initially with a 7-mm balloon; but it slipped distally out of the orifice excessively and was replaced by a 6-mm balloon that partially slipped but stabilized with 6 mm protruding from the orifice (~37%), which gave a satisfactory dilation. The contralateral ET from the same head was dilated with a 6-mm balloon that slipped inferiorly, but stabilized with 8 mm (50%) protruding and yielding a satisfactory dilation. During the dilation of one ET (specimen 4R), a 7-mm balloon began to distract distally but was successfully maintained in position by stabilizing the catheter against the floor of the nose. In the event that a balloon slipped out more than 50%, the dilation was repeated. In all cases, the dilation caused medialization of the posterior cushion, rotating the free portion of the medial cartilaginous lamina.

Average intraluminal volumes of the cartilaginous ET increased from predilation of 0.16 cm³ to postdilation of 0.49 cm³ (increase of +357%), which was statistically significant ($P < .001$).

Measurements of the lengths of the cartilaginous portion of the ET are presented in Table 2. Cross-sectional areas were measured at approximately 4-mm intervals through the cartilaginous ET, with the results depicted in Fig. 9. At the ET orifice (0-mm distance) and at the bony-cartilaginous junction (average of 26.3 mm), there were no significant

differences between pre- and postdilation areas ($P = .61$ and $P = .54$, respectively). For the remaining distances, postdilation areas were significantly larger ($P < .001$ for each distance).

Cross-sectional major and minor axis dimensions in pre- and postdilated ETs are presented in Table 3.

There were minor adverse effects in 3 one-half head specimens, all of which were lacerations of the luminal mucosa. Specimen 1R had a partial-thickness mucosal tear of no significance. Specimen 3L had a full-thickness tear superiorly in the anterolateral wall near the bony-cartilaginous isthmus (Fig. 10). The contralateral ET from the same head sustained a smaller tear in the same location. There were no other soft tissue injuries, no fractures of the cartilage of the ET or separation from the basisphenoid, and no bony fractures detected on palpation or on postdilation CT images. There were no adverse effects noted in the 4 ETs dilated in the whole head specimens.

4. Discussion

Recurrent and chronic OMEs are common problems in children and adults. Attempts are made to ascertain the underlying etiology in each case and to treat it with medical therapy as indicated. Refractory cases are typically managed with the insertion of tympanostomy tubes, but there is a

Table 2
Eustachian tube straight line and curvilinear lengths

	Postdilated length (mm)
Average	26.32
SD	1.7830
Max	28.96
Min	23.34

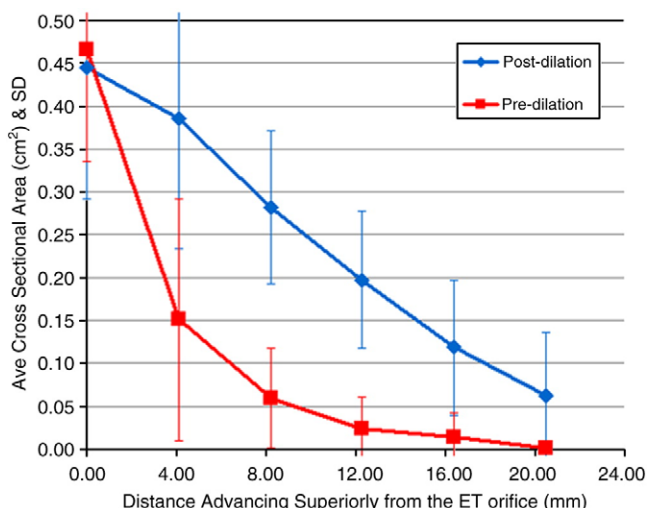


Fig. 9. Plot of average cross-sectional areas along the cartilaginous ET length; pre- and postdilation.

subset of patients in whom OME repeatedly recurs after extrusion of the tubes. Multiple or prolonged tube placements are associated with an increased risk of tympanic membrane atrophy at the tympanostomy site or persistent perforation. Eustachian tuboplasty has shown some early effectiveness in reducing the rate of OME in otherwise refractory cases [10,11].

