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Preface

Otosclerosis is one of the most fascinating diseases in the field of otology. Its familial or spontaneous occurrence, its histological appearance, its clinically sex-dependent frequency with female predominance, its still mysterious etiology and the intellectual challenges it poses as well as the aesthetics involved in its surgical treatment make otosclerosis a subject for continuous clinical research. In April 2004, we organized an international symposium in Saas Fee titled ‘Otosclerosis and Stapes Surgery’ where leading international experts in the field gathered to pass on their latest knowledge on the current aspects of basic and clinical research. This symposium was so successful that we decided to publish some selected and updated papers in this book. In this manner, we have been able to put together a unique work encompassing all the aspects of otosclerosis from its clinical development, histopathology, molecular biology, genetics, diagnostics and differential diagnostics to its various surgical options. The editors as well as the authors are certain that this modern and current overview will provide the reader with fundamental information, whether basic researcher, clinician or student.

Wolfgang Arnold, Munich
Rudolf Häusler, Bern
General History of Stapedectomy

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Abstract

The article gives an overview of the historical development of stapedectomy beginning with Kessel in 1876. Then, from the beginning to the middle of the 20th century, surgery on the oval window became obsolete, opening the way for an era of fenestration operations until Shea in 1956 performed the first modern stapedectomy using a Teflon stapes replacement prosthesis. Since then, numerous surgeons worldwide have used this procedure with great success. Many of them have contributed towards progressively refining the surgical techniques, e.g. by changing the total removal of the footplate for the less traumatic small fenestra stapedectomy or stapedotomy.

Early Attempts at the Surgical Treatment of Stapes Ankylosis

The first description of a stapes ankylosis as the cause of hearing loss that has been passed down to us comes from Valsalva [1] from Bologna [2]. It is not known when the first attempts at stapes mobilization to improve hearing were carried out. A reference to this is to be found in Ménière, 1842 [3]. This is the description of a patient who was able to temporarily improve his hearing by tapping directly on the stapes with a small gold rod. Kessel (1876) from Graz, and later Jena [4, 5] is considered to be the actual founder of stapes surgery. On the basis of experimental investigations in the pigeon, he demonstrated that opening of the oval window did not necessarily result in destructive damage to the inner ear as was generally feared. He subsequently published a description of transtympanal stapes mobilization and stapedectomy as a method for the improvement of hearing in stapes ankylosis. The German otologists, Schwartze [6] and Lucae [7], also carried out stapes mobilization and removal of the stapes. In France, Miot [8] reported that he had achieved a hearing gain in
74 cases out of 126 stapes mobilizations. The operation was also performed in France by Boucheron [9] and Pottier [10] and in Italy by Feraci [11]. In the USA, Blake [12] and Jack [13–15] at the Eye and Ear Infirmary in Boston and also Sexton [16] and Alderton [17] in New York practised mobilization and removal of the stapes. Since the postoperative hearing gain often only lasted for a period of days to weeks and cases of fatal labyrinthitis with lethal intracranial complications could occur, this early stapes surgery fell into disrepute. It was vehemently criticized, in particular also by the leading otologists of the time – Politzer, Siebenmann and Moure – who in 1899 at the 6th International Otology Congress in London declared that stapes surgery was useless, dangerous and unethical [18]. The early stapes surgery that had started with great enthusiasm therefore came to an abrupt end for the time being.

The Era of Fenestration Operations

Since surgical operations on the fixed stapes were considered too dangerous, the idea of an inner ear opening outside of the oval window was taken up. The suggestion of a promontory fenestration made by Passov in 1897 [19] did not become established, but in 1899 Floderus [20] suggested an opening of the vestibular labyrinth, which in 1913 was described by Jenkins in London as a ‘fenestration of the lateral semicircular canal’ [21]. In the 1920s, the electric head light was then introduced by Sexton in New York and in Sweden Nylen [22] was the first to use a microscope for ear surgery. With these tools, Holmgren [23, 24] propagated a closed, microsurgical fenestration operation on the lateral semicircular canal, with which he achieved, admittedly only slight but relatively permanent, improvements of hearing in patients with otosclerosis. The Frenchman Sourdille, a pupil of Holmgren, was the first to develop the fenestration of the lateral semicircular canal towards the outside in a two-stage operation. In 1937 he achieved a lasting hearing improvement in 64% of 109 operated patients with his ‘tympano-labyrintho-pexie’ [25]. In 1938 Lempert in New York [26] finally simplified the semicircular canal fenestration into a one-stage operation. Both he himself and also a number of other otologists achieved considerable and lasting hearing gains in fairly large series with the use of this well-standardized operation [27].

Start of the Era of Modern Stapedectomy

Rosen [28] from New York used a transcanal approach from 1952 in order to test the mobility of the stapes prior to a semicircular canal fenestration, and
rediscovered the effect that stapes mobilization had in the improvement of hearing. Meanwhile great advances had been made in otological microsurgery, which was now routinely performed under the binocular operating microscope, chiefly through the work of Wullstein and Zöllner. After a study of the early literature, Shea [29], who as Clinical Fellow learnt the technique of ear surgery in Vienna with Novotny and Burian, came to the conclusion that it must be possible to replace an otosclerotic stapes with a prosthesis. In collaboration with the engineer Treace, he created a stapes prosthesis made of the then newly discovered biocompatible material Teflon (fig. 1). In a female patient with otosclerosis, after removal of the stapes and covering of the oval window with a vein he used this Teflon stapes prosthesis for the first time on May 1st 1956, with complete success [29, 30, 31].

From this date onwards, stapedectomy for the treatment of otosclerotic conductive hearing loss started on a triumphal march around the whole world. In the 1960s, thousands of hearing-impaired patients with otosclerosis were treated with great success. After the Teflon stapes, Shea used a hollow polyethylene tube for a certain period of time, but this sometimes caused inner ear fistulæ. Later he used a piston made entirely of Teflon, which is still used today by many surgeons. In 1960, Schuknecht developed a steel wire-adipose tissue prosthesis made directly during the operation, which became used worldwide [32]. This prosthesis also had its disadvantages, because lateral displacements of the wire and adhesions in the vestibulum could develop, which represented a certain inner ear risk during revision surgery. The combination of a Teflon shaft in the vestibulum with a metal wire for fixation to the incus led to the metal wire–Teflon piston prosthesis, which is still routinely used in many centres [33, 34].

At the beginning of the ’60s Plester [35] suggested the technique of partial stapedectomy, in which only the posterior third of the footplate was removed. A further development of this principle led Shea et al. [36] and Marquet [37] and Martin from 1962 [38] to just make a small opening in the middle of the
footplate into which the prosthesis piston fitted exactly, in order to reduce the inner ear risk. This initiated the era of ‘stapedotomy’, which is now used worldwide.

As an alternative, Portmann and Claverie in 1957 [39] and Zangemeister in 1958 [40] suggested that the superstructure of the stapes should be left in situ and one of the stapes crura used as an interposition. The advantage of this is that no foreign material is implanted. For the same reason, Zöllner in 1960 [41] replaced the extracted stapes with an autologous cortical bone chip. After covering the oval window with periosteum, Pfaltz [42] made a graft with a cartilage chip. Stapedectomy methods without the use of foreign material are still used today in modified form.

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General History of Stapedectomy
Prevalence of Histologic Otosclerosis: An Unbiased Temporal Bone Study in Caucasians

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Abstract

Background: ‘Histologic otosclerosis’ refers to a disease process without clinical symptoms or manifestations that can only be discovered by sectioning of the temporal bone at autopsy. ‘Clinical otosclerosis’ concerns the presence of otosclerosis at a site where it causes conductive hearing loss by interfering with the motion of the stapes or of the round window membrane. Various authors have studied the prevalence of histologic otosclerosis on laboratory collections of temporal bones. Some 12–15% of the temporal bones with histologic otosclerosis have demonstrated stapedial fixation. Using these figures for calculating the prevalence of clinical otosclerosis gives an extrapolated clinical prevalence of 0.99–1.2%. This does not correlate well with the clinical data on otosclerotic families from which a clinical prevalence of 0.3% has been estimated. Objective: To study the prevalence of histologic otosclerosis in an unselected series of temporal bones. Study Design: During a 1-year period, 118 consecutive pairs of temporal bones of deceased patients at a tertiary center were collected to determine the prevalence of otosclerosis. Although histology remains the gold standard for evaluation of otosclerosis, the gross observation of temporal bone slices combined with microradiography was used to screen for otosclerotic lesions more rapidly and with a lower cost-benefit ratio. The temporal bones with suspected otosclerosis shown with these techniques were further analyzed by conventional histology. Results: 2.5% of the 236 temporal bones (or 3.4% of patients) studied demonstrated histologic otosclerosis. Conclusions: Although the prevalence of 2.5% is much lower than previously published figures on histologic otosclerosis, the extrapolated data (extrapolated clinical prevalence = 0.30–0.38%) correlate well with clinical studies of otosclerotic families. The previous studies based on laboratory collections were likely biased by the presence of hearing loss or other otological diseases.
Otosclerosis is a term used to describe a primary disorder of the bony capsule of the labyrinth, first identified and reported by Adam Politzer [1, 2]. This lesion is found only in the human labyrinthine capsule and stapes footplate and may interfere with the functions of hearing or balance, depending on the site, size, and histologic features of the pathologically involved area.

In commenting on otosclerosis, Guild [3] emphasized the importance of distinguishing between clinical and histologic otosclerosis. ‘Histologic otosclerosis’ refers to a disease process without clinical symptoms or manifestations that can only be discovered by routine sectioning of the temporal bone at autopsy. ‘Clinical otosclerosis’ concerns the presence of otosclerosis at a site where it causes conductive hearing loss by interfering with the motion of the stapes or of the round window membrane [4, 5]. It is hypothesized that in response to various gene defects, the physiological inhibition of bone turnover in the otic capsule is overruled due to a greater susceptibility to environmental factors, resulting in a localized bone dysplasia known as otosclerosis [6].

Several authors have studied the prevalence of clinical otosclerosis in the Caucasian population. Otosclerosis is predominantly a Caucasian disease, correlating with their geographic distribution throughout the world. Clinical otosclerosis is quite rare among Blacks, Orientals, and American Indians [7] (table 1). The early studies only gave an approximate clinical estimate of its prevalence [4, 8, 9], since no attempt was made to relate the clinical condition to a known population at a given time. These estimates are based on a more or less subjective extrapolation from the available data. Taking into account the more recent studies of Morrison [10], Hall [11], Pearson et al. [12] and Gapany-Gapanavicius [13], the mean prevalence in later studies can be estimated at 3/1,000 (0.3%).

Several authors have also studied the prevalence of histologic otosclerosis (table 2). Although histologic otosclerosis strictly speaking refers to the subclinical and asymptomatic variety in which the areas of otosclerotic bone within the otic capsule have not caused stapedial fixation or cochlear degeneration, all authors, except for Schuknecht and Kirchner [15], use this definition in a broader sense. To calculate the prevalence, they include without distinction all individuals with otosclerotic temporal bones as diagnosed by serial sectioning and histologic examination. Measured in this way, the mean prevalence in the Caucasian population can be estimated at 8.3% [7]. In a recent study of Othani et al. [20], the histologic prevalence among Japanese people was reported to be 2.56%.

According to Guild’s figures [3], 15% of the temporal bones with histologic otosclerosis demonstrated ankylosis of the stapediovestibular articulation. In the review by Altmann et al. [7], in which data of Engström [16] and Guild [3] on histologic otosclerosis were combined, 12% of the temporal bones with otosclerosis had ankylosis. Using Guild’s 15% and Altmann’s 12%, the extrapolated clinical prevalence amounts to 8.3 × 15/100 = 1.2% and
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8.3 × 12/100 = 0.99%, respectively. These extrapolations for calculating the prevalence of clinical otosclerosis do not correlate well with the clinical data on otosclerotic families with a clinical prevalence of 0.3% [10–13].

**Materials and Methods**

**Selection Procedure**

During a 1-year period, 118 consecutive pairs of temporal bones of deceased patients were collected from the allograft temporal bone bank at the University Hospital of Antwerp. Their selection was based only on the medical donor criteria and quality control for tympano-ossicular allografts as determined by governmental regulations [21, 22]: in Belgium, each deceased person is regarded as a donor candidate unless he or she has entered his or her name in an official antidonor registry. Hence, in contrast to previous studies, the selection was not made based on the presence of hearing loss or otological diseases. Patients from whom only one temporal bone could be harvested were excluded from this study.
Sample Characteristics
Since the temporal bones were processed by the allograft bank to provide allograft material for middle ear surgery, the tympanic membrane, ossicles, external auditory canal and tegmen tympani had already been removed. However, all the collected samples had an intact otic capsule. In about 46% of the samples, the stapedial footplate was no longer present since the stapes had already been taken out of the oval window as allograft material. The removal of the stapes was always performed under the operating microscope so as not to damage the oval window or the otic capsule itself. All deceased patients were Caucasians. The age range was 16–79 years with a mean age of 63 years. The male/female ratio was 50/68.

Tissue Processing
The methodology is summarized in figure 1. The temporal bones were removed by the technician of the allograft temporal bone bank. Schuknecht’s [23] bone plug method was used. Fixation was performed in a 4% buffered formaldehyde solution with acidic pH (pH 5.6). This acidic fixation is essential to get stiffer allograft material for middle ear surgery, which allows these tympanic membranes to be handled more easily during surgical implantation. Fixation had been carried out for approximately 4 weeks. Once the allograft material was taken from these temporal bones, the bony labyrinths were incorporated into this study and further preserved in a 4% buffered formaldehyde solution (pH 7.4). Following fixation, the whole temporal bones were sliced. Slicing was done with the Exact® cutting system, as described by Declau et al. [24]. Cutting was performed in the axial plane. The slices of the temporal bones were examined then under a stereomicroscope (Zeiss SV11) at a magnification of ×10. If otosclerosis was suspected by this method, the microslice was further analyzed with conventional histologic techniques: decalcification was performed by immersion in a mixture of 5% EDTA and 4% buffered formaldehyde solution. The tissue blocks were further embedded in paraffin and sectioned at a thickness of 20 μm. The sections were stained with hematoxylin-eosin. The slices that seemed to have a normal appearance under the stereomicroscope were further examined by microradiography (see Michaels [25] for a full description of the method). Each microslice was X-rayed with a Faxitron 4380 5N (Hewlett Packard). Careful examination of the X-rays with a hand lens (magnification ×10) was performed in order to reveal any hypodensities possibly indicating otosclerosis. All specimens with hypodensities were also

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subjected to conventional histology. Additionally, in order to test the validity of this methodology, 15 temporal bones in which no sign of otosclerosis could be detected either by slice macroscopy or microradiography were randomly chosen for further histologic analysis.

**Results**

The combined application of slice microradiography and macroscopic evaluation of temporal bone slices revealed 44 out of 236 temporal bones (19%) with suspected otosclerosis (fig. 2). These temporal bones were further processed by conventional histologic techniques. In 6 temporal bones, otosclerosis was histologically confirmed. In order to prove the validity of the selection procedure on false negatives, 15 temporal bones from the collection without any sign of otosclerosis either on macroscopy or microradiography were randomly selected for histologic evaluation. No otosclerosis could be detected in these specimens. The results are summarized in table 3.

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Fig. 2. Microslicing, microradiography and histology of an otosclerotic temporal bone (TB 1 L). *a* Microsliced temporal bone: normal overview. C = Cochlea; V = vestibule. *b* X-ray of the microslice shown in *a*. Arrowheads indicate the otosclerotic focus that appears as a radiolucent area in the region of the fissula ante fenestram. *c* Histologic overview of the stapes and oval window region shown in *a* and *b*. Arrowheads indicate the otosclerotic focus, which has replaced normal bone in the area of the fissula ante fenestram. Size: 1.4 mm (H & E stain). *d* Detail of the active otosclerotic focus shown in *c* (H & E stain).
Table 3. Summary of identified otosclerotic foci

<table>
<thead>
<tr>
<th>Temporal bone no.</th>
<th>Side</th>
<th>Age</th>
<th>Gender</th>
<th>Otosclerotic activity</th>
<th>Initial identification mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB 1 L</td>
<td>50</td>
<td>F</td>
<td>+</td>
<td>microradiography</td>
<td></td>
</tr>
<tr>
<td>TB 1 R</td>
<td>50</td>
<td>F</td>
<td>+</td>
<td>microradiography</td>
<td></td>
</tr>
<tr>
<td>TB 2 L</td>
<td>57</td>
<td>F</td>
<td>+</td>
<td>slice macroscopy</td>
<td></td>
</tr>
<tr>
<td>TB 2 R</td>
<td>57</td>
<td>F</td>
<td>+</td>
<td>slice macroscopy</td>
<td></td>
</tr>
<tr>
<td>TB 48 L</td>
<td>48</td>
<td>F</td>
<td>–</td>
<td>slice macroscopy</td>
<td></td>
</tr>
<tr>
<td>TB 110 R</td>
<td>70</td>
<td>M</td>
<td>–</td>
<td>slice macroscopy</td>
<td></td>
</tr>
</tbody>
</table>

Macroscopy of Temporal Bone Slices

Evaluation of the temporal bone slices under the dissecting microscope revealed four temporal bones with otosclerosis (TB 2 L and R, TB 48 L and TB 110 R). Evaluation of the activity may be done even on gross inspection, active foci being fragile and hyperemic, while inactive ones being dense and pale.

The case with bilateral lesions (TB 2) demonstrated a large bilobed active focus in each temporal bone. Neither the crura nor the footplate of the stapes seemed invaded by the otosclerotic process. The round window was free of otosclerosis on both sides. No gross invasion of the labyrinth was seen.

The other two temporal bones (TB 48 L and 110 R) revealed limited inactive foci of otosclerosis in the region anterior to the oval window at the fissula ante fenestram where an altered bone architecture was seen. In neither of these cases did the otosclerotic process proper involve the footplate of the stapes.

Microradiographic Evaluation

Application of the microradiographic technique resulted in further two temporal bones (TB 1 L and R) in which small but active otosclerotic foci were revealed. They appeared as hypodensities in the region of the oval window at the fissula ante fenestram.

Histologic Characteristics

The otosclerotic lesion in each of the affected temporal bones was sharply delineated from the normal bone. Because of the use of acidic fixation, the otosclerotic foci did not appear as basophilic. However, this could easily be characterized by the disturbed bone architecture which they displayed.

In both right and left temporal bones of TB 1, a highly vascular area was observed in the region of the fissula ante fenestram. Between the vessels, and at
the edges of the bone trabeculae, osteocytes and osteoblasts were found to be very numerous and also appeared enlarged and hyperchromatic. The focus on the right side measured 1.6 mm and that on the left side 1.4 mm.

In both right and left temporal bones of TB 2, a large otosclerotic bilobed focus was found. The otosclerotic foci were located within the otic capsule at the lateral aspect of the cochlea and the anterior side of the vestibule. The thickness of the affected area in the region of the fissula ante fenestram was almost twice that in normal conditions.

On the right side, the focus measured 7.5 mm along its longest axis. The lesion was polymorph: active and less active regions could be found along the same focus. The active regions showed increased vascularity and large bone marrow spaces that contained many cells, mostly fibroblasts, osteoblasts and some multinuclear osteoclasts. In the less active regions, the degree of lamellar bone formation was higher and the vascular channels less pronounced. The endosteal layer of the cochlear capsule remained intact and no hyalinization of the spiral ligament was found. However, the otosclerotic process had invaded the endosteal layer at the vestibule and the marginal cartilage of the oval window was partially replaced by otosclerotic tissue. Unfortunately, the stapes was missing in the histologic sections.

On the left side, the focus measured 4.8 mm along its longest axis. Here also, the focus was polymorph and showed the same histologic characteristics as on the left side. The otosclerotic process had invaded the endosteal layer at the apical turn of the cochlea. No hyalinization of the spiral ligament was found and the endosteal layer at the vestibule remained intact. No direct involvement of the stapedial footplate was visible. However, the morphology of the oval window niche was greatly disturbed by bony overgrowth as the marginal cartilage of the oval window was partially replaced by otosclerotic tissue.

The other two cases (TB 48 L and 110 R) demonstrated smaller foci in the anterior region of the oval window.

In TB 48 L, the focus measured 2 mm and was located anterior to the oval window, in the region of the fissula ante fenestram. The lesion only involved the endochondral and periosteal layers while the endosteal layer remained intact and no hyalinization of the spiral ligament was found. This focus was rather of the inactive type: the marrow spaces were narrow with small vessels and a lot of fibrous tissue. The footplate of the stapes was missing in the histologic sections.

In TB 110 R, the focus measured 1.8 mm and was also rather sclerotic: the lesion had a mosaic-like appearance because of irregular patterns of resorption and new bone formation associated with the deposition of fatty tissue in the marrow spaces. The otosclerotic process had very locally destructed the endosteal layer at the vestibule. However, the endosteum of the cochlear capsule remained
intact and no hyalinization of the spiral ligament could be recognized. Focal mineralization of the annular ligament was identified. Although the annular ligament was partially replaced by otosclerotic tissue and the footplate appeared to be in actual contact with the focus, a clear stapedial fixation could not be defined.

Discussion

The results on the prevalence of otosclerosis in this study are not in agreement with previous findings reported in the Caucasian population. Although its prevalence has been estimated to be up to 8.3% (table 2), in the present study only 6 of 236 temporal bones revealed otosclerotic foci (2.5%) or 4 of 118 autopsy cases (3.4%). In most studies, the frequency of stapedial fixation is 12–15% of histologic otosclerosis cases [7]. If the prevalence figure of the present study is used for extrapolation to calculate the prevalence of clinical otosclerosis, the calculated figure (0.30–0.38%) correlates well with the clinical data of otosclerotic families (clinical prevalence = 0.3%).

Our results are interestingly well in agreement with the histologic prevalence found in the Japanese population [20] suggesting a common biochemical pathway for the otosclerotic process.

In the present study, light microscopy has only been used to confirm the diagnosis in temporal bones with suspected otosclerosis when investigated by microradiography or slice macroscopy. Histology remains the gold standard to detect histologic otosclerosis. However, this method is not suitable to examine a large nonselected group of temporal bones within a reasonable period of time. Therefore, an alternative method with better cost-effectiveness was worked out, using a combination of microradiography and macroscopic evaluation of temporal bone slices. The temporal bone slices with suspected otosclerosis were further processed by conventional histologic techniques.

Since the smallest focus detected by this combination of methods measured 1.4 mm, any smaller foci would have remained undetected. However, the selection procedure was validated on the presence of false negatives: no histologic otosclerosis could be found in 15 randomly chosen temporal bones without any signs of otosclerosis either on slice macroscopy or microradiography.

According to Jørgensen and Kristensen [18], the smallest focus that can be detected by light microscopy is about 80 μm in diameter; only with this dimension can a medullary space and vascularized connective tissue be demonstrated. In the temporal bone collection at the University of Minnesota [19], about 31% of the otosclerotic foci were less than 2 mm. Schuknecht and Barber [26] detected small foci (<2 mm) in 23.9% of the collection at the Massachusetts
Eye and Ear Infirmary. When applying these figures to the present study, the true prevalence might have been one third higher: 3.3% of the temporal bones or 4.5% of the autopsy cases. Even then, the prevalence remains significantly lower.

With respect to otosclerosis, no selection of the material has been made in the present study. In contrast, previous publications were all based on existing laboratory collections and may have contained results biased by the presence of hearing loss or other otological diseases. Many of these publications include audiometric data recorded during life, questioning the unselected character of these temporal bone banks. Also many of these authors candidly admit that a certain selection had taken place when ascertaining the reasons for which the various institutions had sent them the temporal bones for histologic investigation.

Weber [17] examined temporal bones of the Leipzig clinic that were prepared for histologic study and found otosclerosis in about 10%. In 25%, blue strands as described by Manasse [27] were discovered in the bones. It is not clear if these lesions were interpreted as otosclerosis.

Engström [16] found 8 with otosclerosis out of 61 temporal bones (4 out of 34 autopsy cases), which is 11.8% of the sample population. He did not mention the origin of the temporal bones. Two of these 8 otosclerotic temporal bones are questionable because they displayed no real foci but merely areas of blue strands as described by Manasse [27]. Engström [16] interpreted these lesions as otosclerosis.

Guild [3] reported 43 otosclerotic individuals out of 518 autopsy cases (8.3% of the sample population) among whites older than 5 years. The percentage of otosclerotic temporal bones could not be calculated from his material. The temporal bones were from a laboratory collection. The hearing status of all patients was known from antemortem audiometry or from anamnestic data.

Jørgensen and Kristensen [18] were able to establish otosclerosis in 27 of 237 temporal bones (18 out of 155 autopsy cases), which is 11.4% of the temporal bones. They admitted that a certain selection had taken place when ascertaining the reasons for which the various institutions had sent them the temporal bones for histologic investigation.

Schuknecht and Kirchner [15] collected 910 serially sectioned temporal bones from 582 individuals. In the white population of 734 ears, the prevalence of histologic otosclerosis was 4.4%. In this investigation, only temporal bones without stapedial ankylosis were counted as true histologic otosclerosis cases. These authors also admitted that their material reflects the acquisition at autopsy of cases of otologic interest.

Hueb et al. [19] studied the entire collection of human temporal bones of the Otopathology Laboratory at the University of Minnesota. In this temporal bone collection, 82 otosclerotic cases were found in 643 individuals (12.75%).
However, in 37 ears, an antemortem audiogram was present, questioning the unselected origin of the material.

Morrison [10] suggested that the diagnosis of histologic otosclerosis may also be biased by the (histologic) overestimation of otosclerotic foci in the temporal bone sections.

In the past, much emphasis has also been placed on the presence of lesions known as ‘blue mantles’ [27]. According to some authors [18], these lesions represent pre-otosclerotic manifestations. However, according to Sørensen [28], blue mantles are incomplete perivascular secondary osteons, which can be found in every capsular layer of a normal temporal bone, including in the zone of ‘no remodeling’, and therefore they may not be regarded as pre-otosclerotic lesions. However, these blue mantles seem to be greatly exaggerated in otosclerotic temporal bones and merely indicate a local enhancement of capsular bone remodeling.

Finally, a correct interpretation of the prevalence figures is not always obvious since it is not always clear whether these figures refer to the percentage of persons or to the percentage of temporal bones studied. Moreover, Schuknecht and Kirchner [15] regarded all specimens with evidence of stapedial fixation as clinical otosclerosis, whereas other authors included such cases in the category of histologic otosclerosis.

However, there is no doubt that histologic otosclerosis (genotype) may occur in the absence of clinical otosclerosis (phenotype).

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Evidence of Increased Average Age of Patients with Otosclerosis

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Abstract

Otosclerosis is an inflammatory disease of the human temporal bone which was assumed to affect up to 10\% of the Caucasians. Histologic otosclerosis has an incidence of 3.4\%. It is considered as a major cause of hearing loss in Western countries while a low incidence is observed among Africans. Many hypotheses about its origin had been formulated in the past. Otosclerosis genes (\textit{OTSC1–5}) and collagen 1 genes are mutated in some familial cases of otosclerosis. On this genetic background, a common environmental factor such as a measles virus infection might be the triggering factor. Studies in the past indicated a distribution of otosclerosis among men and women of 1:1.4. Our study was designed to analyze the age of patients with otosclerosis at the time of surgery in the eighties and the nineties of the last century. Patients suffering from clinical otosclerosis who underwent stapedectomy between 1978 and 1999 with complete clinical data available (n = 1,351) were included in the study. Age and gender distribution, the age difference between men and women and the influence of gender and the year of recruitment were evaluated. Statistical analyses demonstrated an increase in the average age of patients with clinical otosclerosis from the eighties to the nineties (p = 0.012). The gender distribution showed no statistically significant variation (p = 0.398). These data might reflect an improved health consciousness among the elder population or could be the result of increased health awareness in the seventies and eighties. Finally, in the early seventies, measles virus vaccination was introduced in Germany and the shift of age could be the result of the measles virus immunization campaign.

Otosclerosis is considered among the major causes of hearing loss in the Western world [1–3]. The incidence of histologic otosclerosis is assumed at 10\% of temporal bones, but Declau et al. [4], in their study of unselected temporal bones,
found otosclerotic foci in 3.4%. This disease restricted only to the human temporal bone develops with foci of bone resorption and reactive bone formation in the ontogenetically weak border region between bone and cartilage. Epidemiologic investigations in the past confirmed a higher incidence of otosclerosis in women than in men and in about 50% of cases familial inheritance has been described, suggesting a role of hereditary and genetic factors [1]. The age of onset of hearing loss due to otosclerotic fixation of the stapes has been considered to be between 15 and 40 years with a 1.4–2.0 times higher incidence in women [1, 2].

The incidence in Caucasians and South Indians is higher than in Europeans, while people from China and Indonesia suffer less frequently from otosclerosis. About otosclerosis in Africa, there are only rare reports in the literature [2]. Early epidemiologic data suggested low frequency of otosclerosis among the Japanese population, but recent investigations showed an incidence similar to that in Europeans [5, 6]. In the United States, 15 million people suffer from otosclerosis and it is considered to be among the most common causes of acquired deafness. In the last 30 years, a clear decrease in surgical otosclerosis occurred [3].

Histologic investigations of otosclerotic foci gave evidence of a chronic inflammatory process within the temporal bone. Many etiopathogenetic reasons such as mechanical distress, enzymatic imbalance, particular localization of Paget’s disease, disease of the collagen tissue and others have been formulated. In some patients with otosclerosis, a particular genetic background could be detected. Mutations in otosclerosis genes (OTSC1–5) and collagen 1A1 were found in few families but no candidate genes have been sequenced up to now [7–9]. As a triggering factor, a measles virus (MeV) persistence was considered. Investigations by electron microscopy [10] and immunohistochemistry [11, 12] have shown the presence of MeV structures and proteins. Biochemical investigations have confirmed the strong MeV association with otosclerosis [13–15]. We and others observed MeV RNA within the otosclerotic tissue [13, 14, 16], but Grayeli et al. [17] failed to detect MeV RNA in otosclerotic tissue and cell culture. However, up to now no real proof has been found that MeV causes otosclerosis.

Since we felt that the average age of our patients increased over the years, we attempted to reevaluate the age of clinical onset of otosclerosis and the gender distribution considering the increased consciousness of health.

**Patients and Methods**

We included all patients with clinical otosclerosis who had undergone stapedectomy or stapedotomy in our Department of ENT, Head and Neck Surgery, Munich, Germany, between 1978 and 1999 (n = 1,351). Clinical diagnosis of otosclerosis was based on ear microscopy, air and bone conduction audiogram and speech data for Freiburger monosyllabic words, tympanogram, stapedial reflex and radiography of the mastoid. The footplate fragments were
fixed, decalcified and paraffin embedded. Histologic examination of the hematoxylin/eosin-stained fragments confirmed sclerosis of the ligamentum annulare in all cases. All patients had spent the major part of their lives in Germany. The study group consisted of 798 (59%) women and 553 (41%) men and all clinical data were available. The distribution of age was analyzed for normal distribution. The gender distribution over the recruitment period was tested with the \( \chi^2 \) test. The differences of age between women and men were evaluated with Student’s t test. A multivariate analysis of variance was performed to determine the influence of gender and year of recruitment. The level of significance was fixed at 5%. SPSS version 10 was used.

**Results**

Univariate analysis of the age of patients showed a statistically significant increase in the period examined (\( p = 0.012 \); table 1, fig. 1). An increase in the proportion of women at the limit of significance (\( p = 0.054 \)) was observed in the

<table>
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<tr>
<th>Year of surgery</th>
<th>Patients ( n )</th>
<th>Mean age ± SD years</th>
</tr>
</thead>
<tbody>
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<td>1978</td>
<td>42</td>
<td>39.60 ± 10.83</td>
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<tr>
<td>1979</td>
<td>43</td>
<td>40.12 ± 9.93</td>
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<tr>
<td>1980</td>
<td>60</td>
<td>37.88 ± 13.54</td>
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<tr>
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<td>1999</td>
<td>38</td>
<td>45.05 ± 10.88</td>
</tr>
<tr>
<td>Total</td>
<td>1,351</td>
<td>43.57 ± 12.5</td>
</tr>
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</table>
Fig. 1. Statistical analysis of the patients’ average age over the period of recruitment.

univariate analysis of the distribution of gender. The difference of age between women and men \( (p = 0.398) \) (figs. 2, 3) was not statistically significant. The multivariate analysis confirmed that there is a significant increase in the patients’ age over the period of recruitment \( (p = 0.012) \) while the increase in the incidence of otosclerosis in women in comparison with men from 1978 to 1999 was not statistically significant \( (p = 0.418; \) fig. 4).

**Discussion**

The statistical analysis of the available data gave evidence of an increase in the average age of patients with clinical otosclerosis in the recruitment period from 1978 through 1999, while no change in the distribution among gender and incidence in women and men occurred. The prevalence of otosclerosis in women is well known and our results are in good agreement with data published in the past. Various reasons were discussed: estrogens induce the proliferation of osteoblasts and calcification. The fact that otosclerosis occurs in women in particular after pregnancy supports this hypothesis. Furthermore, the administration of estrogens as contraceptives could explain the higher incidence of otosclerosis in women, whereas the low dose of hormones in the new generation of
**Fig. 2.** Distribution of females in the years from 1978 to 1999.

**Fig. 3.** Distribution of males in the years from 1978 to 1999.
contraceptives may prevent the development of otosclerosis in early years. Administration of estrogens in the postmenopausal phase could explain the cases of otosclerosis in advanced age. However, in a large study, the influence of estrogens on the development of otosclerosis could not be confirmed [18].

The increase in the average age of onset of otosclerosis was clearly demonstrated in this study, considering some socioeconomic factors. The disattention of young patients regarding a progressive hearing loss because of social problems such as unemployment may play a role. This is confirmed by the fact that otosclerosis seems to be more frequent among people of higher social classes with minor social problems. However, in the last few years, concern about a high quality of life has increased and today patients do not put up with even small hearing problems. Another explanation for the increase in the age of patients with otosclerosis could be that large numbers of young patients with even a small air bone gap were operated in the seventies and eighties because of increased health awareness.

An increase in the use of fluoridated water was discussed as a reason for the decrease in otosclerosis. However, in a large study, this hypothesis could not be confirmed [19].

Finally, we have noted that the decrease in the incidence of otosclerosis in younger people coincides with the introduction of MeV vaccination in Germany. The distribution of otosclerosis among women and men showed no significant change in the period of recruitment (women:men = 1.4–1.6:1). Our data
confirm the results from previous reports [1, 2]. Garenne [20] has reported a statistically significantly increased measles mortality for women during the reproductive period which is 1.4 times higher. One explanation discussed by Garenne is an immunologic weakness in the defense against MeV in women. However, our findings are in good agreement with investigations reported in the past.

Morphological and biochemical investigations in the past have shown a strong association between MeV and otosclerosis [15]. Since 1965, MeV vaccination with attenuated live Edmonston-strain-derived virus has been employed [21]. The administration of MeV vaccines has dramatically decreased the incidence of measles in all countries in which it has been effectively delivered (data from Centers of Disease Control and Prevention). In 1979, the USA identified as a goal the elimination of measles. Vaccination in the USA has led to a statistically significant reduction of MeV-related diseases, MeV inclusion body encephalitis and subacute sclerosing panencephalitis [22]. Otosclerosis has also decreased in the USA over the past 30 years. The authors state that the widespread immunization against MeV is a plausible reason [3].

However, the mechanisms of immunity are not completely understood. The duration of vaccine-induced immunity appears to be variable and the secondary vaccine failure rates have been estimated to be approximately 5% at 10 years after immunization [23]. Recently, we have genotyped MeV within the otosclerotic tissue of patients born in the sixties to group A which circulated in Europe before 1970 [unpubl. data]. This result confirms that MeV persists over several decades within the otosclerotic tissue. Studies on tissue from young patients immunized in the past could clarify which genotype – even the vaccination strain – can persist in the human temporal bone. We do not have any data which ascertain MeV persistence as the true cause of otosclerosis. MeV affects only humans and the genetic background certainly plays an important role. Thus, animal studies do not seem to be helpful to elucidate the causal role of MeV; however, epidemiologic data may contribute to answer this question.

In conclusion, there is evidence of a decrease in otosclerosis in patients aged between 20 and 40 years; however, the gender distribution did not change. The use of low-dose contraceptives, socioeconomic factors and vaccination strategies may partly explain these data. Further studies should be undertaken in the future to reevaluate the incidence and age of onset of otosclerosis.

References


Some Remarks on the Histopathology of Otosclerosis

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Abstract

The histopathology of otosclerosis is described in detail in classical textbooks like Schuknecht's *Histopathology of the Ear* or Friedmann and Arnold's *Pathology of the Ear*. In this article, some of the important and new facts will be summarized which might affect the understanding of the pathomechanism of this unique measles-virus-associated inflammatory disease of the temporal bone.

The pathological process of the disease can be summarized as follows: lacunar resorption of the bone by osteoclasts (macrophages), initiated by an unknown pathological, probably viral stimulus affecting the cartilaginous cell nests (globuli interossei) at certain sides of anatomical predilection. The term ‘otosclerosis’ refers, of course, to the final inactive stage of the process (scar formation), whereas the essential pathological lesion is in fact an inflammatory replacement of the lamellar bone by a bone of greater thickness, cellularity and vascularity. The term ‘otospongiosis’ refers to the active inflammatory vascular stage of the process. The disease may be present for years without causing deafness. (The histopathology of otosclerosis is described in detail in Schuknecht [1] and Friedmann and Arnold [2].)

The most frequent onset of the progressive hearing impairment has been between the age of 20 and 30; however, today there is a shift to the age of 40 and 50. The histological lesion of the otic capsule begins several years before the onset of stapes ankylosis. The rate of progression depends on the individual, i.e. periods of rapid extension alternating with quiescent phases in some patients, while in others, the lesion steadily progresses. Pregnancy, puberty and the menopause may stimulate the rate of progress probably under the influence of
Estrogens [3]. Estrogens are known to activate osteoblasts, so estrogens may have some influence on the otospongiotic lesion changing it into a sclerotic scar. That is why during pregnancy the former otospongiotic lesion near the oval window changes into a sclerotic stage causing conductive hearing loss.

Often a familial disease (30–50%), otosclerosis may be inherited as a mendelian dominant trait and is more common in females: the microscopical incidence of otosclerosis in routine postmortems is about 1 in 8 middle-aged white females, and 1 in 15 adult white males [4]. Histological otosclerosis without symptoms of any kind is about 10 times more common than clinical otosclerosis with stapes fixation producing a conductive hearing loss [5]. In the largest series of temporal bones analyzed to date [4] among 1,161 specimens, 4.39% exhibited otosclerosis. Many of the temporal bones, however, were from black people and it is now well recognized that otosclerosis is rare in the African races. Data collected by Seifer et al. [6] indicated that among 601 temporal bones of white American adults, the histological incidence of otosclerosis was 8.3%. The incidence of stapedial fixation amounted only to 0.99% [7]. Thus, although every 10th adult person has otosclerotic foci within the temporal bone, hearing problems of the conductive type may affect only 1 in every 100 people.

Although any part of the petrous temporal bone may be the side of otosclerosis, the abnormal bone tends to form at particular points, most commonly at the ‘otosclerotic angle’, which is between the anterior part of the stapedial footplate, the cochleariform process and the bulge of the promontory. By extension posteriorly, this focus infiltrates and fixes the stapes, producing conductive deafness. The entire footplate may be involved, the anterior end only, or both ends, leaving the middle of the footplate intact (fig. 1).

There are certain local anatomical features of the osseous labyrinth, e.g. the fissula ante fenestram and the cartilagenous rests of the enchondral bone of the otic capsule near the oval window, which may offer a locus minoris resistentiae to some inflammatory agents like measles viruses. It should be underlined that more than 90% of all otospongiotic or otosclerotic lesions are in contact with the middle ear mucous membrane as well as with the perilymphatic space (fig. 2a, b).

Otosclerotic foci in other areas of the labyrinthine capsule or in the walls of the internal acoustic meatus can occur simultaneously or in rare cases isolated. In about 70–80% of patients, both temporal bones are affected and the otosclerotic lesions more often than not display a striking similarity in regard to localization, extent and direction of growth. Unilateral histological otosclerosis only occurs in about 20–30%.

The fundamental pathological process of otosclerosis can be summarized as lacunar resorption of the bone by macrophages, initiated by an inflammatory stimulus. Within otospongiotic lesions, a mixed cellular infiltrate can be
observed, consisting of lymphocytes, macrophages and plasma cells. Macrophages which are capable of presenting antigen in association with major histocompatibility antigens (MHC) class I and class II to CD8+ and CD4+ T-cells, respectively, were found in otospongiotic lesions based on their expression of the MAC387 antigen. Furthermore, HLA-DR-positive cells and complement C3 have been found in resorption lacunae of otosclerotic lesions. Several osteoblasts and chondrocytes in active otosclerotic lesions reveal a strong surface expression of β2-microglobulin, indicating an increased MHC class I antigen expression in active otosclerotic lesions. In agreement with
recently published data, we found that a large fraction of the lymphoid cells are antigen-primed T-cells expressing an \( \alpha/\beta \) T-cell receptor in association with CD3 molecules on their surfaces. CD4+ lymphocytes which functionally represent lymphokine-secreting cells are activated through the specific recognition of antigen, presented in context with MHC class II molecules such as HLA-DR. Therefore, the presence of MHC-class-II-positive cells is crucial for the initiation of a local immune response. The observation of HLA-DR-positive cells in otospongiotic lesions is of particular interest. Cells expressing the MHC-class-I-associated protein \( \beta_2 \)-microglobulin are potential target cells for CD8+ T-lymphocytes which functionally mainly represent cytotoxic T-lymphocytes that are also capable of secreting distinct lymphokines, such as interferon-\( \gamma \) (fig. 3a–d). In this context, the observed strong expression of \( \beta_2 \)-microglobulin by osteoblasts and chondrocytes may be of importance for the pathogenesis of otospongiotic lesions. The significance of these findings for an improved understanding of the etiology of otosclerosis remains open, but the findings point at an infectious agent, such as a virus infection, as the primary cause of the inflammatory response of the bone [8–10].