Balloon dilation of the cartilaginous portion of the ET has been proposed as a novel, minimally invasive method for treating refractory OME. ET dilation with a sinus balloon dilation catheter is not indicated on the labeling of the device. The present study has demonstrated that the procedure is feasible and safe to the best extent that can be judged from a cadaver trial. There was significant dilation of the lumen

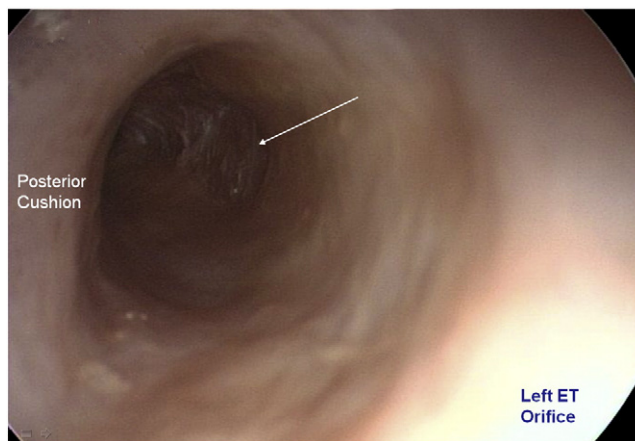


Fig. 10. A 30°, 4-mm-diameter Hopkins rod endoscopic view of left ET postdilation. A mucosal tear in the anterolateral wall is noted (arrow).

without any significant adverse effects. There was no significant effect at the tubal orifice, where the medial cartilaginous lamina is most mobile, or near the bony-cartilaginous junction, where the cartilage becomes circumferentially fixed. The greatest dilatory changes occurred between 4 and 16 mm from the orifice, where the cartilage is less mobile; and the balloon was forced to expand into the soft space of the anterolateral wall, toward Ostmann fat pad, TVP muscle, and pterygoid fossa. Our measurements of the length of the adult cartilaginous ET were similar to the average length of 26.6 mm previously reported by Sudo et al [12] in measurements from reconstructions of histologic sections.

Unlike with dilation of sinus ostia, there was no intentional fracturing of bone. However, soft tissue balloon dilation of stenotic vessels, biliary tree, urinary strictures, and other tubular organs has been demonstrated to have lasting benefits. It is known that one of the mechanisms of successful balloon dilation of vascular stenoses is tearing of the intima and sometimes the media [13]. In a histologic study of balloon-dilated aortic valves, there was evidence of young-appearing scar tissue that filled the small tears and lacerations observed in the dense collagenous tissue stroma rather than healing by regrowth of the collagen. The scar tissue consisted of a cell-rich pattern of fibroblasts, capillaries, and an inflammatory infiltrate composed of lymphocytes, plasma cells, and histiocytes that was present even at 24 months [14]. In the present study, endoscopically observed tears occurred in the mucosa in 3 (19%) of 16 dilated ETs; and it is likely that microscopic examination would reveal an even higher number of tears. Although the mucosa, submucosa, and cartilage are all flexible, it is possible that similar submucosal and intracartilaginous injury or tears may result. It is also possible that compression of irreversibly injured hypertrophic mucosa and submucosa may cause them to regrow with thinner and healthier layers. Histology after laser removal of posteromedial mucosa and submucosa has shown such a healing pattern with return of normal ciliated epithelium, reduced inflammatory infiltrate,

Table 3
Cross-sectional major and minor axis dimensions in pre- and postdilated ET

Average distance from ET orifice (mm)	0.00	4	8	12	16	20
<i>Predilation</i>						
Major axis ave (mm)	1.11	0.77	0.55	0.56	0.32	0.26
SD	0.2115	0.4723	0.3062	0.0644	0.0922	0.0000
Max	1.436	1.73	1.092	0.65	0.427	0.258
Min	0.794	0.109	0	0	0	0
Minor axis ave	0.38	0.22	0.14	0.15	0.13	0.08
SD	0.0951	0.1086	0.0441	0.0344	0.0314	0.0000
Max	0.593	0.42	0.2	0.185	0.166	0.081
Min	0.266	0.086	0	0	0	0
<i>Postdilation</i>						
Major axis ave	1.04	1.03	1.01	0.74	0.57	0.53
SD	0.2364	0.1455	0.2593	0.2530	0.1612	0.1563
Max	1.529	1.284	1.61	0.74	0.805	0.746
Min	0.656	0.809	0.707	0.191	0.291	0
Minor axis ave	0.47	0.46	0.33	0.36	0.24	0.21
SD	0.1454	0.1917	0.1103	0.1945	0.1124	0.0776
Max	0.657	1.019	0.527	0.906	0.559	0.345
Min	0.23	0.299	0.18	0.19	0.148	0