Fig. 3. Infiltration of CD8+ lymphocytes around new vessel formation in a resorption lacuna. Expression of HLA-DR in pervascular macrophages. Expression of \( \beta_2 \)-macroglobulin within pericapillary cells. Complement C3 in the perivascular tissue.
What is the factor stimulating the proliferation and aggressive infiltration of the blood vessels (angiogenesis) into the bone of the otic capsule, accompanied by a variety of inflammatory cells including lymphocytes, granulocytes, macrophages and occasional mast cells? The author has examined parts of the footplates from patients at various histological stages of otosclerosis by immunohistochemical methods with particular reference to the distribution of specific antibodies (IgG, IgA, IgM) and the presence and distribution of the viral antigens of measles [9]. Antibodies IgG, IgA and IgM were found to be bound to the vascular connective tissue of the resorption lacunae and IgG also to osteocytes. In specimens showing inactive otosclerosis, no IgG or IgM were present. The active phase of otosclerosis (otospongiosis) appears to be related to IgG fixation (together with C1q and C3 complements), stimulated by a humoral immunological process. The application of antibodies against measles antigens showed the expression of the relevant viral antigens in the large cells of the resorption lacunae, in the vascular connective tissue and in osteocytes, osteoclasts (macrophages) and chondrocytes, present in or around the otospongiotic areas (table 1).

This investigation has provided evidence of the presence of measles virus antigens in all the otospongiotic specimens studied. In contrast, the sclerotic specimens as well as the unaffected parts of the otosclerotic stapes, used as controls, expressed none of the viral antigens. The viral antigens are more strongly expressed by the cells of the perivascular tissue and by various inflammatory cells and macrophages present in the resorption lacunae. This suggests that the

| Table 1. Cell type distribution and immunohistochemical reaction of characteristic cell elements within the otospongiotic and otosclerotic focus |
|---------------------------------|------------------|------------------|
| T-lymphocytes (80%)             | ++               | –                |
| B-lymphocytes (20%)             | +                | –                |
| Plasma cells (mainly B-lymphocytes) | +        | –                |
| Complement C3 (lytic activity)  | +++              | –                |
| HLA-DR+ (MHC) (activity of macrophages) | +++     | –                |
| β₂-Microglobulin (activation of macrophages) | +++     | –                |
| IgG                             | +++              | (+)              |
| IgA                             | ++               | –                |
| IgM                             | –                | –                |
| Measles virus antibodies        | +++              | (−)              |
| (chondrocytes, osteocytes, perivascular spaces, middle ear mucous membrane) |          |                  |

Histopathology of Otosclerosis
aggressive proliferation of the vascular connective tissue might be initiated in
the early stages of otospongiosis and subsequently maintained by the measles
viruses. However, otospongiosis today must be respected as an inflammatory,
osteolytic bone disease associated with a measles virus infection. There is other
unproven but logical support for this pathogenesis as the incidence of otoscle-
rosis has markedly decreased as immunization practices have improved.

This today well-accepted concept of a measles-virus-associated inflamma-
tory disease is supported by recent convincing results from Niedermeyer et al.
[11], Lolov et al. [12], Niedermeyer and Arnold [13] and Karosi et al. [14].

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Otosclerosis and Associated Otopathologic Conditions

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Abstract

Otosclerosis occurring with other pathologies has received little attention in the literature although these concomitant occurrences can be clinically relevant. We studied the clinical and histopathological characteristics of 182 cases of otosclerosis from our human temporal bone collection, and found 81 (44\%) to have associated pathologies. Clinical pathological findings included vestibular symptoms and findings (e.g. Ménière’s syndrome), otitis media in various forms, and to a lesser extent labyrinthine anomalies, tumors and other associated pathologies. Whether these coexisting pathologies are coincidental (usually) or causative as in the case of Ménière’s syndrome with extensive otosclerosis, appropriate diagnosis and treatment of the patient with otosclerosis requires recognition of these potential clinical pathological relationships.

Otosclerosis is a disorder limited to the bony labyrinth and stapes. First described by Politzer in 1893, it was later confirmed by Siebenmann, who recognized the progression from otoporosis during the active and vascular stage of the disease to the eventual final stage of sclerosis of the otic capsule. He later proposed a change of nomenclature from otosclerosis to otospongiosis [1]. The prevalence of otosclerosis has been estimated to be 0.1–1.0\%, with an average of 0.3\% [2]. Hueb et al. [3] studied the entire collection of human temporal bones at the University of Minnesota, excluding infants and individuals of races other than white and found the incidence of histologic otosclerosis to be 12.75\%. The disease is probably autosomal dominant with incomplete penetrance (estimated at 40\% by several epidemiological studies) [4]. On the other hand, otosclerosis is rare among blacks, Asians, and American Indians [5].
Stapedial surgery dates back to 1878 when Kessel mobilized the stapes. In 1924, Sourdille reported tympanolabyrinthopexy, a two-staged procedure that demonstrated long-term results. In 1941, Lempert made it a single-staged procedure. Shea was credited with the first successful stapedectomy in 1956 and since has revolutionized stapedial surgery. Other otopathologic conditions associated with otosclerosis, frequently overlooked, can affect diagnosis and treatment of this disease. The purpose of this study was to identify the prevalence and types of associated otopathologic conditions in our collection of temporal bones with otosclerosis.

**Materials and Methods**

The entire collection of the temporal bone bank at the University of Minnesota was searched for those bones with otosclerosis. Out of 1,884 temporal bones, 182 from 103 patients with a histologic diagnosis of otosclerosis were examined for the presence of associated pathologic conditions. The conditions searched for included: otitis media, acoustic neuroma, endolymphatic hydrops, enlarged vestibular aqueduct, labyrinthine dysplasia, and labyrinthitis. The category of otitis media was divided into serous, mucoid and chronic. Fibrous labyrinthitis confined to the site of stapedectomy was excluded.

Classification of otitis media was based on the characteristics of fluids and pathologic changes in the middle ear. For serous otitis media, the middle ear had to exhibit serous fluid containing a few inflammatory cells and no epithelial hyperplasia. For mucoid otitis media, the middle ear cavity had to exhibit mucoid effusion and hyperplastic and hypersecretory changes of the mucoperiosteum. For chronic otitis media, the temporal bone had to show intractable pathologic conditions such as cholesteatoma, cholesterol granuloma, or granulation tissue. Ménière’s disease was a clinical diagnosis obtained from review of the medical charts with histologic confirmation. Definitions of the rest of the pathologic conditions in temporal bones were based only on histologic findings. Clinical data and histopathologic findings were tabulated, and the data were examined for comparison and correlation.

**Results**

Of the 182 temporal bones from 103 patients with otosclerosis that we examined, 81 (44%) in 57 patients (55.3%) were found to have associated conditions. Of these, 20 temporal bones (24.7%) in 15 patients (26.3%) had more than one associated condition. Two otopathologic changes occurring in the same ear were detected in 18 of those 20 temporal bones, and three otopathologic conditions were observed in the remaining 2 temporal bones. The 57 human donors (30 men, 27 women) of the 81 temporal bones with otosclerosis and associated otopathology ranged in age from 21 years to 90 years, with a mean age of 68 years.

The frequencies of pathologic conditions associated with otosclerosis are listed in table 1. Multiple conditions in the same ear are reported for each
condition. The most frequently occurring with otosclerosis were chronic otitis media (34%), endolymphatic hydrops without Ménière’s disease symptoms (28%), and serous labyrinthitis (15%). The remaining otopathologic conditions each occurred in less than 10% of the ears. Both of the two acoustic neuromas were identified by histologic diagnosis. There was more than one otopathologic condition in 12 out of 35 (34%) temporal bones with chronic otitis media, 10 out of 29 (34%) temporal bones with endolymphatic hydrops, and 9 out of 16 (56%) temporal bones with serous labyrinthitis (tables 1, 2). Bilateral associated otopathologies were observed in 24 patients (42%).

**Otosclerosis and Genetic Labyrinthine Anomalies**

In this study, 3 patients demonstrated enlarged vestibular aqueducts. Other anomalies are possible. The relationship of otosclerosis and anomalies of the inner ear should be considered coincidental and not causative.

**Categorical Description of Histological Anomalies**

Vestibular aqueducts were enlarged in 3 patients (6 temporal bones). Histopathologic examination of these 3 patients revealed that otosclerosis was located anterior to the oval window. In only 1 case was stapedial fixation due to otosclerosis observed. Involvement of the cochlear endosteum was not

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Ears</th>
<th>More than one pathologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic otitis media</td>
<td>35 (34)</td>
<td>12</td>
</tr>
<tr>
<td>Endolymphatic hydrops</td>
<td>29 (28)</td>
<td>10</td>
</tr>
<tr>
<td>Serous labyrinthitis</td>
<td>16 (15)</td>
<td>9</td>
</tr>
<tr>
<td>Ménière’s disease</td>
<td>8 (8)</td>
<td>3</td>
</tr>
<tr>
<td>Large vestibular aqueduct</td>
<td>6 (6)</td>
<td>5</td>
</tr>
<tr>
<td>Ossicular (non-stapes) fixation</td>
<td>4 (4)</td>
<td>1</td>
</tr>
<tr>
<td>Acoustic neuroma</td>
<td>2 (2)</td>
<td>1</td>
</tr>
<tr>
<td>Purulent labyrinthitis</td>
<td>1 (1)</td>
<td>1</td>
</tr>
<tr>
<td>Serous otitis media</td>
<td>1 (1)</td>
<td>–</td>
</tr>
<tr>
<td>Mucoid otitis media</td>
<td>1 (1)</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>103 (100)</td>
<td>–</td>
</tr>
</tbody>
</table>

Figures in parentheses indicate percentages.
seen in any of these cases. No other histological areas of involvement were observed (fig. 1).

Clinical Interpretations

If symptoms and findings in the inner ear indicate, a CT scan with enhancement should be ordered. We do not routinely order CT scans in patients considered for stapedectomy. In the absence of significant symptoms in the inner ear, and in the presence of a significant conductive hearing loss, stapedectomy should provide a safe and satisfactory result.

Otosclerosis and Adjacent Tumors of the Temporal Bone

In 2 temporal bones, vestibular schwannomas (acoustic tumors) were identified in addition to otosclerosis. Here too, the coexisting histopathology should

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Table 2. Cases of multiple pathologic conditions associated with otosclerosis

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Multiple otopathologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>38R</td>
<td>Endolymphatic hydrops Serous labyrinthitis</td>
</tr>
<tr>
<td>136L</td>
<td>Endolymphatic hydrops Large vestibular aqueduct</td>
</tr>
<tr>
<td>136R</td>
<td>Endolymphatic hydrops Large vestibular aqueduct</td>
</tr>
<tr>
<td>155L</td>
<td>Serous labyrinthitis Large vestibular aqueduct</td>
</tr>
<tr>
<td>155R</td>
<td>Serous labyrinthitis Large vestibular aqueduct</td>
</tr>
<tr>
<td>159R</td>
<td>Chronic otitis media Large vestibular aqueduct</td>
</tr>
<tr>
<td>216R</td>
<td>Endolymphatic hydrops Chronic otitis media</td>
</tr>
<tr>
<td>225L</td>
<td>Chronic otitis media Serous labyrinthitis</td>
</tr>
<tr>
<td>225R</td>
<td>Chronic otitis media Serous labyrinthitis</td>
</tr>
<tr>
<td>269L</td>
<td>Chronic otitis media Ménière’s syndrome</td>
</tr>
<tr>
<td>276R</td>
<td>Endolymphatic hydrops Chronic otitis media</td>
</tr>
<tr>
<td>357L</td>
<td>Endolymphatic hydrops Chronic otitis media</td>
</tr>
<tr>
<td>365L</td>
<td>Chronic otitis media Acoustic neuroma</td>
</tr>
<tr>
<td>365R</td>
<td>Chronic otitis media Endolymphatic hydrops</td>
</tr>
<tr>
<td>374R</td>
<td>Endolymphatic hydrops Purulent labyrinthitis</td>
</tr>
<tr>
<td>559L</td>
<td>Ménière’s syndrome Serous labyrinthitis</td>
</tr>
<tr>
<td>559R</td>
<td>Ménière’s syndrome Serous labyrinthitis</td>
</tr>
<tr>
<td>648L</td>
<td>Chronic otitis media Serous labyrinthitis</td>
</tr>
<tr>
<td>693L</td>
<td>Endolymphatic hydrops Chronic otitis media</td>
</tr>
<tr>
<td>912L</td>
<td>Endolymphatic hydrops Chronic otitis media</td>
</tr>
</tbody>
</table>

L = Left; R = right.
be considered coincidental in its occurrence and not causative. If our series were large enough, it is likely that other tumors might be associated with otosclerosis, including glomus jugulare tumors and primary and secondary carcinomas.

**Categorical Histological Description**

One of the temporal bones with acoustic neuroma showed otosclerosis located anterior to the oval window and involving the stapedial footplate. The other temporal bone had multiple otopathologic conditions containing otosclerosis that fixed the stapedial footplate and was located anterior to the oval window. The temporal bone also had cholesteatoma, cholesterol granuloma, acoustic neuroma, and serous labyrinthitis (fig. 2).

**Clinical Interpretations**

It seems not only prudent but also obvious that a patient should not have a stapedectomy if a tumor exists in the temporal bone (intrinsic or extrinsic). Some might argue that a small, non-growing vestibular schwannoma might be an exception; however, since the future cannot be predicted, we believe a hearing aid would be preferable. The primary effort should be to diagnose and manage the tumor, medically or surgically, as indicated.

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*Fig. 1.* This temporal bone with a large vestibular aqueduct has an otosclerotic focus (O) anterior to the oval window involving the footplate. The arrow indicates the internal opening of the vestibular aqueduct. HE. ×20 (original magnification).
Otosclerosis is a disease of the inner ear with an occasional (approximately 10%) manifestation in the middle ear, particularly a conductive hearing loss due to secondary fixation of the stapes. It is a disease of the osseous labyrinth (in particular the membranous labyrinth) and can occur in 14 predilective sites, the most frequent being in cartilaginous arrest sites such as the fissula ante fenestram and, to a lesser degree, the fossula post fenestram. Otologists agree, and it is easy to understand how otosclerosis from these closely adjacent sites invades the annular ligament and footplate of the stapes, causing fixation.

It is well established by many studies that otosclerosis can frequently cause a sensorineural hearing loss as well as a conductive loss. They can occur as concomitant hearing losses or either can be the dominant loss. Many theories and mechanisms of how otosclerosis causes sensorineural hearing loss have been described. The two most generally accepted mechanisms appear to be (1) direct invasion of otosclerosis into the endosteal layer of the cochlea with secondary possible involvement of the spiral ligament, stria vascularis, osseous spiral lamina, fluid spaces, and sensorineural cellular elements, or (2) the release of toxins or metabolites from adjacent otosclerotic foci into the membranous labyrinth.

The first such relationship was described in 1966 [6]. It is somewhat surprising that the literature has paid scant attention to vestibular symptoms and

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**Fig. 2.** This 86-year-old woman had chronic otitis media with cholesteatoma (arrow). Cholesterol granuloma (C), labyrinthitis, otosclerosis (O) and vestibular schwannoma (VS). HE. ×20 (original magnification).
Otosclerosis and Associated Pathologies

This is especially so when we observe the immediate proximal location of common otosclerotic foci and critical vestibular structures such as, to mention two, otosclerotic foci in the fissula ante fenestram in its close proximity to the utricle, and an otosclerotic focus adjacent to and involving the utricular nerve and the elliptical utricular macula. Vestibular symptoms can occur with otosclerosis and may include a sense of disequilibrium, positional and motion-related vertigo, and dizziness, as well as incapacitating vertigo from Ménière’s disease. To repeat: otosclerosis is a disease of the inner ear, and it is true that cochlear symptoms (especially sensorineural hearing loss and tinnitus) are more common than vestibular symptoms. Theoretical reasons might include the fact that the pars superior is phylogenetically and embryologically much older than the pars inferior.

Categorical Histological Descriptions

In this group, 6 patients (8 ears) had a clinical diagnosis of Ménière’s disease, and their endolymphatic hydrops was very profound. Three patients had otosclerosis encircling so as to obstruct the vestibular aqueduct [9, 10] (fig. 3). However, 1 patient showed only a small focus of otosclerosis in the region of the round window. In other cases with no history of vertigo, the histologic appearance of endolymphatic hydrops was mostly slight in character in the cochlea and saccule. Involvement of the area anterior to the oval window was observed in all these temporal bones. Nine temporal bones also showed involvement of the endosteum of the cochlea. The footplate was affected in 20 temporal bones.

Fig. 3. There is active otosclerosis (O) surrounding the endolymphatic duct in this temporal bone. HE. ×20 (original magnification).
Other sites of involvement were the round window membrane (in 2 temporal bones), and posterior to the oval window (in 2 temporal bones) in addition to involvement of the area anterior to the oval window [9, 10] (fig. 4a, b).

Clinical Interpretation
In our clinic, a patient with a conductive loss considered to have otosclerosis and vestibular symptoms will receive a workup comparable to that for a patient with typical Ménière’s disease including a comprehensive audiogram that consists of behavioral pure-tone and bone conduction testing, testing of speech reception threshold, testing of word discrimination, and a tympanogram. In addition, electronystagmography, auditory brainstem response tests, and electrocochleography will take place. An MRI with gadolinium is ordered if indicated by the clinical picture and findings on auditory brainstem response tests. In this group of patients, we have found some with vague disequilibrium or positional vertigo or positional dizziness. We have also diagnosed and treated patients with vertigo, including more than 40 with incapacitating vertigo and a clinical syndrome of Ménière’s disease. This group of patients may or may not reveal electronystagmography caloric hypofunction.

Typical features of patients with Ménière’s disease and otosclerosis include episodes of vertigo associated with nausea and vomiting, associated concomitant symptoms of pressure, tinnitus, inability to tolerate loudness, and to a lesser extent fluctuating sensorineural hearing loss. Patients with otosclerosis and Ménière’s disease are first diagnosed and then managed medically. For these patients and for the treating otologist, vertigo is usually more important than hearing loss. If they become intractable and fail medical therapy, we have successfully performed
stapedectomy/sacculotomy in this group [7] (fig. 5). Results in this category are rewarding, with the majority of patients having loss or significant reduction of vestibular symptoms. In no patient had vertigo become worse, and no patient developed significant sensorineural hearing loss. One patient with persistently severe sensorineural hearing loss and continued vestibular symptoms received a labyrinthectomy, and 3 patients ultimately received endolymphatic sac enhancement because of continued symptoms.

The relationship of the histopathology of vestibular otosclerosis and vestibular symptoms is correlatable in some cases. For example, if otosclerosis invades and obstructs the vestibular aqueduct so as to cause endolymphatic hydrops, it is readily understood why endolymphatic sac surgery might not be beneficial. We look forward to more correlative studies in the future to assess the causative or coincidental relationship of otosclerosis and vertigo.

**Otosclerosis and Otitis Media**

The most common associated finding was otitis media in its various forms (36%) and its sequelae, including eustachian tube dysfunction and atelectasis.
In general, these findings, usually insidious and not obviously detected, are commonly coincidental and not causative. Various forms of otitis media were associated with otosclerosis in this group: (1) serous otitis media, (2) mucoid otitis media, and (3) chronic otitis media and mastoiditis (associated with cholesteatoma, cholesterol granuloma, and granulation tissue). Sequelae, almost always associated with eustachian tube dysfunction, included atelectasis, ossicular fixation, and ossicular dysfunction. Tympanosclerosis and osteoneogenesis are also seen, and stapedial fixation can, in addition to otosclerosis, result from tympanosclerosis and osteoneogenesis.

**Categorical Histological Descriptions**

The histopathologic diagnosis of chronic otitis media was based on pathologic changes in the middle ear such as cholesteatoma, cholesterol granuloma, or granulation tissue. The histologic appearance of endolymphatic hydrops was mostly slight in character in the cochlea and saccule. Involvement of the area anterior to the oval window was observed in 29 out of 35 (83%) temporal bones. In 26 (74%), this was the only site of involvement. Five temporal bones also showed involvement of the endosteum of the cochlea. The footplate was affected in 7 temporal bones (20%). Other sites of involvement were the round window membrane (in 6 temporal bones), and posterior to the oval window (in 3 temporal bones) in addition to involvement of the area anterior to the oval window (fig. 6).

![Fig. 6. This temporal bone contains an otosclerotic focus (O) anterior to the oval window with active chronic otitis media in the middle ear. MEE = Middle ear effusion. HE. ×20 (original magnification).](image-url)
Clinical Interpretation

Certainly, stapedectomy should never take place in the presence of active infection from purulent otitis media or chronic otitis media. In recent years, we have found it preferable to perform stapedectomy under general anesthesia to avoid sudden movements on the part of the patient. We routinely perform a small myringotomy in the anterosuperior quadrant to avoid changes in pressure during postoperative recovery. In occasional select cases, if a patient has a negative tympanogram, slight or moderate atelectasis, or a history of eustachian tube ventilation dysfunction, a myringotomy and a No. 1 Paparella ventilation tube is placed in the anterosuperior quadrant, which also allows the patient to fly sooner postoperatively than otherwise. If a patient has stapedial or other ossicular fixation due to tympanosclerosis, careful removal of tympanosclerosis and mobilization of the stapes is done, which obviates stapedectomy in our experience in all cases to date.

In earlier years, we performed a second stage so as to make the ear dry and safe in cases of tympanomastoidectomy for chronic otitis media/chronic mastoiditis. The risk is too high for type 5 tympanoplasty in this group, and this procedure had been abandoned years ago. If, however, after tympanoplasty, the mesotympanum and ossicles are intact, a stapedectomy can be very successful, and again a myringotomy and ventilation tube compensates for possible eustachian tube ventilation dysfunction thereafter [11].

The incudal long process might be missing, either from previous stapedial surgery or as a sequela of otitis media, particularly in cases of atelectasis. Here we have used 2 procedures successfully, either (a) a stapedectomy with a custom-made malleus-to-oval window prosthesis, using stainless steel wire and collagen, or (b) a total ossicular replacement prosthesis (TORP) can be used with a graft of the oval window and the TORP stabilized under the malleus after incising the tensor tympani muscle and enlarging the mesotympanum. In the latter case, it is important to use a ventilation tube to prevent the TORP from invading the vestibule.

Associated Clinical Pathologic Conditions

There are 2 other associated clinical pathologic conditions revealed in our study of otosclerosis. One is otosclerosis and cochlear implantation, and the other is otosclerosis as a cause of conductive hearing loss due to obstruction of the round window.

A patient may appear deaf on the audiogram. It is always important to take a history and provide a thorough examination. Using an electronic Barany box in one ear, spondee words are shouted in the other ear while masking the opposite ear. Tuning forks are used for Rinne testing, again while masking the opposite
ear. If a patient has a conductive component, even in the presence of complete deafness, revealed by testing with a tuning fork and not the audiogram, then an exploratory tympanotomy and a stapedectomy should and can be done. These are the happiest patients of all our patients with stapedectomies. A deaf ear can be brought to a speech reception threshold of, e.g., 60 dB, and a hearing aid can be used very successfully. We feel certain that some of the best results for cochlear implantation occur in these patients who might otherwise benefit from stapedectomy and a hearing aid (fig. 7).

Another occasional clinical phenomenon is continued postoperative conductive deafness after a routine stapedectomy. Upon revision, the prosthesis and oval window may look perfect. One cause of persistent conductive deafness is otosclerosis that can selectively obstruct the round window and primarily occurs in the scala tympani and may be difficult to detect during exploratory tympanotomy (fig. 8).

**Discussion and Conclusion**

The idea of multiple coexistent pathologic conditions occurring in the temporal bone has been described in previous publications [12]. Here we concentrate on those pathologic conditions associated with otosclerosis as determined from a study of our histological collection of human temporal bones. Coexisting

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*Fig. 7.* There is active otosclerosis (O) anterior to the oval window in this patient who received a cochlear implant. The electrode sites (arrows) are seen in the basal turns of the cochlea. HE. ×20 (original magnification).
Pathologic conditions can be coincidental, as is the case for most patients, but still preoperative and postoperative diagnostic considerations should include these possibilities. Another possibility is that these pathologic conditions can be causative, as is seen in the examples of advanced Ménière’s disease following otosclerosis with obstruction of the vestibular aqueduct. Recognition of these histological relationships has direct clinical application to the diagnosis and treatment of patients with otosclerosis. It is hoped that this study encourages a heightened awareness of appropriate diagnosis for this category of patients. Sometimes these pathological findings can only be assessed during exploratory tympanotomy for consideration of stapedectomy.

References


Fig. 8. In this temporal bone, otosclerosis obstructs the round window, involving the scala tympani (ST) of the cochlea. ME = Middle ear. HE. ×20 (original magnification).

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Expression of Collagens in the Otosclerotic Bone

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Abstract

The etiopathogenesis of otosclerosis is still controversially discussed. The major hypotheses discussed are a viral infection on a genetic background and an (autoimmune) collagen disease. The aim of our study was to investigate by immunohistochemistry the expression pattern of collagens within the otosclerotic focus. Stapes footplates from 30 patients with clinical otosclerosis undergoing stapedectomy were formalin fixed, decalcified and paraffin embedded. As controls, 30 autopic temporal bone specimens were employed. We investigated the expression of collagens I–V with immunohistochemistry. The expression of collagen I showed a diffuse homogeneous distribution with increased staining of the otosclerotic focus. Collagen II was exclusively expressed in chondrocytes including the globuli interossei. The pattern of collagen III in the otosclerotic bone was web-like in contrast to a lamellar pattern in the control bone. The mucoperiosteal layer and connective tissue such as the vessels of the resorption lacunae expressed collagen IV. An increased expression of collagen V around osteocytes was observed in the otosclerotic focus. In conclusion, in the otosclerotic tissue, in comparison with the control bone, a high expression of collagen IV occurred. The immunohistochemical analysis of collagen II, which has been suggested to be implicated in the etiopathogenesis of otosclerosis, revealed no differences between control and otosclerotic bones. The intense staining of the otosclerotic focus with collagen I is in good agreement with an inflammatory process but in contrast with lesions like those in osteogenesis imperfecta.

Otosclerosis is the major cause of hearing loss in western countries, the southern part of India and Japan, but its etiopathogenesis is not clear [1, 2]. The current etiopathogenetic hypothesis includes a measles virus infection as the triggering event on a genetic background although neither measles virus nor the genetic changes could be ascertained as a cause of otosclerosis. Histologically,
the otosclerotic foci exhibit all signs of a chronic inflammatory process which develops in three phases with the final formation of a scar. Otosclerosis shows some similarities with Paget’s disease and osteogenesis imperfecta [3]. In the past, some authors reported blue sclera in patients with otosclerosis, suggesting a common pathogenetic base. A collagen (auto-)immune etiopathogenesis was supported by induction of lesions very similar to otosclerosis in rats which were immunized against collagen II [4, 5]. Chondrocytes are known to express collagen II. Antibodies against collagens II and IX in the serum of patients with otosclerosis supported a collagen involvement [6, 7]. To support a collagen pathogenesis in otosclerosis, McKenna et al. [8, 9] found mutations in COL1A1 which occur in the mild form of osteogenesis imperfecta. There is no doubt that otosclerosis develops in the border region of the enchondral and endosteal layer of the cochlea characterized by the presence of the unique globuli interossei. Thus, a collagen etiopathogenesis is possible.

The aim of this study was to investigate by immunohistochemistry the expression pattern of collagens I–V within the otosclerotic focus in comparison with normal temporal bone specimens.

**Materials and Methods**

Footplates from 30 consecutive patients with clinical otosclerosis subjected to stapedectomy were collected. The ratio of males:females was 1:1.3. The age ranged from 27 to 52 with an average of 41 years. As controls, 30 autopic gender- and age-matched temporal bone specimens were employed. The specimens were formalin fixed (4% paraformaldehyde), decalcified (15% EDTA) and paraffin embedded. Two-micrometer sections were prepared.

Specific antibodies against collagens I–V (Quartett, Berlin, Germany; Eurodiagnostics, Apeldoorn, the Netherlands) were used for immunohistochemistry. For detection, the ABC peroxidase method (Vektor, Burlingame, USA) and the nonconjugated APAAP technique (Dianova, Hamburg, Germany) were employed.

**Results**

In 15 footplates, we observed areas of bone resorption and reorganization and the stage of scar formation in the other 15 samples. The control tissue did not present otosclerotic foci. The expression of collagen I showed a diffuse homogeneous distribution with enhanced staining of the otosclerotic focus (fig. 1). Collagen II was exclusively expressed in the globuli interossei and chondrocytes of the stapes footplate (fig. 2). The pattern of collagen III in the otosclerotic bone was web-like in contrast with a lamellar pattern in the control bone.
The mucoperiosteal layer and connective tissue such as the vessels of the resorption lacunae expressed collagen IV. A slightly increased expression of collagen V around osteocytes was observed in the otosclerotic focus.

**Discussion**

Otosclerosis develops in the ontogenetically ‘weak’ border region of the otic capsule. In the past, results of animal studies and serologic analysis of
patients with otosclerosis suggested a collagen etiopathogenesis of otosclerosis. Mutations of COL1A1 in familial cases of otosclerosis support this view [8]. In our immunohistochemical analysis, we found a slightly increased expression of collagen I in the otosclerotic focus. Collagen I is part of the extracellular matrix of the normal bone and an increased expression can be expected in regions of new bone formation. This observation is in contrast with the reduced expression of collagen I in osteogenesis imperfecta [10]. However, we cannot exclude mutations of COL1A1.

Experimental data from rats immunized against collagen II suggested an autoimmune process in otosclerosis [4, 5]. At the protein level, we could not find any difference in the expression of collagen II between otosclerotic and control tissue. This finding is supported by a case control study where the mutations in patients with otosclerosis could not be confirmed [11] (see also Solvsten-Sorensen et al. [12]). Finally, if a collagen II autoimmune etiopathogenesis was true, we would expect other inflammations of cartilage tissue in patients with otosclerosis.

We suppose that the increased expression of collagens IV and V is a consequence of the well-known inflammatory process that occurs in otosclerosis. Further studies on the RNA level could help to elucidate the role of collagens in otosclerosis.

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Otosclerosis Associated with Ménière’s Disease

A Histological Study

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Abstract

A histological study of a pair of temporal bones was performed in a case of Menière’s disease. A severe endolymphatic hydrops and extensive capsular otosclerosis bilaterally was found. Severe endolympathic hydrops results from otosclerotic endolympathic duct occlusion. Our unique histopathological findings show that a causal association exists between these two entities.

The etiology of endolymphatic hydrops in Ménière’s disease is still unknown and may have multiple causes. The speculation about the association between otosclerosis and Ménière’s disease has often been described, however, the causal relationship of these two entities remains unknown.

A female patient noted at the age of 31 postpartum bilateral hearing loss in stages, which led to profound hearing loss at the age of 41. She subsequently developed three vertiginous attacks lasting for several days and persistent bilateral tinnitus in the following 5 years. In 1945, she consulted an ENT specialist because of severe otalgia and nausea.

The examination yielded the following results: tuning fork testing revealed no pure-tone bone conduction, and only loud speech was perceptible 5 cm from the left ear and not at all from the right ear. There was a spontaneous nystagmus to the left and no caloric response on the right side. The diagnosis of Ménière’s disease was entertained.
Neurosurgical transection of the right 8th cranial nerve according to Dandy was performed. Postoperatively, the patient reported initial relief of her symptoms, but 3 months later the vertigo and bilateral tinnitus plagued her until her death at the age of 71 years.

Both temporal bones were prepared in our laboratory for histology and cut in the horizontal plane. All sections were stained with hematoxylin-eosin. The pathological findings are basically the same on both sides: multiple, partially confluent otosclerotic foci are located in the area of the oval window and surroundings and deforming the bony cochlea (fig. 1). The bone changes of the stapes footplate as well as the posterior margins of the oval window lead to partial ankylosis of the footplate. Extension until the endosteal bony layer of the cochlea was found. There was a marked endolymphatic hydrops throughout the ductus cochlearis with multiple ruptures of Reissner’s membrane (fig. 2a). The stria vascularis is atrophic, and the organ of Corti can no longer be identified. New bone formation in form of ossifying labyrinthitis is found in the scala tympani of the right cochlea probably as a reaction to the massive invasion of the endosteal layer (fig. 1). The endolymphatic duct revealed complete occlusion in its distal segment, over a depth of 1.2 mm on the left side, and over a depth of 2.0 mm on the right side (fig. 1). There was an extensive saccular hydrops on both sides so that its membranous wall directly comes into contact with the stapes footplate (fig. 2b).

**Fig. 1.** Overview at the midmodiolar level of the left and right temporal bone showing multiple partially confluent otosclerotic foci on the labyrinthine capsule and obstruction of the endolymphatic duct (arrow). New bone formation in the scala tympani (asterisk) of the right cochlea. ED = Endolymphatic duct; IAC = internal auditory canal.
The severe endolymphatic hydrops manifesting itself as Ménière’s disease is the result of otosclerotic endolymphatic duct occlusion. Our unique histopathological findings show that a causal association between these two entities exists.

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Dynamic Bone Studies of the Labyrinthine Capsule in Relation to Otosclerosis

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Abstract

The pathological perilabyrinthine bone remodelling of otosclerosis is associated with a genetic predisposition and triggered by mechanisms so far unknown. A proposed viral aetiology of otosclerosis originates from a similar concept of Paget’s disease. However, at present, it is not clear why a virus should cause otosclerosis, confined to the bony otic capsule with no effects on the general skeleton in some patients, and systemic Paget’s disease with only occasional involvement of the bony otic capsule in others. Moreover, the extent and distribution of pathological bone remodelling is different in Paget’s disease of the temporal bone and in otosclerosis. Bone resorption and consequently bone remodelling which turns over the general skeleton at a rate of 10% per year is normally highly restricted in perilabyrinthine bone to a minimum of 0.13% per year except in otosclerosis, and systemic remodelling rates are normal even in otosclerotic patients. This suggests the existence of a local inner ear mechanism in control of capsular remodelling activity, which is either overruled, bypassed or most likely defective in otosclerosis, no matter what may have triggered the disease process. We present experimental data related to this mechanism, which may offer a truly local pathogenetic factor in otosclerosis.

The Anatomy of Compact Bone Remodelling Revisited

The process of bone remodelling is responsible for the continuous turnover and renewal of the skeleton throughout life. Since bone is a hard tissue with living cells embedded in a tough, mineralised intercellular matrix, this process requires the actions of surface resorption and surface formation operating in concert. Normally, compact bone turnover is a quantum-based process occurring in
discrete packets or bone remodelling units. A remodelling event is initialised when mononuclear phagocytic cells recruited from the bone marrow exit the circulation, fuse to form multinuclear osteoclasts and tunnel through solid bone as a cutting cone. This cutting cone drills out a canal, which is invaded by proliferating blood vessels and lined by osteoblasts that subsequently refill the defect with lamellae of new bone matrix, and trapped osteocytes as reviewed in Sørensen [1]. Numerous local and systemic factors are known to influence this activity but the exact role and importance of the individual components in the regulation of physiological and most pathological remodelling conditions remain unclear.

**Paget’s Disease, Otosclerosis, Virus and More**

In human Paget’s disease of the bone, the skeleton is slowly deforming because bone resorption and consequently bone remodelling is pathologically enhanced. Multifocal pathology develops in long bones, in the axial skeleton and in the skull and may involve the outer part of the bony otic capsule as well. It has been suggested that Paget’s disease may result from a slow virus infection of bone cells with paramyxoviruses such as measles virus, respiratory syncytial virus or canine distemper virus [2, 3]. This idea, which is still controversial [4, 5], has inspired a similar idea of otosclerosis, claiming that pathological bone remodelling occurring in the endochondral and sometimes the endosteal (inner periosteal) bony otic capsule could be the result of a virus infection [6–9]. However, the extent and distribution of pathological bone remodelling differ in pagetic lesions of the temporal bone and otosclerosis, and as in Paget’s disease, there are some controversies regarding the presence of virus in otosclerosis [10].

**Are We Missing Something?**

While it may seem possible that a systemic virus infection can cause systemic or multifocal Paget’s disease of the bone with occasional involvement of (but no special preference for) the otic capsule, it is not obvious why the same type of virus infection in other cases should initiate otosclerosis, in which abnormal bone remodelling occurs exclusively in the otic capsule, whereas the general skeleton remains unaffected [11–14].

A systemic virus infection may well contribute to the pathogenesis of a highly localised disease process such as otosclerosis. However, in addition, a local pathogenetic factor is required to explain why otosclerosis is present only in perilabyrinthine bone and absent from any other bone tissue. This argument applies
similarly to other systemic factors suggested in the pathogenesis of otosclerosis such as autoimmunity [8, 9] and collagen type I mutations [8, 9, 15, 16].

For this reason, any deviation of otic capsular bone remodelling from the general pattern of compact bone remodelling is important, since it may point to missing factors in the aetiology and pathogenesis of otosclerosis.

**Perilabyrinthine Bone Modelling and Remodelling in vivo**

Newly formed bone can be labelled with certain fluorochromes in vivo and subsequently demonstrated in histological sections. Used as tissue time markers, these osteofluorochromes permit studies of bone dynamics, but because they are removed by decalcification, undecalcified histological bone sections are needed. Time-labelled bone remodelling units are easily identified and counted in undecalcified sections from the bony otic capsule and from any other compact bone, and remodelling activity and distribution may be measured by histomorphometry [17, 18]. The turnover can be calculated to a rate of 10% per year in long bones but only amounts to a crude rate of 2% per year in the otic capsule. Moreover, in the otic capsule, turnover rates decline from a normal 10% per year at the capsular periphery towards 0.13% in perilabyrinthine bone close to the inner ear spaces (fig. 1) [19, 20]. This unique decline of bone remodelling around the inner ear spaces indicates that bone resorption is highly restricted in perilabyrinthine bone.

*Fig. 1.* Spatial distribution of perilabyrinthine bone remodelling in 8 dogs labelled with a sequence of osteofluorochromes [20].
During the ossification, growth and modelling of the otic capsule and the surrounding cranial base, most of the primary fetal bone tissue is swept away and replaced by successive generations of bone by spatially oriented, coordinated osteoclastic and osteoblastic drifts shortly after its formation. However, perilabyrinthine bone once formed is bypassed in this process and preserved as a consequence of the perilabyrinthine restriction of bone resorption (fig. 2) [21].

This unique rate and distribution of perilabyrinthine bone resorption (and consequently remodelling) may result from either an extreme resistance of perilabyrinthine bone matrix against resorption (evident in vivo and in vitro) or a sustained in vivo inhibition of osteoclast activity by some mechanism of local origin.

**Perilabyrinthine Bone Modelling or Remodelling in vitro**

To answer the questions ‘Is perilabyrinthine bone more resistant than other compact bone tissues against resorption in vitro?’ and ‘Is inner capsular bone
more resistant than outer capsular bone?’, rabbit osteoclasts were isolated and seeded in plastic wells onto compact bony tablets prepared from bovine long bones, cranial bone and inner/outer parts of the bony otic capsule. After 3 days of culture, tartrate-resistant acid phosphatase per osteoclast was measured in the conditioned medium for each bone tissue type as an indicator of osteoclast activity, and collagen type I telopeptide per unit of tartrate-resistant acid phosphatase was measured as an indicator of the amount of bone resorbed, i.e. the result of the osteoclast activity. No significant difference was found between the different bone types [22]. This indicates that all the tested bone types are equally susceptible to bone resorption in vitro and supports the alternative option of sustained in vivo inhibition of perilabyrinthine bone resorption.

**Conclusion**

The existence of a unique pattern of the rate and spatial distribution of bone remodelling around the inner ear spaces indicates that there is indeed a local factor in the remodelling of the bony otic capsule. Perilabyrinthine bone resorption is normally highly suppressed in vivo, possibly by some local inner ear mechanism, which suppresses bone modelling and remodelling, except in otosclerosis, in which abnormal bone remodelling occurs within the restricted compartment. Such a local inner ear mechanism in control of bone resorption must be either overruled, bypassed or most likely defective in otosclerosis, no matter what may have initially triggered the disease process.

Consequently, this mechanism must play a role in the pathogenesis of otosclerosis and points to bone-regulating signal molecules as major candidates for gene substrates of interest in future molecular biological studies.

**References**


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Stapes Pathology in Otosclerosis

Scanning Electron Microscopic Examination

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Abstract

The human stapes is still a subject of considerable interest both to the clinician and to the research investigator. This is due to the stapes position between the middle and inner ear, and because of its involvement in the otosclerotic process. The purpose of this study was to determine scanning electron microscopic and histopathological features of normal and otosclerotic stapes. The specimens were obtained from adult human temporal bones and during operation of patients with otosclerosis. Our results show that the surface of the normal stapes had various degrees of structural features. The otosclerotic stapes is characterized by a typical irregular pattern. Histological examination of the stapedial footplate or its fragments showed three types of otosclerotic lesions: fibrotic, sclerotic, and spongiotic. Our observations could support the hypothesis that otosclerosis is not a static disease.

Although numerous studies have dealt with morphological characteristics of otosclerotic lesions, there is still limited information on the actual structural features of the otosclerotic stapes. The study of bony tissue of the human stapes is still technically difficult, and most studies include a relatively small number of cases. The purpose of this study was to present the scanning electron microscopic features of the otosclerotic lesions in the stapes.