and some collagenous scar tissue developing in the thinner submucosa [10]. Therefore, it is possible that balloon dilation could cause some permanent changes in the cartilaginous ET that could provide lasting benefit in widening the lumen and facilitating the dilatory action of the TVP muscle.

Risks of the balloon dilation could be development of a circumferential stricture, fracture of the medial cartilaginous lamina, injury to the TVP muscle, hemorrhage into the pterygoid space, and excessive widening to cause a patulous ET. Circumferential strictures have been predicted since the introduction of balloon dilation procedures, but vast experience has shown that it rarely occurs because of the permanent histologic changes that are induced. Gross fracture of the cartilage could theoretically cause the posterior cushion to flail loosely, which could be detrimental to the action of the TVP; but no fractures occurred at all in this trial, and the cartilage would be expected to be more flexible in live patients. There was no evidence of muscle tears in the TVP or LVP in any of the specimens, and it would therefore be unlikely for hemorrhage to occur. Patulous ET could theoretically occur, even on a temporary basis. Although physiologically harmless and likely to resolve a patient's OME, it could cause significant disturbing symptoms of autophony that would be undesirable. Patients selected for the procedure would have considerable mucosal swelling as an indication for dilation such that the risk of causing an incompetent, patulous valve would be minimized. Techniques to repair a persistently patulous ET are now available [15].

Another risk of the procedure would be with the introduction of the guide wire. Excessively deep insertion could pass the wire into the middle ear, causing injury to the ossicles, tympanic membrane, or inner ear. It could also present a risk to an internal carotid artery that would be dehiscent into the floor of the bony ET. In the course of this study, we found that the C-arm fluoroscopy was unnecessary. Inserting the wire with only 5 mm protruding from the balloon catheter should absolutely minimize the risk of entry into the middle ear, keep the wire within the cartilaginous ET, and prevent any proximity to the internal carotid artery. A preoperative CT scan to ensure that the carotid is covered with bone would be initially prudent until more experience is gained with the procedure. *The guide wire should be removed before inflation to prevent any potential overpressure from occurring in the proximal ET and middle ear.*

It is important to monitor the balloon for movement during the dilation. The optimal position for the balloon appeared to be protruding by about one quarter to one third out of the tubal orifice. A deeper insertion, such as occurred in specimen 3L with the initial 6-mm balloon, was the likely cause of the largest mucosal tear. If the balloon were to begin to slip out during the inflation, it may be possible, as was done in one case, to maintain it in place by allowing the catheter to rest on the nasal floor to provide some counterpressure. If the balloon were to slip out more than

50%, the dilation could be repeated with the same size catheter if it appears that some dilation has successfully occurred, or a smaller balloon could be used.

If balloon dilation of the ET were ultimately demonstrated to be effective with the benefits sustained over time, it would be a useful and minimally invasive alternative to tympanostomy tubes in patients with chronic OME. Careful selection of patients with medically refractory tubal dilatory dysfunction should be done. A thoughtful evaluation of the risks and potential benefits of the procedure should be made in every case. In the future, it may also be beneficial to patients with atelectasis or scuba or flight barotrauma. After accumulating experience in adults, it would have to be determined whether the procedure should be performed in children, in whom the mechanisms of OME remain less clear than for adults.

5. Conclusions

This study demonstrated that balloon dilation of the cartilaginous portion of the ET was feasible and appeared to be safe in a cadaver trial. The hypotheses for this study were supported by the significant dilation of intraluminal volumes and cross-sectional areas within the middle section of the cartilaginous ET. No significant adverse effects were encountered.

On the basis of this study, it is reasonable to proceed with a human pilot study to judge safety and efficacy in patients with medically refractory dilatory dysfunction of the ET.

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