The stapes studied included 20 intact normal stapes from adult temporal bones and 30 otosclerotic stapes obtained from patients with clinical otosclerosis who underwent stapedectomy. The majority of the otosclerotic specimens were large posterior fragments of the footplate. Upon removal, all specimens were placed in cold buffered 2% glutaraldehyde, dehydrated in graded ethanol solution, then frozen with liquid nitrogen and dried. The specimens (fractured and nonfractured) were oriented and mounted on aluminum stubs using carbon
suspension in alcohol, and coated with gold and aluminum to obtain a fine surface. The examination was performed using a Philips 500 scanning electron microscope which provides surface views with a magnification between 20 and 10,000 times.

At first we presented the morphological features of the normal stapes observed at low magnification. The posterior crus is generally longer, more arched, while the anterior crus is shorter and more delicate. It was apparent that the stapes showed a high degree of structural specialization, particularly on its footplate and crura. The footplate varies in shape and thickness. Its tympanic surface showed a fibrillar appearance with irregularly arranged mineralized collagen fibers. The vestibular surface of the footplate is covered by cartilage and demonstrated a pebbled appearance at high magnification.

The specimens of the otosclerotic footplate are characterized by the disappearance of the cartilaginous plate. The otosclerotic bones showed a typical irregular pattern, and this seemed to be formed by irregularly laid down poorly mineralized fibers. In some cases, the otosclerotic microfoci were evident as small patches of poorly mineralized nests. These microfoci were seldom seen near the blood vessels. The hallmark of the obvious otosclerotic bone was the presence of lacunar spaces. These spaces were varied in size and shape. Typical lacunae were abundant in some cases. The surrounding bone appeared as a sponge due to removal of minerals. This type of lesion appears spongiotic owing to the porous appearance of the bone. In some specimens, the lacunar spaces were filled with numerous spherical structures and covered with a crystalline substance. The area containing such lacunae appeared denser showing the sclerotic type of lesion. Occasionally, both types of lesions were found in certain specimens. Overall findings of otosclerotic specimens can be categorized as spongiotic, sclerotic and mixed form. This is essentially in agreement with what has previously been reported. Our observations support the hypothesis that otosclerosis is not a static disease. The exact mechanism by which the bone is destroyed is still not wholly understood.

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Too Much Bone: The Middle Ear in Sclerosing Bone Dysplasias

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Abstract
The middle ear changes in Sclerosteosis and Van Buchem disease are described. Reduced bone resorption occurs due to faulty activity of the sclerostin molecule, a product of the recently discovered SOST gene in chromosome 17. Syndactyly draws attention to sclerosteosis, and a conductive hearing loss develops before age six in both conditions. Acute, repeated attacks of facial palsy, similar to Bell’s palsy, are usually the first symptoms in both conditions. Total facial nerve decompression can stop the attacks of facial paralysis. The hearing loss is a problem because new bone formation continues up to age 21. Life saving craniectomy becomes necessary when increased intracranial pressure develops, and this may have to repeated. The sclerostin molecule is now of major interest to the researchers who want to develop a treatment for osteoporosis.

Sclerosing bone dysplasias are rare genetic disorders of bone remodeling. Only a few cases were published before X-rays were discovered. In 1904, Albers-Schönberg, professor of radiology in Hamburg (who later died from overexposure to radiation), published the X-rays of a patient who had very strong hard bones and a very thick skull. The terms ‘marble bone disease’ and ‘osteopetrosis’ then came into use until the various genetic syndromes were identified and new names given. The case of Albers-Schönberg was identified as rare, benign, dominant osteopetrosis. ‘Malignant’ recessive osteopetrosis occurs more often and children rarely survive for more than a few years. This presentation deals with sclerosteosis, a relatively benign form of excessive bone formation of which 67 cases have been identified in the Afrikaner community in South Africa (from Dutch, French and German descent) and 30 cases in the rest of the world [1]. Van Buchem disease, of which less than 30 cases have been identified, is very similar and occurs mostly in Holland (figs. 1–5) [2].
Craniometaphyseal dysplasia and Camurati-Engelmann disease are even less common but show similar involvement of the skull and middle ears. The term ‘marble bone disease’ is now only used as a nonspecific collective name for the skeletal dysplasias with dense bones, especially sclerosteosis and Van Buchem disease.
The SOST gene, which is involved in sclerosteosis and Van Buchem disease, was discovered a few years ago on chromosome 17. Bone metabolism researchers are very excited about this discovery, and are researching the characteristics of this gene in order to develop a treatment for osteoporosis. Patients suffering from sclerosing bone dysplasias sincerely hope that one day it may also become possible to treat excessive bone formation, because their thick bones not only press on the brain and sometimes cause premature death, but
they also press on cranial and spinal nerves where they exit the skull and reduce the size of the middle ear, causing conductive hearing loss.

The dense bone, similar to the sclerotic mastoid bone, compresses the facial nerve, reduces the size of the middle ear, encroaches upon the middle ear ossicles, the eustachian tube, as well as the oval and round windows of the inner ear (figs. 6 and 7). The volume of the mesotympanum is decreased because the walls of the mesotympanum are thickened, and ventilation tubes will touch the promontory because of the shallow middle ear space (fig. 7).

Patients are normal at birth, except for syndactyly in many cases of sclerosteosis. Acute, recurrent attacks of facial paralysis, identical to Bell’s palsy, occur in childhood, and a few cases had paralyses at birth! The paralyses recover partially after 3–5 months, and if they recur frequently, result in severely compromised facial movements. Therapeutic as well as prophylactic total facial nerve decompressions were performed in 30 ears. These are very difficult procedures but are worthwhile [3]. Because the skull becomes 3 cm thick in adults, it is best to do the surgery before age 6. In the case of tympanic and mastoid segments of the facial nerve, a canal wall down method may be the best, because the compromised middle ear ventilation often causes retraction pockets in a canal wall up mastoidectomy plus posterior tympanotomy.

Narrowing of the external auditory canal requires widening in order to accommodate a hearing aid. A bone-anchored hearing aid was successfully fitted to a patient with Van Buchem disease in Groningen [Dikkers, F., pers. commun.].
Extensive drilling is required to mobilize the malleus, incus and stapes. Because the bone regrows quickly, it is usually necessary to remove the head of the malleus as well as the incus. The stapes can be mobilized by drilling on the promontory. Similarly, the round window niche can be opened by drilling away the rim of the round window niche. At least one of the windows has to be patent in order to utilize a hearing aid. Unfortunately, the whole mesotympanum gets smaller. The bone does not grow into the cochlea, but the internal auditory
canal becomes extremely narrow. The umbo of the malleus handle is often fused to the promontory, and this compromises a malleostapedotomy. The results of middle ear surgery are therefore very unsatisfactory, and bone-anchored hearing aids are advised as soon as problems are encountered wearing an ordinary hearing aid. Successful cochlear implantation has been reported in a case of Camurati-Engelmann disease in Canada.

The neurosurgeon is an important member of the team caring for these patients. The increased pressure on the brain is often lethal – the patient can

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**Fig. 8.** Same patient as in figures 6 and 7. Encroachment of the bone onto the anterior crus of the stapes is visible (from Dort et al. [6]). The asterisk indicates the stapes.

**Fig. 9.** Sclerosteosis. Part of the dome of the skull was removed from Miss. W., and then replaced by a thin acrylic prosthesis. The posterior fossa was decompressed at a second operation.
suddenly go into coma and die within hours. Emergency craniectomy is life saving. When elective craniectomy is done, the dome of the skull is removed and thinned by drilling on the internal surface of the skull cap [4]. This requires extensive drilling, and we hope that laser techniques, e.g. femtosecond laser, may be developed one day to cut this bone. The use of the presently available lasers for middle ear surgery has not been successful because of the very thick bone. Also, drilling on the otic capsule results in some loss of hearing in the high tones due to the noise of the drill.

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Molecular Biology of Otosclerosis

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Abstract

Otosclerosis is a bone disease of the human otic capsule, which is among the most common causes of acquired hearing loss. The pathologic process is characterized by a wave of abnormal bone remodeling in specific sites of predilection within the endochondral layer of the temporal bone. Although the cause of otosclerosis remains uncertain, there is a clear genetic predisposition with half of all cases occurring in families with more than one affected member. There is also compelling evidence that measles virus may play a role in some cases. Ultimately, how genetic factors and viral infection result in otosclerosis must be explained by effects on the molecular factors that control bone remodeling.

Unlike all other bones in the body, the human otic capsule undergoes very little remodeling following development. Otosclerosis is a process of pathologic remodeling within a bone that is normally refractory to remodeling. Fundamental to elucidating the molecular biology of otosclerosis is an understanding of the molecular factors that promote and inhibit bone remodeling. Bone is a dynamic tissue controlled by various biochemical, hormonal and biomechanical stimuli. Cytokine factors that include osteoprotegerin (OPG), receptor activator of nuclear factor kappa B (RANK) and RANK ligand (RANK-L) play a major role in the system that directly controls bone turnover. RANK-L is expressed in a variety of cells including osteoblasts. RANK-L expressed by osteoblasts that are involved in bone turnover promotes differentiation (in the presence of macrophage stimulating factor) \cite{1}, activation \cite{2} and survival \cite{3} of osteoclasts by activation of its specific receptor RANK on osteoclasts. OPG acts as a soluble neutralizing antagonist that binds and inactivates RANK-L \cite{4}. OPG inhibits the differentiation, survival and fusion of osteoclastic precursor cells, suppresses activation, and promotes apoptosis of osteoclasts \cite{5}.
At the cellular level, bone turnover follows a pattern of bone resorption by osteoclasts derived from monocytic/macrophagic lineage followed by new bone formation by osteoblasts that differentiate from pluripotent mesenchymal stem cells. The molecular coordination of the remodeling process is influenced by a large number of factors, most of which act by influencing OPG, RANK, and RANK-L.

Although the factors that serve to inhibit postdevelopmental remodeling within the otic capsule have yet to be established, there is recent evidence to suggest that OPG which is produced within the spiral ligament, secreted into the perilymph, and diffuses into the surrounding bone may be an important factor [6].

**Genetics and Otosclerosis**

Otosclerosis is most common among whites, uncommon among Asians, and extremely rare in blacks. Otosclerosis is estimated to occur histologically in 10% of the white population and results in hearing loss in approximately 1% [7, 8]. The clinical prevalence of otosclerosis is estimated to be twice as common in females as in males [9].

Familial aggregation of individuals affected by otosclerosis has been recognized for many years [10]. The most compelling evidence for an underlying genetic cause for otosclerosis comes from monozygotic twins with clinical otosclerosis [11, 12] in which concordance has been found in nearly all cases. However, because information does not exist on the genetic transmission of histologic otosclerosis, it is not known whether the genetic basis of inheritance is related to the formation of an otosclerotic focus within the temporal bone or the tendency for a lesion to progress once it has begun, or both. Most studies on families with otosclerosis support a pattern of autosomal dominant transmission with incomplete penetrance [13–16]. A recent study on 65 pedigrees with otosclerosis in Tunisia suggests that otosclerosis is primarily heterogenetic, and that in 13% of the clinical cases studied, affected individuals carry a dominant gene with nearly complete penetrance [17]. Linkage studies between otosclerosis and the ABO, MN, and Rh blood groups and haptoglobin genotypes have failed to show evidence for linkage [16]. Linkage analysis of three large and unrelated families has revealed linkage to at least three separate loci indicating that otosclerosis is heterogenetic [18–20]. Each of these families is atypical in that the penetrance is nearly complete with approximately half of all individuals in each family being affected.

Although a strong familial component exists, several studies have reported that sporadic otosclerosis represents 40–50% of all clinical cases [14–16,
There appears to be no significant difference in the degree of clinical severity between sporadic and familial cases [16]. There is evidence to suggest that some cases of otosclerosis may be related to defects in the expression of the COL1A1 gene. Association analysis has revealed a significant association between both familial and sporadic cases of clinical otosclerosis and the COL1A1 gene using multiple polymorphic markers within the COL1A1 gene [24]. The association has been found to increase from the 3-prime to the 5-prime region of the gene. Studies of the allelic expression of the COL1A1 gene in patients with clinical otosclerosis have revealed reduced expression of one COL1A1 allele in some cases, similar to that which has been described in many cases of type 1 osteogenesis imperfecta [25–28]. Type 1 osteogenesis imperfecta shares both clinical and histologic similarities with otosclerosis. Approximately half of all patients with type 1 osteogenesis imperfecta develop hearing loss that is clinically indistinguishable from clinical otosclerosis [29, 30]. It is also well known that some patients with clinical otosclerosis have blue sclerae [31], a feature that is found in virtually all patients with type 1 osteogenesis imperfecta [32]. The histopathology of temporal bones from patients with type 1 osteogenesis imperfecta is identical to that observed in patients with otosclerosis. Most patients with mild osteogenesis imperfecta and conductive hearing loss have mutations in the COL1A1 gene [33]. Additional studies on the association of COL1A1 and otosclerosis have revealed an even more significant association between clinical otosclerosis, both familial and sporadic, and an Sp1 binding site polymorphism in the first intron of the COL1A1 gene [34]. A similar and practically identical association has been described between osteoporosis and the Sp1 binding site in the first intron of the COL1A1 gene. A preliminary study has demonstrated that osteoporosis may be more common in patients with otosclerosis, and these two common bone diseases may share an underlying molecular pathologic mechanism [35].

**Measles Virus and Otosclerosis**

The possibility that otosclerosis may be related to a persistent viral infection of the bone was first considered because of the similarity between otosclerosis and Paget’s disease of the bone, and the mounting evidence of a viral etiology in Paget’s disease [36, 37]. The evidence which has emerged thus far is suggestive of a possible persistent measles virus infection similar to what occurs in the central nervous system in subacute sclerosing panencephalitis. Support for this hypothesis comes from ultrastructural and immunohistochemical evidence of measles-like structures and antigenicity in active otosclerotic lesions [38–40]. In addition, measles RNA has been found in archival and fresh
footplate specimens with otosclerosis [41–44]. Elevated levels of antimeasles antibodies have also been reported in the perilymph of patients undergoing stapedectomy for otosclerosis as compared to controls [44]. Others have reported lower levels of circulating antimeasles antibodies in patients with otosclerosis as compared to healthy controls [45]. This hypothesis is further strengthened by recent evidence that the incidence of otosclerosis has declined since the introduction of measles vaccination [46].

**Discussion**

Otosclerosis is an abnormal remodeling process of the otic capsule, a bone in which remodeling is extremely limited after development. It is a complex disease with genetic heterogeneity. It could result from intrinsic abnormalities in bone metabolism or be initiated by some other stimulus such as measles infection, the spread and extension of which are determined by underlying defects in bone metabolism. It is likely that a variety of gene defects result in a similar phenotypic expression by affecting fundamental mediators of bone remodeling.

The key factors which regulate bone remodeling are RANK which is found on osteoclasts and their precursors, RANK-L which is produced as both a soluble and membrane-bound form by osteoblasts and stromal cells in the bone marrow, and OPG which acts as a decoy receptor for RANK-L and is produced by osteoblasts and stromal cells. Upregulation of RANK-L results in increased formation and activation of osteoclasts and increased bone resorption. Upregulation of OPG results in inhibition of osteoclast formation and activity and decreased bone resorption. Each of these factors is subject to a complexity of upstream and downstream regulation by a variety of hormones, cytokines and transcription factors.

Several studies have examined the effects of measles infection on bone cells and the above-mentioned pathway. Measles infection and cells transduced with measles gene products express increased amounts of RANK and appear to be capable of RANK activation independent of RANK-L. Furthermore, inflammatory cytokines such as IL-1, TNF-α, and IL-6 result in further upregulation of RANK and RANK-L. It is clear from these studies that measles infection can have direct effects that result in active resorption and remodeling.

Perhaps most fundamental to understanding the molecular biology of otosclerosis is elucidation of the factors which serve to uniquely inhibit bone remodeling in the otic capsule. The elegant studies of Frisch et al. [47, 48] have demonstrated that otic capsule remodeling is most reduced in proximity to the inner ear. We have recently found that OPG is produced in high quantity within
the spiral ligament and directly secreted into the perilymph. We have also shown that proteins within the perilymph can diffuse into the surrounding otic capsule bone. Since OPG is a potent inhibitor of osteoclast formation and activation, it may be one important factor that prevents otic capsule remodeling.

With a better understanding of the molecular factors which serve to inhibit normal otic capsule remodeling and promote abnormal remodeling as occurs with otosclerosis comes the possibility of developing better forms of treatment for otosclerosis. We suspect that compounds that have been and are being developed for the treatment of other metabolic bone diseases such as Paget’s disease and osteoporosis may have direct application in the treatment of otosclerosis.

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The Genetics of Otosclerosis: Pedigree Studies and Linkage Analysis

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Abstract

Otosclerosis is one of the commonest causes of hearing loss in adults. The hereditary nature of the disease has been acknowledged for over a century but the precise genetic basis of the disorder has as yet not been characterised. It is currently recognised that familial otosclerosis exhibits autosomal dominant inheritance with variable penetrance and expression. More recently, family linkage studies have identified three chromosomal regions that can be ascribed to this disorder: otosclerosis 1 on chromosome 15, otosclerosis 2 on chromosome 7 and a third locus on chromosome 6. The genes responsible for the disease within these regions remain to be defined. The work presented in this paper firstly examined the familial nature of the disease in a cohort of individuals that had undergone surgery for otosclerosis. Following detailed ascertainment, pedigrees were constructed for subsequent genetic analysis. The laboratory analysis included linkage analysis of the candidate region on the long arm of chromosome 15, linkage analysis of the aggrecan protein gene within the 15q region and linkage analysis to chromosome 7q. The pedigree studies confirmed the hereditary nature of otosclerosis and the recognised mode of inheritance. Linkage to the chromosome 15 locus, the candidate aggrecan gene and the chromosome 7 locus was excluded, confirming that otosclerosis exhibits locus heterogeneity.

The hereditary nature of otosclerosis has been recognised for nearly 150 years [1]. Despite this, the precise genetic basis of the disorder remains to be defined. The aims of this study were firstly to confirm the familial nature of the disease and secondly to examine two of the specific chromosomal loci that have been described as harbouring genes implicated in the pathogenesis of otosclerosis, OTSC1 and OTSC2 [2, 3].
**Materials and Methods**

**Source of Data**

The starting point for the acquisition of study material was individuals in whom the diagnosis of otosclerosis had been confirmed surgically. The operating theatre records for the period from 1990 to 1995 were examined retrospectively by the authors and prospectively during the study at several hospitals in the North-West of England. In addition, a single large family with otosclerosis was identified by colleagues in Leeds and made available for collaborative research. Details were also made available from the personal stapedectomy series of an otologist in London. The details of all these patients were entered into a database constructed by the authors under the regulations of the Data Protection Act.

**Identification of Potentially Informative Families**

The case notes of the patients identified from the operating theatre records were individually studied for historical evidence of a positive family history of otosclerosis. Ethical approval for subsequent contact and entry into the study of those patients with a family history was confirmed by the Manchester Health Authority. Those patients consenting to take part in the study were then either evaluated by the first author in the University Department of Audiology, Manchester, or at the individual’s home.

**Construction of Pedigrees**

Detailed ascertainment of families through the index case was undertaken historically and pedigrees constructed. Evaluation of index cases and relatives included otoscopic and tuning fork examination, audiometric analysis and the collection of a venous blood sample. Individuals were designated as affected or unaffected on this basis. The surgically confirmed affected status of individuals in a family was also noted.

**Audiometric Analysis**

Pure-tone audiometry was undertaken by the authors in all individuals available for evaluation in accordance with the guidelines of the British Society of Audiology. Where indicated, masking of the non-test ear was undertaken in accordance with accepted guidelines. Hard copies of the pure-tone audiograms were made for subsequent analysis.

**Collection of Blood Samples and Extraction of Constitutional DNA**

Between 10 and 20 ml of venous blood was collected from each individual studied and anticoagulated with ethylenediaminetetraacetic acid (0.5 ml 0.5 M, pH 8.0). Constitutional DNA was extracted from leucocytes from the venous blood samples using standard techniques.

The homogenous solution of DNA was stored at −70°C until required.

Stock DNA was diluted with deionised water in the ratio DNA 10 μl:1,000 μl deionised water. The optical density machine was calibrated with a 1-ml deionised water blank and the optical density of the DNA solution was read at 260 nm against the water blank in a quartz cuvette.

**Chromosome 15q and 7q Linkage Analysis**

Linkage analysis using microsatellite markers for the 14.5-cM region on chromosome 15 (15q25–q26) and the 16-cM region on chromosome 7 (7q33–q36) was undertaken in families A–G. A summary of the oligonucleotide primers utilised for the study is presented in...
The forward primer in each pair was fluorescently labelled. The DNA was diluted with deionised water to give 50–100 ng of genomic DNA per reaction. The reaction volumes were all made up to 10 μl with deionised water. The PCRs were set up and run in an automated thermal cycler. Following an initial step at 93°C for 3 min, 40 cycles were utilised with the following reaction conditions: denaturing at 94°C for 1 min, annealing at 55°C for 1 min and synthesis at 72°C for 1 min. The fluorescent product for each primer pair was visualised on an automated ABI PRISM 377 DNA sequencer/genotyper and computed using the Genotyper® 1.1.1 software. Multipoint linkage analysis was undertaken using Genehunter 2.1.

**Aggrecan Gene Analysis**

A summary of the intragenic oligonucleotide primer utilised for this study is presented in table 2. The DNA was diluted with deionised water to give 50–100 ng of genomic DNA per reaction. The reaction volumes were all made up to 10 μl with deionised water. The PCRs were set up and run in an automated thermal cycler. Forty cycles were utilised with the following reaction conditions: denaturing at 94°C for 1 min, annealing at 67°C for 1 min and synthesis at 70°C for 2 min. The amplified products were separated on a 3.5% agarose gel and visualised with ethidium bromide staining.

### Results

**Identification of Potentially Informative Families**

The demographic details of individuals that had undergone stapes surgery for otosclerosis were entered into a database. In total, 225 such individuals were

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**Table 1.** Summary details for the oligonucleotides used for the chromosome 15q and 7q studies

<table>
<thead>
<tr>
<th>Locus</th>
<th>Oligonucleotide markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>15q25–q26</td>
<td>D15S996</td>
</tr>
<tr>
<td></td>
<td>D15S127</td>
</tr>
<tr>
<td></td>
<td>D15S158</td>
</tr>
<tr>
<td></td>
<td>D15S963</td>
</tr>
<tr>
<td></td>
<td>D15S652</td>
</tr>
<tr>
<td></td>
<td>D15S531</td>
</tr>
<tr>
<td></td>
<td>D15S1004</td>
</tr>
<tr>
<td></td>
<td>D15S649</td>
</tr>
<tr>
<td></td>
<td>D15S130</td>
</tr>
<tr>
<td></td>
<td>D15S657</td>
</tr>
<tr>
<td>7q33–q36</td>
<td>D7S509</td>
</tr>
<tr>
<td></td>
<td>D7S497</td>
</tr>
<tr>
<td></td>
<td>D7S2560</td>
</tr>
<tr>
<td></td>
<td>D7S684</td>
</tr>
<tr>
<td></td>
<td>D7S2513</td>
</tr>
<tr>
<td></td>
<td>D7S2426</td>
</tr>
</tbody>
</table>
identified and the number of subjects with a positive family history for each source of data is summarised in table 3.

The 33 individuals in London that had undergone stapes surgery and had a positive family history were not ascertained during the study period. The 35 individuals from the North of England that had undergone stapes surgery and had a positive family history according to their clinical records were contacted by the methods described previously. Of these individuals, there was no response despite repeated attempts to contact them in 3 individuals and 11 individuals did not in fact have a positive family history on direct questioning. The remaining 21 index cases were ascertained in detail. Of these, 2 did not have a positive family history and in 1 the affected status of the relative was equivocal. In 5 families, the only living affected individual was the proband. In 3 families, there were 2 living affected individuals including the proband and there were 6 families with 3 affected living individuals. One family contained 4 living affected individuals including the proband and in 3 families, there were 5 or more affected individuals still alive. These findings are summarised in table 4.

**Table 2. Summary details for the oligonucleotides used for the aggrecan gene study**

<table>
<thead>
<tr>
<th>Marker</th>
<th>Primer sequence</th>
<th>Allele size, bp</th>
<th>Heterozygosity, %</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGC1.PCR</td>
<td>forward: 5’-TAGAGGGCTCTGTCTCTTGGAGTTG-3’</td>
<td>775–1,915</td>
<td>70</td>
<td>[4]</td>
</tr>
<tr>
<td></td>
<td>reverse: 5’-AGGTCCCCCTACCG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CAGAGGTAGAA-3’</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 3. Patient data summary**

<table>
<thead>
<tr>
<th>Region</th>
<th>Number</th>
<th>Positive family history</th>
<th>Sex ratio (M:F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North of England</td>
<td>97</td>
<td>35 (36)a</td>
<td>0.39</td>
</tr>
<tr>
<td>London</td>
<td>128</td>
<td>33 (26)</td>
<td>0.50</td>
</tr>
<tr>
<td>Total</td>
<td>225</td>
<td>68 (30)</td>
<td>0.46</td>
</tr>
</tbody>
</table>

*Figures in parentheses indicate percentages.*

*aNineteen percent after more detailed ascertainment.*

Chromosome 15q Studies

The 7 study families were typed for the candidate region using between 3 and 8 markers. One family was uninformative and one family generated a small
positive lod score. The remaining 5 families generated maximum lod scores between –3.62 and –5.00 at 0% recombination (table 5), thereby excluding linkage to the candidate region in the study material.

**Chromosome 7q and Aggrecan Studies**

Parametric multipoint linkage analysis to chromosome 7q generated a maximum lod score of –0.4, excluding linkage. Non-parametric linkage analysis also excluded linkage to 7q.

Six of the 7 study families were also typed for linkage to the aggrecan gene. One family was uninformative (family E) and 3 families generated a weak positive lod score (families D, F and G). The 2 remaining larger families (B and C) generated maximum lod scores of –4.30 and –4.03 at 0% recombination, thereby excluding linkage to the aggrecan gene.

**Table 4.** Family history details for the North of England families

<table>
<thead>
<tr>
<th>Family history</th>
<th>Number of families</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not contactable</td>
<td>3</td>
</tr>
<tr>
<td>No true/equivocal family history</td>
<td>14</td>
</tr>
<tr>
<td>Only proband alive</td>
<td>5</td>
</tr>
<tr>
<td>2 affected alive</td>
<td>3</td>
</tr>
<tr>
<td>3 affected alive</td>
<td>6</td>
</tr>
<tr>
<td>4 affected alive</td>
<td>1</td>
</tr>
<tr>
<td>5 or more affected alive</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
</tr>
</tbody>
</table>

**Table 5.** Maximum lod score at 0% recombination

<table>
<thead>
<tr>
<th>Family</th>
<th>Maximum lod score at 0% recombination</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>–3.62</td>
</tr>
<tr>
<td>B</td>
<td>–5.00</td>
</tr>
<tr>
<td>C</td>
<td>–4.21</td>
</tr>
<tr>
<td>D</td>
<td>–4.09</td>
</tr>
<tr>
<td>E</td>
<td>0.40</td>
</tr>
<tr>
<td>F</td>
<td>0.00</td>
</tr>
<tr>
<td>G</td>
<td>–4.33</td>
</tr>
</tbody>
</table>

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Discussion

Despite the fact that the hereditary nature of otosclerosis has been recognised for 140 years [1], the precise genetic basis of the disease and its pathogenesis remain elusive. Recent advances in molecular biology have given a new impetus to the study of deafness genetics and this is reflected in the ongoing recognition and refinement of the genetics of syndromic and non-syndromic hereditary hearing loss [5, 6]. Whilst otosclerosis is one of the commonest causes of familial hearing loss, there are a number of reasons why to date, the genes implicated in the development of the disease have not been defined. Firstly, in a given individual presenting with hearing loss, the diagnosis is presumptive rather than absolute, based on the history, clinical examination and audiometric findings being compatible with such a diagnosis. The diagnosis is proven either at surgery or if high-resolution computed tomography scanning (CT scanning) demonstrates the lesion in the oval window or otic capsule. Since a negative CT scan does not exclude the disease and many individuals presenting with deafness due to otosclerosis elect not to undergo surgery, the phenotype of the index case and kindred cannot be ascribed with absolute certainty. Secondly, even if the index case is defined as one that has undergone surgery for otosclerosis, the construction of informative pedigrees can be difficult. The fundamental starting point in the study of a familial disorder is the ascertainment of cases and the construction of robust pedigrees. For a disorder that shows an autosomal dominant mode of inheritance, the ideal family for linkage analysis comprises around 10 informative meioses allowing the identification of recombinant individuals with unambiguous characterisation of the affected and unaffected individuals in the family. These criteria are rarely met, particularly in smaller families in the Western World. In addition, anamnestic data may be unreliable. On this basis, in order to reach statistical significance, data from several smaller families are combined using the lod score as a statistical tool. The identification of affected and unaffected individuals is further hampered by the fact that the classical mendelian inheritance of otosclerosis is complicated by incomplete penetrance and variable expression. This would account for the difference between clinical and histological otosclerosis as described by Guild in 1944 [7]. Despite these difficulties, otosclerosis is a recognised familial deafness disorder and as such should be amenable to the application of modern clinical and molecular biological techniques. Such techniques have been applied successfully to less common familial deafness disorders such as non-syndromic hereditary hearing loss, Usher’s disease and Wardenburg’s syndrome [8]. Many of the studies characterising the genetics of these disorders have been collaborative research projects in large kindreds emanating from areas such as the Middle East.
In addition, these studies have not been hampered by incomplete penetrance and are based on a firm audiometric diagnosis. Finally, in otosclerosis the pathological lesion itself is not generally available for molecular analysis unless at surgery the stapes is inadvertently removed in its entirety. This is in contrast to the familial cancer syndrome neurofibromatosis type II (NF2) in which the hearing loss is due to the presence of bilateral vestibular schwannomas (acoustic neuromas). At the time of surgical removal, tumour samples together with a sample of the individual’s blood can be made available for genetic studies. This has led to novel molecular studies culminating in the detailed genetic characterisation of this familial disorder and ongoing research into the molecular biology of the sporadic form of the disease in which individuals develop a unilateral tumour [9, 10]. Such a strategy would be immensely helpful in the molecular study of otosclerosis.

**Pedigree Studies**

The fundamental basis of this study was a group of individuals that had undergone surgery for otosclerosis in several Otolaryngology Departments in the North of England over a 6-year period. These 225 individuals were therefore a selected group and not representative of the population suffering with otosclerosis as a whole for several reasons. The first of these is motivation on the part of the person presenting for a specialist opinion. Such individuals would have sought medical advice at a point when he or she felt that their hearing loss was causing a significant disability in terms of day-to-day living or work. This is more likely to be the case the greater the hearing loss and in particular if both ears are affected by the disease process. The point at which a given hearing loss constitutes a disability is variable from individual to individual and is itself subject to differences between people depending on their age, sex, vocation, lifestyle and expectations. In addition, some individuals may have positive or indeed negative family experiences of the management of otosclerosis which will also influence their own threshold for seeking medical advice. Secondly, once a presumptive diagnosis of otosclerosis is reached by the clinician, three management options are available to the patient: observation, provision of a hearing aid or surgery. This process is also subject to bias depending on the surgeon’s understanding and experience of the management of this disorder. Finally, any retrospective case record study will be subject to the vagaries of hospital record keeping. This was found to be the case in several instances where the clinician seeing the patient had not documented the presence or absence of a family history despite dealing with a patient with a recognised familial disorder. The issues raised in this discussion are therefore based on selected material subject to analysis and cannot be extrapolated to the population suffering with otosclerosis at an epidemiological level.
The findings from this study confirm that otosclerosis can be a familial disorder. Interestingly, prior to detailed ascertainment, 36% of the North of England index cases yielded a positive family history. Following detailed assessment, this figure fell to 19%. This serves to highlight the dangers of relying on anamnestic data, a point made by Larsson in 1960 [11]. Patients will not necessarily differentiate between otosclerosis and other causes of deafness when questioned about the presence or absence of hearing loss in their relatives. Commonly deafness in relatives due to the aging process or suppurative middle ear disease will be assumed to be due to otosclerosis by the index case. The issue is only clarified once the relatives of the proband are ascertained and this study confirms the great importance of examining the relatives of the index case to avoid erroneous conclusions [12]. Based on this study, the prevalence of familial otosclerosis is close to 1 in 5, which is lower than the accepted figures in the literature which range from 30 to 50% [13, 14]. The wide range probably reflects a selection bias and variable ascertainment of relatives of the proband. The male to female ratio however for affected individuals in this series was close to 40%, which is comparable to other epidemiological studies. The number of affected individuals within a pedigree is subject to three main factors: the size of the family, incomplete penetrance and variable expression. This study group confirms this observation in that the number of living affected individuals in the pedigree ranged from 1 to 10. However, only 4 pedigrees had 4 or more living affected individuals and this illustrates one of the difficulties cited previously in subjecting such families to linkage analysis. Overall family size is an important determinant and it is well recognised that family size in part is subject to personal, religious, cultural and political factors. Consanguinity however was not a complicating factor in this study. Larger families in a population in whom otosclerosis is prevalent such as those seen in the Indian subcontinent are in theory a good source for linkage analysis and indeed the study by Tomek et al. [2] was based on a large Indian kindred.

The process of detailed ascertainment was based on a clinical and audiometric assessment. In those individuals that had undergone surgery for otosclerosis the affected status was secure. Characterisation of affected and unaffected non-operated relatives however poses a potential problem as the characterisation is necessarily presumptive. The presence of a normal tympanic membrane which is mobile on pneumatic otoscopy, appropriate tuning fork test results, a type A tympanogram and a characteristic conductive hearing loss on pure-tone audiometry is highly suggestive of a diagnosis of otosclerosis. This is particularly the case if there is a known affected relative such as the proband. However, congenital or acquired fixation of the malleus or incus will give exactly the same picture though incudomalleolar fixation is considerably rarer than the stapedial fixation seen in otosclerosis. In this respect, the history of the hearing
loss assumes considerable importance. The sensitivity and specificity of tuning fork tests have been debated amongst otolaryngologists in more recent times and are probably unreliable as a single screening modality [15]. In addition, field audiometry is subject to errors due to adverse environmental issues such as noise. In reality, classification of relatives as affected or unaffected proved less difficult than anticipated as the process is a constellation of clinical and audiometric compatibility. In those cases where doubt remained, audiometry was repeated at the university and unless unequivocal, the individual was labelled as clinically unaffected for the purposes of this study.

Allowing for the potential sources of error outlined above, observation of the inheritance patterns in this group is possible. An autosomal dominant mode of inheritance was observed in 7 of the 21 families ascertained. Of these, incomplete penetrance was noted in 2 families. X-linked dominant inheritance was observed in 1 family with the remaining families being too small to ascribe a mode of inheritance. However, autosomal or X-linked recessive inheritance was not observed. These findings are consistent with the currently accepted inheritance patterns and characteristics in this disorder despite the study group being selected in the manner described above. Overall, the pedigree studies were consistent with the accumulated literature and the families were deemed suitable for subsequent molecular studies.

Chromosome 15 and Chromosome 7 Linkage

This study was unable to provide evidence of linkage to the candidate regions on 15q and 7q. The implication of excluding linkage to these regions is locus heterogeneity. More recently, an additional family has been studied by the Manchester group. The family was ascertained in India and comprises 32 individuals across 4 generations. Nine affected individuals were identified and haplotypes constructed utilising the markers for the 15q candidate region in the manner described in this paper. Typing was undertaken on 21 individuals and again linkage to the candidate region was excluded [unpubl. data]. This adds weight to the observation of locus heterogeneity in otosclerosis, and indeed a third locus has been identified more recently on chromosome 6 [16].

Aggrecan Gene Linkage

The most important gene that maps to the candidate region identified by the Tomek group is the gene for the aggrecan protein. The aggrecan gene is a good candidate gene for the pathogenesis of otosclerosis. Six of the 7 study families were typed for linkage to this gene. Not surprisingly, linkage was excluded (maximum lod scores of $-4.30$ and $-4.03$ at 0% recombination). One cannot however conclude that the aggrecan gene is not implicated in the pathogenesis of otosclerosis based on this work, as this work excluded linkage to the whole 15q region.
The key step will be to look for evidence of linkage to the aggrecan locus in a family that first links to the 15q region. Such data have not been forthcoming from the Tomek group but the search for pedigrees that link to this region should continue in addition to a wider genome search.

**Conclusions**

The following conclusions may be drawn from the studies described in this paper.

Of the 97 individuals studied that had undergone surgery for otosclerosis, an overall positive family history of the disease was found in 19% with a male to female ratio of 0.39. An autosomal dominant mode of inheritance was demonstrated with evidence of incomplete penetrance.

Linkage to the candidate regions on the long arm of chromosomes 15 and 7 was excluded in the 7 study families typed for these regions. In addition, linkage to the aggrecan protein gene was also excluded, thereby demonstrating that familial otosclerosis exhibits locus heterogeneity.

Clearly, the current evidence both in the literature and amongst investigators interested in this particular field warrants continuing research at a molecular level utilising pedigrees that have been ascertained in addition to families ascertained in the future.

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**References**


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Measles Virus and Otosclerosis

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\textbf{Abstract}

Measles virus (MeV) might play an important role as an environmental stimulus in the etiopathogenesis of otosclerosis. Chronic inflammation was shown in morphologic investigations of otosclerotic foci and MeV N, P, and F proteins were detected within cells of the otosclerotic focus by immunohistochemical investigations. MeV RNA was extracted from fresh-frozen otosclerotic tissue by the use of in vitro RT-PCR. This result was validated through amplification of MeV genome sequences by RT-PCR from celloidin-embedded sections with morphologically ascertained otosclerotic foci. In searching for an immune response of the inner ear immune system against MeV proteins, elevated anti-MeV IgG levels were detected in the perilymph of patients with otosclerosis in comparison with the serum levels. In situ RT-PCR allowed the localization of MeV sequences in osteoclasts, osteoblasts, chondrocytes, macrophages, and epithelial cells in middle ear mucosa of otosclerotic tissue. Further evidence for MeV persistence has recently been given. Genotyping of MeV in otosclerotic foci demonstrated the presence of MeV genotype A, which circulated in Europe around 1960. All the above results confirm a strong association between MeV and otosclerosis.

Otosclerosis was described for the first time by Antonio Maria Valsalva in 1735 [1] as a disease of the human temporal bone. More than one century later, Toynbee [2] recognized otosclerosis as a cause of hearing loss. Otosclerosis may occur as a histological type within the human temporal bone without affecting the stapes footplate. In only 10% of patients with otosclerosis is the focus localized near the oval window niche leading to fixation of the stapes with consecutive (characteristic) conductive or mixed hearing loss. Women are affected 1.4 times more frequently than men and the age of onset has risen in Caucasians in the last decades [3]. Otosclerosis is the most important cause of hearing loss
in Europe and the USA, whereas it appears to be uncommon in developing countries and among the Japanese population [4].

**Morphologic Analysis of the Otosclerotic Focus**

Otosclerosis only affects the human temporal bone, but otosclerosis-like lesions were observed in the crura of LP/J mice leading to conductive or combined hearing loss [5].

Histologically, three different phases can be distinguished: the first phase shows bone resorption. The tissue is highly vascularized and macrophages and activated osteoclasts are present. The second phase is characterized by new bone formation beginning around the vessels leading to the characteristic blue mantles of Manasse. Finally, in the last phase, the otosclerotic focus appears as a scar with rare cells and calcification [6].

**Immunohistochemistry**

A variety of immunocompetent cells including macrophages (MAC 387 antigen positive), HLA-DR-positive cells, cells expressing β2-microglobulin, T suppressor cells and complement C3 were found in otosclerotic tissue by immunohistochemical investigations [7, 8]. Deposits of immunoglobulins (IgG, IgM and IgA) and complement C3 are present along the resorption lacunae, as well as in osteocytes and chondrocytes surrounding the destructive process [9].

*What Is the Reason for This Inflammatory Process?*

The etiopathogenetic hypothesis for the development of otosclerosis includes mechanical distress, enzymatic imbalance, disease of the collagen, and viral infection. The current hypothesis considers otosclerosis as an inflammatory disease with a genetic background. Five otosclerosis genes have been localized in familial cases of otosclerosis [10, 11], but the presence of these genes could not be confirmed by case-control studies. Mutations of collagen genes are also discussed as a cause for the otosclerotic process. However, a genetic inheritance is accepted in up to 50% of cases. The triggering event could be an environmental stimulus such as a common viral infection [12].

Electronmicroscopic studies in Paget’s disease, which is histologically very similar to otosclerosis, revealed the presence of paramyxoviral structures in pagetic bone [13]. Analogously, filamentous structures very similar to paramyxoviral nucleocapsids were observed in otosclerotic bone specimen [14]. Immunohistochemical studies were undertaken to characterize these nucleocapsid-like structures. The expression of measles virus (MeV) N, F, and
H antigens in osteoclasts and macrophages of otosclerotic tissue strongly supports the hypothesis that MeV is involved in otosclerosis [15–17].

**Detection of MeV RNA within the Otosclerotic Tissue**

Studies on the RNA level were undertaken to determine the presence of MeV-related sequences within the otosclerotic tissue since specificity and sensitivity of MeV antigen detection have been discussed controversially. Total RNA from fresh-frozen otosclerotic bone chips obtained during stapes surgery was analyzed by RT-PCR for MeV RNA (fig. 1) [18]. MeV-related sequences were amplified in an average of 84% in several studies, whereas the negative controls always remained negative [19–21]. A possible explanation for the negative cases is primarily the true absence of MeV in the otosclerotic tissue. Alternatively, the absence of an otosclerotic focus might explain the negative results, since RNA has been extracted from the stapes fragments without histologic controls. Finally, technical problems and limitations of the RNA extraction technique from small eburnized bone chips have to be considered.

McKenna et al. [22] were able to detect MeV RNA in 8 out of 11 temporal bones with morphologically confirmed otosclerotic foci. All negative controls remained negative. The true absence of MeV within the otosclerotic tissue might explain the 3 negative cases. However, false-negative results could be related to technical problems which may occur dealing with celloidin-embedded tissues.

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Fig. 1. Detection of MeV by RT-PCR. Lanes 1, 2, and 4 with the amplicons of the expected length (120 bp). MW = Molecular weight marker; + = positive control; − = negative control.
Recently, Karosi et al. [23] have found MeV RNA in 14 out of 20 fresh-frozen footplates from patients with otosclerosis. They amplified RNA from minced and crushed bone chips by in vitro RT-PCR. In contrast, Grayeli et al. [24] could not confirm the presence of MeV neither in cells cultured from the otosclerotic foci nor in bone chips after RNA extraction and amplification by RT-PCR. They concluded that MeV is not involved in otosclerosis. However, it cannot be excluded that the negative results are due to the absence of otosclerotic foci in the examined tissue, as morphologic controls were not available. Furthermore, only few copies of MeV RNA are expected in a persisting infection and highly sensitive techniques including RNA extraction procedures are needed.

The controversial discussion about MeV RNA within the otosclerotic focus asked for a technique such as in situ RT-PCR, which combines morphology and amplification of the genetic material. In situ RT-PCR has been successfully used in research on hematologic tumors, but only few studies with bony tissue are available [25]. These studies were related to a paramyxoviral etiopathogenesis in Paget’s disease and performed on decalcified bone. The authors demonstrated the presence of canine distemper virus in all cases examined [26, 27]. Up to now, we had analyzed stapes footplate specimens of 15 patients with clinical otosclerosis by in situ RT-PCR. The bone chips were decalcified and paraffin embedded and the histological examination demonstrated the presence of otosclerotic foci within the decalcified and paraffin-embedded tissue. In all cases, osteoblasts, osteoclasts, chondrocytes, and epithelial cells of the middle ear mucosa close to the otosclerotic focus contained MeV RNA amplification products [unpubl. data].

Recently, we have managed to genotype the MeV within the otosclerotic tissue. Cells cultured from otosclerotic bone chips of 5 patients had the morphological and biochemical characteristics of preosteoblasts. After RNA extraction and reverse transcription, the C-terminal part of the MeV N gene was amplified and sequenced by two independent companies. The phylogenetic analysis revealed that all MeV were of the genotype A. This genotype was present in Europe before the vaccination era and contains several wild-type strains isolated before 1970. Sequencing enabled us to distinguish MeV found in our patients from all other strains known up to now [unpubl. data]. This result proves the persistence of the MeV genome for more than 40 years within the temporal bone of patients with otosclerosis and excludes any speculation of contamination or false-positive results.

**MeV Antibodies within the Perilymph**

The otosclerotic focus usually has intimate contact with the perilymph spaces so that antigens from the otosclerotic focus might reach the immune target
organ localized in the endolymphatic sac [28, 29]. It is known that antigenic stimulation of the endolymphatic sac via the perilymph can trigger a specific immune reaction [30]. We analyzed the perilymph and serum of patients with otosclerosis or Ménière’s disease, and of controls for the content of albumin, total IgG and specific MeV IgG by nephelometric assay and ELISA. The MeV IgG fraction of total IgG was significantly higher in the perilymph compared to the serum of patients with otosclerosis (fig. 2) [21]. In contrast, evidence for local production of antibodies against herpes simplex virus type I was found in patients with Ménière’s disease [31]. The reactivity of antibodies against MeV is decreased in patients with otosclerosis [32].

**Conclusion**

There is convincing evidence for a chronic inflammatory reaction in otosclerosis. MeV involvement was demonstrated in morphological, biochemical and immunological studies. Epidemiological data show a decrease in occurrence of otosclerosis and an increase in the average age of onset during the past 10 years, which could be due to the introduction of MeV vaccination in 1970 in Germany. Taken together, there is a strong association between MeV and otosclerosis. Further investigations will elucidate the role of MeV in the etiopathogenesis of otosclerosis.

**Fig. 2.** Analysis of IgG in the serum and perilymph. Perilymph samples from patients with otosclerosis, or Ménière’s disease, and from patients subjected to cochlea implantation were investigated by ELISA. The amounts of specific (MeV, herpes simplex virus, cytomegalovirus) IgG from total IgG in the perilymph in comparison with the amounts in the serum are expressed as index.
Acknowledgement

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Measles Virus Prevalence in Otosclerotic Foci

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Abstract

The etiology of otosclerosis is still unknown. Persistent measles virus infection of the otic capsule is supposed to be one of the etiologic factors in otosclerosis. The presence of measles virus was shown in otosclerotic patients by RT-PCR amplification of the viral RNA, detecting the viral proteins by immunohistochemistry and antimeasles immunoglobulin G in the perilymph samples. Nucleic acid (mRNA, vRNA, DNA) was extracted from pulverized, frozen stapes footplate samples of otosclerotic patients. Measles virus RNA was amplified by RT-PCR: reverse transcription and the first-round PCR amplification were performed by heat-stable recombinant *Thermus thermophilus* polymerase, while in the nested round PCR Taq polymerase was employed. Oligonucleotide primers specific to measles virus nucleoprotein and matrix protein RNA were used in these reactions. Edmonston- and Schwartzte-type measles viruses served as positive controls and cortical bone fragments, stapes superstructures, cadaver stapes, incus and malleolar samples served as negative controls. Among 102 otosclerotic patients, 62 stapes footplate samples contained measles virus RNA. Measles virus RNA was not detected in other bone specimens of the patients. The etiologic role of measles virus in the pathogenesis of otosclerosis should be considered. The 40 negative samples may be genetically determined otosclerotic cases or stapes fixations due to other causes.

Otosclerosis (otospongiosis) is a disease of unknown etiology causing conductive and/or sensorineural hearing loss. In the Caucasian population, the prevalence of otosclerosis is 0.3–0.4% of the general population and 5–7% of those with hearing loss [1, 2]. In Hungary (population is 10 million), less than 200 stapedectomies have been performed annually in the latest years. The characteristic histologic findings in active otosclerosis only occur in the otic capsule [1, 2]: focal, resorptive bone lesions with high cellularity and vascularization in
the pericochlear region, near the oval window and in the stapes footplate. The fissula ante fenestram usually is the barrier against focal bone resorption [1, 2]. There are a lot of osteoclasts (in Howship’s lacunae), giant cells, fibroblasts and proliferating endothelial cells in the active otosclerotic foci [2]. The osteoclasts of resorptive foci show an increased metabolic and osteolytic activity confirmed by enzyme cytochemistry [2, 3, 4]. There is no animal model of otosclerosis.

The etiologic role of measles virus in the pathogenesis of otosclerosis arose in the past 15 years. Measles virus is an RNA virus (with negative, single-stranded RNA) that belongs to the paramyxovirus family. It does not have neuraminidase but contains fusion protein (important in syncytium formation), hemagglutinin and hemolysin [5]. Nucleoprotein (NP) and matrix protein (MP) are necessary for the stabilization and replication of the viral RNA [5]. The human cellular receptor of measles virus is the CD46 molecule, which is a transmembrane glycoprotein and can be found on all nuclear cells [5].

McKenna et al. [6] and McKenna and Mills [7] have discovered pleomorphic filamentous structures similar to paramyxovirus particles in the osteoclasts of otosclerotic foci by electron microscopy. Niedermeyer and Arnold [4] and Arnold et al. [5, 6] have detected measles-virus-specific immunoglobulin G in the otosclerotic perilymph. The presence of MP and NP of measles virus was also confirmed in the stapes and postmortem cochlear samples of otosclerotic patients. A large amount of measles-virus-derived proteins were detected on the surface of osteoclasts, fibroblasts, embryonic chondrocytes and the proliferating endothelial cells (i.e. fusion protein, MP and hemagglutinin) [2, 8–10]. Lower antimeasles immunoglobulin G titers were measured by ELISA in the sera of otosclerotic patients compared to controls [11].

The presence of measles virus in otosclerotic stapes footplates was also shown by using RT-PCR [12–15]. However, there are conflicting results. The RT-PCR method applied by Grayeli et al. [16] revealed an absence of measles virus RNA in otosclerotic bone.

There are only hypotheses on the role of measles virus in the pathomechanism of otosclerosis [17–20]. In the background of primary otosclerotic cases (when there are no other lesions in the skeletal system, i.e. Paget’s disease, osteogenesis imperfecta, or osteopetrosis), there could be a persistent measles virus infection of the otic capsule or genetic abnormality [15, 21–24]. Three autosomal dominant genes were identified by the analysis of peripheral leukocytes of otosclerotic patients [OTSC1 (15q26.1-qter), OTSC2 (7q34-q36), and OTSC3 (6p22.3-p21.3)] [24]. Functions, exact genomic locations and the protein products of these genes are unidentified. There may be other genetic factors in the background of otosclerosis. The genetic susceptibility is probably not mediated by human leukocyte antigens [25]. Also, no antigens were found to
belong to the major histocompatibility complexes (MHC-I) that could be more frequent in patients with otosclerosis [25]. This study assessed the prevalence of measles virus in otosclerotic stapes footplate samples by a highly sensitive RT-PCR method.

**Materials and Methods**

**Extraction of RNA**

Extraction of nucleic acids from bone fragments requires the removal of inorganic material [15, 16]. Treatment with EDTA is a feasible decalcifying method since EDTA also inhibits the enzymatic digestion of the nucleic acids [13]. Other decalcifying agents, i.e. organic acids, will probably result in degradation of the RNA. The fixation of specimens by formaldehyde or paraformaldehyde can lead to fragmentation of the viral RNA genome, therefore fixative agents were not used in the pretreatment protocol of the specimens [12–15]. The nucleic acid extraction method used in this study consists of pulverization of the stapes footplates, enzymatic release of nucleic acids from the protein matrix, spinning out the gross insoluble material and affinity purification of the nucleic acids. The latter step is performed with a filter device that removes any insoluble material left after the spinning step and ensures the elution of purified nucleic acids.

Otosclerotic stapes footplate samples (n = 102) were stored in sterile plastic tubes (volume 1.5 ml) at −70°C until analysis. Bone fragments were frozen in liquid nitrogen and pulverized in sterile dry rubber cups without decalcification and formaldehyde fixation. The pulverized bone was suspended in 200 μl diethyl-pyrocarbonate-treated, thermosterilized distilled water. These procedures exclude the possibility of RNase contamination of the solvent. Human and viral nucleic acids (mRNA, vRNA, DNA) were extracted by a nucleic acid isolation kit (High Pure Viral Nucleic Acid Kit, Roche, Basel, Switzerland). This kit operates on selective nucleic acid binding and elution. The extraction was done according to the manufacturer’s instructions, except that extra- and intracellular proteins were digested by proteinase K for 50 min instead of the prescribed 10 min because of the compact composition of the stapes bone fragments. The isolated nucleic acid samples were eluted in a final volume of 50 μl and stored at −70°C.

**Reverse Transcriptase and Complementary DNA Polymerase Chain Reaction for Nucleoprotein RNA**

The NP RNA segment of the measles virus genome was amplified using seminested PCR. The target RNA segment that contains the connection points of primers is 440 bp long (5'- to 3'-segment: 1091–1531) (fig. 1). The recombinant *Thermus thermophilus* (rTth) DNA polymerase enzyme (500 units, 2.5 units/μl; Applied Biosystems, Foster City, Calif., USA) was used for the RT and cDNA PCR (first round) [25]. rTth DNA polymerase is suitable for both RT and cDNA PCR steps in the presence of 25 mM manganese-oxaloacetate electrolyte solution. Oligonucleotide primers specific to MV2 (0.4 μM) and MV3 (0.4 μM) measles virus NP RNA were used in RT-PCR (table 1, fig. 1). In the final volume of the reaction mix, there were 25 μl that included 4 μl of previously isolated RNA samples and 2.5 units of rTth DNA polymerase. The following temperature cycling scheme was applied for 40 cycles of
Fig. 1. The whole negative single-stranded RNA genome of measles virus. The connection points and target sequences of measles virus NP- and MP-specific oligonucleotide primers (MV2, MV3, MV4, NP14 and OMP1–6, IMP1–6). C = Constant protein; F = fusion protein; H = hemagglutinin; L = large protein; M = matrix protein; N = nucleoprotein; P = phosphoprotein. The Arabic numerals show the nucleotid sequence from the 5’ to the 3’ end.

RT-PCR in an automatic thermal cycler (Applied Biosystems): incubation at 60°C for 30 min, initial denaturation at 94°C for 2 min (RT reaction), 40 cycles of amplification (denaturation at 94°C for 30 s, annealing primers at 62°C for 1 min), and final extension at 60°C for 7 min [25]. RNA sample-free negative controls were used that could be suitable for the detection of random viral RNA contamination.

**Seminested Polymerase Chain Reaction**

First-round PCR products (cDNA) were amplified to obtain a higher sensitivity in a conventional PCR (seminested round of the whole PCR). Red Taq DNA polymerase (250 units, 1 unit/μl; Sigma-Aldrich, St. Louis, Mo., USA) was used in this reaction. In the seminested PCR, two oligonucleotide primer combinations specific to measles virus NP RNA were employed (table 1, fig. 1): MV3-MV4 (first set, 0.4–0.4 μM) and MV2-NP14 (second set, 0.4–0.4 μM). Both primer pairs contained one of the primers used in the first-round RT-PCR (MV2 and MV3). In the final volume of the reaction mix, there were 25 μl that included
Measles Virus Prevalence in Otosclerotic Foci

Table 1. Details of measles virus NP- and MP-specific oligonucleotide primers for RT-PCR detection of viral RNA, and the human ribosomal RNA-specific oligonucleotide probes for cellular control RT-PCR

<table>
<thead>
<tr>
<th>Primer</th>
<th>Sequence (from the 5’ to the 3’ end)</th>
<th>Temperature, °C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Measles NP-specific primers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MV2 (−)</td>
<td>GTT CTT CCG AGA TTC CTG CCA</td>
<td>67.5</td>
</tr>
<tr>
<td>MV3 (+)</td>
<td>GCA TCT GAA CTC GGT ATC AC</td>
<td>59.7</td>
</tr>
<tr>
<td>MV4 (−)</td>
<td>AGC TCT CGC ATC ACT TGC TCT</td>
<td>65.5</td>
</tr>
<tr>
<td>NP14 (+)</td>
<td>GCA AGG AAG ATA GGA GGG TC</td>
<td>61.5</td>
</tr>
<tr>
<td><strong>Measles MP-specific primers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OMP1 (+)</td>
<td>GAC AAG TCG GCA TGG GAC A</td>
<td>63.2</td>
</tr>
<tr>
<td>OMP2 (−)</td>
<td>TTA TCC GAA AGA CGG GTG ATG</td>
<td>62.1</td>
</tr>
<tr>
<td>OMP3 (+)</td>
<td>CAC CCG TCT TTC GGA TAA CG</td>
<td>62.7</td>
</tr>
<tr>
<td>OMP4 (−)</td>
<td>TGC TGG GCA CTA CGG TCT ACA</td>
<td>64.0</td>
</tr>
<tr>
<td>OMP5 (+)</td>
<td>CCC TCA CAA TGA CAG CCA GA</td>
<td>62.3</td>
</tr>
<tr>
<td>OMP6 (−)</td>
<td>TGT CTA GGG AGT CGG ATG CC</td>
<td>62.5</td>
</tr>
<tr>
<td>IMP1 (+)</td>
<td>CTA AGG GCA GGG ACC CAA A</td>
<td>62.3</td>
</tr>
<tr>
<td>IMP2 (−)</td>
<td>GGT GTC GGCG AGA AGA CAC GC</td>
<td>64.0</td>
</tr>
<tr>
<td>IMP3 (+)</td>
<td>CCG AGT TGT GCA TGG AGA GTC</td>
<td>63.2</td>
</tr>
<tr>
<td>IMP4 (−)</td>
<td>TCG CAC TTT GTG GTG AGG G</td>
<td>63.1</td>
</tr>
<tr>
<td>IMP5 (+)</td>
<td>AAT GAC AGC CAG AAG GCC CG</td>
<td>66.9</td>
</tr>
<tr>
<td>IMP6 (−)</td>
<td>GCG GTT CGG TTG TGG AGT TC</td>
<td>65.1</td>
</tr>
<tr>
<td><strong>Human cellular control primers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H36B4+ (+)</td>
<td>AGA TGC AGCA GAT CCG CAT</td>
<td>66.0</td>
</tr>
<tr>
<td>H36B4− (−)</td>
<td>ATA TGA GGC AGG AGT TTC TCC AG</td>
<td>65.4</td>
</tr>
</tbody>
</table>

1 μl of first-round PCR product (cDNA) and 0.5 unit of Red Taq DNA polymerase. The temperature profile of the nested round was (Hybaid, Manchester, UK): initial denaturation at 95°C for 2 min, 35 cycles of amplification (denaturation at 96°C for 20 s, annealing primers at 55°C for 1 min and primer extension at 72°C for 1.5 min). cDNA-free negative controls were used to check cross-contamination.

Amplimers were separated in a 1.5% agarose gel (Sigma-Aldrich) after a previous ethidium bromide labelling (400 mA, 160 V, 45 min). Molecular weight markers (Sigma-Aldrich) were employed in each gels (50–1,000 bp).

Reverse Transcriptase and Complementary DNA Polymerase
Chain Reaction for Matrix Protein RNA

The MP segment of measles virus RNA was also amplified in 36 previously analyzed and virus-positive stapes footplate samples. The target RNA sequence that contains the recognizing points of MP-specific oligonucleotide probes is 1,382 bp long (5’- to 3’-segment: 3460–4842) (fig. 1). The aforementioned RT-PCR profile was used in this reaction. In the planning step of the reaction, the MP target sequence was divided into three equal fragments.
In the RT, three overlapping primer pairs were used: OMP1-OMP2, OMP3-OMP4, and OMP5-OMP6 (0.4–0.4 μM) (fig. 1). In the nested cDNA PCR, also Red Taq DNA polymerase was utilized with the previously described thermoprofile. The following comprehensive oligonucleotide probes were applied in the cDNA PCR: OMP1-IMP2, IMP1-OMP2, OMP3-IMP4, IMP3-OMP4, and IMP5-IMP6 (fig. 1).

**Cellular Control Reverse Transcriptase-Polymerase Chain Reaction**

The confirmation of successful extraction of measles virus RNA was obtained by the detection of human cellular RNA in the isolated nucleic acid samples. Human cellular control oligonucleotide primers targeting human ribosomal RNA were employed in this reaction: h36B4+ and h36B4– (0.4–0.4 μM) (table 1). Enhanced avian reverse transcriptase (EA-RT; 1,000 units, 20 units/μl; Sigma-Aldrich) and genomic Red Taq DNA polymerase (250 units, 1 unit/ml; Sigma-Aldrich) were used in the cellular control RT-PCR. This reaction had two main steps. The previously isolated RNA samples were incubated with housekeeping control primers in the first step (75°C, 10 min, final volume 15 μl). After this incubation, EA-RT enzyme was used for RT-PCR (final volume 20 μl including 20 units of EA-RT). During the RT step, the temperature was increased from the initial 42°C to the final 50°C by 2°C steps after every 10-min interval. cDNA was amplified in a conventional PCR in the second step (final volume 25 ml including 1 unit of genomic Red Taq DNA polymerase) by genomic Red Taq DNA polymerase (Sigma-Aldrich). The temperature profile of the cDNA PCR (Hybaid) was: initial denaturation at 95°C for 2 min, 35 cycles of amplification (denaturation at 96°C for 20 s, annealing primers at 55°C for 20 s, primer extension at 72°C for 1 min), final incubation at 72°C for 2 min. Negative result excluded further analysis. Amplimers were separated in a 1.5% agarose gel (Sigma-Aldrich) after a previous ethidium bromide labelling (400 mA, 160 V, 45 min). Molecular weight markers (Sigma-Aldrich) were employed in each gels (50–1,000 bp).

**Controls**

Live, attenuated, Edmonston- and Schwartzte-type measles viruses were employed as positive controls of otosclerotic stapes footplate samples. Positive control measles virus RNA was extracted from MMR vaccine (MMR-II vaccine, MSD, Haar, Germany) by the aforementioned nucleic acid isolation kit (High Pure Viral Nucleic Acid Kit, Roche). Cortical bone fragments (n = 42) removed during tympanotomies (external auditory meatus), superstructures of stapes samples (n = 19), cadaver stapes samples (n = 2), incus (n = 2) and malleolar specimens (n = 1) were used as negative controls. The virus positivity of cortical bone was only examined when the stapes footplate samples gave a positive reaction against measles virus RNA.

**Results**

One hundred and two otosclerotic stapes footplate samples (n = 102; male = 38, female = 64) removed during stapedectomies were analyzed. The mean age of patients was 39.19 years (range 23–53 years). Air-bone gap at 1,000 Hz was at least 30 dB. Eleven patients remembered that they had had a measles virus infection in childhood and 8 other patients had a documented
Measles Virus Prevalence in Otosclerotic Foci

antimeasles vaccination. No disease similar to otosclerosis was found in the family histories of the patients; therefore, familial otosclerosis was excluded.

The optimal annealation temperature of rTth DNA polymerase in the first round of nested RT-PCR (critical temperature of the cDNA synthesis) was established at 62°C by using the method of thermogradient PCR (56.3–69°C) (fig. 2). The highly sensitive nested RT-PCR protocol used in this study could detect measles virus NP RNA in the amount of as low as 0.01 tissue culture infectious dose (fig. 3).

The hypothesis as to identifying RNA sequences (NP, MP) of persistently infecting measles virus from rather small bone specimens was successful. Persistent infections imply low replication rate, consequently a highly sensitive method was necessary, which covers all different sequences of the measles virus. The major determinants for the specificity and sensitivity of PCR detection are the oligonucleotide primers. Since the sensitivities of the PCR methods used in this field were not always available, we performed a computer-based assessment of the PCR primers described in the literature for optimal combinations and for optimal target recognition. These primers were found optimal (in silico) that had been reported to detect measles virus RNA in otosclerotic bone

\[ \text{Thermic gradient of annealation} \]

\[ \begin{array}{cccc}
69 & 67.6 & 65.3 & 63.3 \\
69 & 67.6 & 65.3 & 63.3 \\
56.3 & 59.4 & 57.7 & 56.3 \\
59.4 & 56.3 & 57.7 & 56.3 \\
\end{array} \]

381bp
231bp
221bp

**Fig. 2.** Optimal annealation temperature assessment of the rTth polymerase enzyme by thermogradient RT-PCR. Optimal annealation temperature of the first-round RT-PCR was established at 64°C. All of the possible, NP-specific primer combinations were applied in this reaction (MV2-MV3, MV3-MV4, MV2-NP14).
specimens [12, 13], while those primers that had not been able to detect measles virus RNA in otosclerosis were found suboptimal [16]. We tested 3 sense and 3 antisense PCR primers, which were found the best in silico. These primers could be used in MV1-MV4, NP14-NP6 nested and MV3-MV4, MV2-NP14 seminested combinations. In the present study, we applied the two seminested combinations that had the highest sensitivities. Therefore, the primers MV1 and NP6 were excluded from further use. It should be noted that using rTth DNA polymerase in the first round proved to be superior to the tested RT plus Taq polymerase systems.

Detection of measles-virus-derived RNA was successful in 62 cases of 102 otosclerotic stapes footplate samples (61% positive) (table 2). The other 40 samples did not give any positive results by the application of primers specific to measles virus NP RNA. Both primer pairs of the nested-round PCR (MV3-MV4, MV2-NP14) gave positive reactions in 42 cases of 62 positive samples (fig. 4a). In 13 cases of the 62 positive samples, only the primer pair MV3-MV4 specific to measles virus NP RNA gave positive reactions against measles virus RNA, and in 7 cases of the 62 positive stapes footplate samples, only the primer pair MV2-NP14 gave positive results (fig. 4b). MP RNA of measles virus was successfully detected in 36 otosclerotic stapes footplate samples that contained NP RNA (fig. 5). Human cellular RNA was successfully detected by cellular control RT-PCR in each of the 102 stapes footplate samples and all specimens were eligible for testing the presence of measles virus RNA (fig. 6).

Cortical bone fragments (n = 42) and stapes superstructures (n = 19) applied as negative controls did not contain any measles virus RNA, but the
Table 2. Results of highly sensitive seminested RT-PCR on otosclerotic stapes footplate samples and controls

<table>
<thead>
<tr>
<th></th>
<th>Otosclerotic stapes footplates</th>
<th>Controls¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MV positive</td>
<td>MV negative</td>
</tr>
<tr>
<td>Number Primers²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MV3-MV4/MV2-NP14</td>
<td>42</td>
<td>0</td>
</tr>
<tr>
<td>MV3-MV4</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>MV2-NP14</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>H36B4+/-</td>
<td>62</td>
<td>40</td>
</tr>
</tbody>
</table>

MV = Measles virus.

¹Cortical bone fragments and stapes superstructures were obtained from otosclerotic patients during stapedectomies. The incus, malleus and cadaver stapes specimens were removed from non otosclerotic patients during tympanoplasty or autopsy.

²Number of positive samples by using the primer pairs below.

Fig. 4. a Seminested RT-PCR of otosclerotic stapes footplate samples. K.G., Z.D., Sz.S. and B.E. are patients with virus-positive stapes footplate samples that gave positive amplification reactions by using both seminested primer pairs (MV3-MV4 and MV2-NP14). B.E.-c is a virus-negative cortical bone specimen of patient B.E. b Patient G.R. showed a positive amplification reaction only by application of MV2-NP14 primers. H.M. is a patient with virus-negative stapes footplate sample. Stapes sample of patient H.V. gave a positive amplification reaction only by using MV3-MV4 primers.
**Fig. 5.** Confirmation RT-PCR method of measles virus detection. Secondary semi-nested RT-PCR of 8 virus-positive stapes footplate samples by using MP-specific primers (lanes 1–8). These samples previously showed a positive reaction against measles virus NP RNA. All of these specimens contained the 3 target sequences of measles-derived MP RNA.

**Fig. 6.** Cellular control RT-PCR of 11 otosclerotic stapes footplate samples (lanes 1–11) by using human cellular control primers (h36B4+ and h36B4−) targeting human ribosomal RNA.

stapes footplates from the same patients showed viral RNA positivity. Cadaver stapes (n = 2), incus (n = 2) and malleolar specimens (n = 1) from nonotosclerotic patients employed also as negative controls did not contain measles virus RNA. Human cellular RNA was successfully detected by cellular control RT-PCR in each negative controls (table 2).
Discussion

The presence of intact measles virus genome was established by application of 12 MP-specific oligonucleotide primers (OMP1–6, IMP1–6). Detection of MP RNA was successful in the 36 previously analyzed and NP RNA-positive stapes footplate samples. This experience demonstrates the presence of intact measles virus genome in otosclerotic bone. However, the question arises whether viable measles viruses are present in the otosclerotic foci. The main evidence for the vitality of measles virus is the detectability of viral RNA, because without active viral replication, RNA is rapidly disintegrated.

We detected the presence of measles virus RNA in 62 stapedial footplate samples. However, only 42 samples gave positive results by application of both primer pairs (MV3-MV4, MV2-NP14) in the seminested PCR. None of the seminested combinations was superior to the other: failure rates to detect the target sequences were similar. Considering an equal sensitivity of the two seminested PCR methods, the most feasible explanation for this finding is the occurrence of mutations within the viral genome. Measles virus being an RNA virus has a high mutation rate. In acute infections, most mutations result in defective functions and in an antigenically uniform virus species circulating in unvaccinated populations. The persistent measles virus infections are, however, associated with deficient viral functions due to the accumulation of mutations. Defective virion production is a common feature of paramyxoviruses, since about 80% of virions are uninfective due to mutations of viral RNA segments that encode MP and fusion proteins [3]. Thus, multiple PCRs targeting different sequences can improve the detectability of persistent measles infections.

The pathomechanism of otosclerosis remains unclear. Measles virus probably exhibits a high affinity to the otic capsule (organotropism) as measles virus cannot be detected in the superstructure (its embryonic origin is different from other parts of the otic capsule) [27].

Defective measles viruses (these viruses have no functional MP) are unable to leave infected cells (osteoclasts, fibroblasts, chondrocytes and proliferating endothelial cells). However, viral antigens are also expressed by the MHC-I molecules of the cytoplasmic membrane on the surface of infected cells [3]. The chronic viral antigen stimulation could induce a secondary autoimmune reaction from the cellular immune system of patients (natural killer cells, lymphokine-activated killer cells, CD8+ lymphocytes, granulocytes) [3, 13, 28–31]. It is supposed that the most important factor in the pathogenesis of otosclerosis is the chronic and continuous viral antigen stimulation of the cellular immune system of the patients, because defective measles viruses cannot induce direct cellular damage [3, 19, 25].

A high amount of cytotoxic enzymes [32] (e.g. elastase, collagenase, cathepsin D/B), inflammatory cytokine mediators and complement fragments [22]
(e.g. interleukine-1, interleukine-6, tumor necrosis factor-α, lymphokines, C1q, C3a, C5a) are reported to be released from otosclerotic foci. These substances enter into the perilymph and change the electromotility of outer hair cells [33–35], which may result in sensorineural hearing loss in otosclerosis [33].

The 40 negative samples may be genetically determined otosclerosis cases [23, 24] or stapes fixations due to other etiology (e.g. inflammation, dystrophic calcification), as viral RNA could not be detected in these samples after repeated analysis. Genetic predisposition in patients who suffer from otosclerosis caused by measles virus can be assumed, because otosclerosis is uncommon in those people who suffered from measles. Measles is a widespread disease in nonindustrialized countries (40 million infections and 1.2 million deaths in 1996), whereas otosclerosis is very rare in these regions [36]. Otosclerosis frequently occurs in northern industrialized countries, where 98% of the population are actively immunized against measles [36]. An unresolved question that remains is why measles virus shows an organotropism to the otic capsule. The absence of an animal model also emphasizes the role of measles virus in the genesis of otosclerosis, since small mammals do not possess the measles-binding protein CD46. The presence of measles virus in the otosclerotic bone may be an epiphenomenon instead of being a causative agent.

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References

Measles Virus Prevalence in Otosclerotic Foci


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Antimeasles Immunoglobulin G and Virus-Neutralizing Activity in Sera of Patients with Otosclerosis

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Abstract

Otosclerosis is considered as an organ-specific measles virus (MV)-induced disease. The majority of people are infected with MV during childhood, and the immune activation is characterized by a lifelong persistence. Any kind of depressed systemic antimeasles reaction can lead to induction of a local immune response in the inner ear. MV proteins were resolved by conventional polyacrylamide gel electrophoresis in the presence of a denaturing detergent. In subsequent Western blot, healthy blood donors demonstrated a stronger reaction against most proteins than age- and sex-matched otosclerotic patients. Different serum dilutions were tested for neutralizing activity against constant MV concentration. Nearly complete viral neutralization was achieved with samples containing inactivated complement and in immunoglobulin-G-containing fractions, and activity in sera from patients with confirmed otosclerosis was significantly weaker than in healthy individuals. Our observations are consistent with viral participation in otosclerotic pathogenesis, but it is difficult to say if the diminished antimeasles humoral response is a consequence of or the cause for a local measles infection.

Background

The etiopathogenesis of otosclerosis is unexplained. There are some data for measles virus (MV) in cases of otosclerosis (fig. 1).

The majority of people are infected with MV during childhood, and the immune activation is characterized by a lifelong persistence. It seems that the average age of patients with otosclerosis has increased since the introduction of the MV vaccination program.
Fig. 1. Suspected routes of MV participation in bone turnover reactivation [1–3, 6–12].
Hypothesis

Any kind of depressed systemic antimeasles reaction can lead to induction of a local immune response in the inner ear and possibly to reactivation of bone turnover in this specific region.

Antimeasles Immunoglobulin G

MV proteins were resolved by conventional preparative SDS-PAGE. After subsequent Western blot, the membranes were air-dried and subjected to densitometry. According to statistical analysis, healthy blood donors demonstrated a stronger reaction against most proteins than age- and sex-matched otosclerotic patients (fig. 2) [4].
**MV-containing mixture:**
(a) virus only;
(b) virus with different dilutions of whole sera;
(c) virus with treated/separated sera

**MTT assay**
1. MTT solution was added to each well and the plates were incubated for 4h under cell culturing conditions.
2. Solubilization solution was added to dissolve the formazan crystals.
3. After 24h, the absorption at 600nm was measured on an ELISA reader

**Fig. 3.** Schematic presentation of the combination between in vitro virus neutralization procedure and quantitative MTT reaction.

**Fig. 4.** Titer for 50% MV-neutralizing activity for several sex-matched pairs of healthy individuals and otosclerotic patients.
Fig. 5. Schematic presentation of sample separation (a) and box-whiskers plots of virus-neutralizing activities (mean ± standard error, see legend in (b) in different fractions: all samples (b), only sera with inactivated complement (c) and IgG fractions (d).
**Measles Virus Neutralization Assay with Whole Sera**

The ability of MV to infect and replicate in the cell monolayer was detected by enumeration of living and growing cells with a colored reaction, constructed especially for this study (fig. 3) [5].

Virus-neutralizing activity in sera from patients with confirmed otosclerosis was significantly weaker than in healthy individuals ($p = 0.032$). When age- and sex-matched pairs were compared, in 5 cases, the neutralizing activity in the healthy counterpart was higher. The opposite situation was observed in 1 healthy/otosclerosis couple only (fig. 4).

**Measles Virus Neutralization Activity in Separated Sera**

Samples from selected sera were incubated at $56^\circ C$ for 30 min to inactivate the complement. Immunoglobulin G (IgG) fractions were isolated using protein G sepharose 4 fast flow affinity columns (fig. 5a).

Nearly complete viral neutralization was achieved with samples containing inactivated complement, and in IgG-containing fractions (fig. 5b), and activity in sera from patients with confirmed otosclerosis was significantly weaker than in healthy individuals (fig. 5c, d) [5].

**Conclusion**

Our observations are consistent with viral participation in otosclerotic pathogenesis, but it is difficult to say if the diminished antimeasles humoral response is a consequence of or the cause for a local measles infection.

**References**


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Phenotype-Genotype Correlations in Otosclerosis: Clinical Features of OTSC2

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Abstract
As part of the GENDEAF consortium, a European multi-centre otosclerotic database is under construction to collect the clinical data of as many otosclerotic patients as possible. Otosclerosis represents a heterogeneous group of heritable diseases in which different genes may be involved regulating the bone homeostasis of the otic capsule. The purpose of the GENDEAF otosclerosis database is to explore the otosclerotic phenotype more in depth. Subtle phenotypic differences otherwise not visible, may become statistically relevant in a large number of patients. Their identification can lead towards the discovery of new genes involved in the pathway of abnormal bone metabolism in the human labyrinth. As soon as one of the otosclerotic genes is identified, it would allow us to identify genotype-phenotype correlations. From other deafness genes, it is know that different mutations in the same gene may cause similar phenotypes of varying severity. Also the variability in treatment outcomes after surgery or fluoride therapy may result not only from differences in practice or surgical skill among physicians, but also on the nature of the underlying disorder. Screening large numbers of patients would make it possible to undertake clinical trials comparing different treatments. Identifying a genetic susceptibility would allow us to dissect out possible environmental factors that prevent the expression of clinical otosclerosis in those that carry the mutated gene and yet retain normal hearing.

Otosclerosis is a disorder in which both genetic and environmental etiological factors are involved [1]. Although a limited number of large autosomal dominant families have been described, most patients occur in small families
with unclear inheritance pattern or have no prominent familial character, pointing to a complex etiology in these cases. Clinical otosclerosis has a reported prevalence of 0.3% among white adults, making it the single most common cause of hearing impairment in this population [2]. Histological otosclerosis even has a prevalence of 3.5% among white adults [3].

Otosclerosis represents a heterogeneous group of genetic diseases in which different genes may be involved regulating the bone homeostasis of the otic capsule. It is hypothesized that in response to various gene variants and environmental factors, the physiologic inhibition of bone turnover in the otic capsule is overruled resulting in a localized bone dysplasia known as otosclerosis [3]. Many different environmental factors have been implicated in the etiology of otosclerosis, including infectious causes such as measles virus, hormones (related to puberty, pregnancy and menopause), and nutritional factors (fluoride intake) [4, 5].

Large autosomal dominant otosclerosis families have been used for gene identification studies, but the first gene responsible for otosclerosis has yet to be cloned. However, five genetic loci, OTSC1–OTSC5, have been published to date, supporting the hypothesis that mutations in any of a number of genes may be capable of causing the otosclerosis phenotype. OTSC1 was mapped to chromosome 15q25–q26 in an Indian family in which hearing loss began in childhood [6]. The OTSC2 locus was mapped to a 16 cM region on chromosome 7 (7q34–36) in a large Belgian family [7]. More recently, the OTSC3 locus has been mapped to chromosome 6 in a large Cypriot family (6p21.3–22.3) [8]. The defined OTSC3 interval covers the human leukocyte antigen (HLA) region, consistent with reported associations between HLA-A/HLA-B antigens and otosclerosis. The localization of OTSC4 in an Israeli family has also recently been reported [9]. A fifth locus for otosclerosis (OTSC5) was mapped to chromosome 3q22–24 in a large Dutch family [10]. Such genetic heterogeneity has been well demonstrated for nonsyndromic sensorineural hearing loss [11].

Materials and Methods

Hearing thresholds obtained in patients from two previously published OTSC2 families were collected. Only patients with a haplotype consistent with the linkage were included. Data from 34 genotypically affected members from two families with a linkage to OTSC2 were included to investigate the phenotype-genotype correlations more in depth. The mean age of the affected members was 52 years ranging between 24 and 89 years. The male/female ratio was 15/24. All subjects had undergone a general otorhinolaryngological examination to exclude nonhereditary causes of hearing impairment. Audiograms were recorded using standard procedures. Both air and bone conduction threshold levels were recorded. Last-visit preoperative audiograms were included. To recognize the maximal effect of the disease on
hearing, only the thresholds of the worst ear were used in the statistical analysis. Pure-tone hearing thresholds were analyzed in relation to age (linear regression analysis) to construct age-related typical audiograms (ARTA) both for bone and air conduction pertaining to age 20, 30, 40, 50, 60, 70 and 80 years. Also age-related air-bone gaps (ARAB) were plotted: the air-bone gap was recalculated from the ARTA by subtracting bone from air conduction. Statistical analysis was performed with the SPSS 11.5.1 software.

**Results**

Data from 34 genotypically affected persons from two families were included. Linear regression analysis demonstrated only weak correlations between hearing loss and age ($R^2$ values for air conduction: between 0.09–0.32; $R^2$ values for bone conduction: between 0.05–0.31).

The air conduction thresholds per frequency as well as the air-bone gap at 500 Hz are illustrated with a box-and-whisker plot (fig. 1). Overall, the audiometric configuration was quite variable resulting in mean hearing thresholds from 250 to 8,000 Hz that were not statistically significantly different.

Figure 2 shows the ARTA for bone and air conduction as well as the ARAB. The ARTA for air conduction had a configuration that was rather flat between 250 and 4,000 Hz. The ARTA for bone conduction demonstrated a

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Fig. 1. Box-and-whisker plot: air conduction versus air-bone gap at 500 Hz.
slight slope towards higher frequencies with a maximal deterioration/year at 2,000 Hz. Yearly deterioration was minimal at 500 Hz.

Also the annual threshold deterioration was calculated for each frequency between 250 and 4,000 Hz. The annual threshold deterioration indicated a progression of 0.37–0.82 dB/year for bone conduction and 0.81–1.32 dB/year for air conduction. On the ARAB plots, the maximal air-bone gap was situated at 500 and 4,000 Hz and the Carhart notch at 1–2 KHz was also clearly visible. The air-bone gap deterioration at 500 Hz amounted to 0.41 dB/year.

**Fig. 2.** ARTA and ARAB of OTSC2 patients. *a* ARTA (air conduction). *b* ARTA (bone conduction). *c* ARAB.

Discussion and Conclusion

The pooled data from two families segregating with the OTSC2 locus demonstrated quite variable audiometric configurations with only a limited contribution of age. Even in this monogenic form of otosclerosis, it seems that other modifying factors are implicated in the mechanism that triggers the osseous change. These results clearly illustrate the complexity of the otosclerotic disease:
the mechanism of removal of normal bone followed by its replacement by otosclerotic bone remains as yet unknown. It is hypothesized that these modifying factors may be both genetic and environmental. Further refinement of the phenotype-genotype correlation will become available as soon as the OTSC2 gene for otosclerosis is cloned and specific mutations recognized.

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Audiological Evaluation of Patients with Otosclerosis

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Abstract

Even though the diagnosis of otosclerosis is confirmed definitively during surgery, preoperative diagnosis and determination of the indication for surgery are made based on audiological evaluation. Audiological tests should firmly establish a conductive component to hearing loss. The measurement of pure-tone air and bone conduction thresholds has limitations that prevent an accurate diagnosis based solely upon these test results. Such limitations include general variability of threshold measurements, individual variations of tests in the bone conduction mode, and complex interactions between changes of middle ear mechanics and threshold. Objective audiometric tests should be added because of these uncertainties. The presence of otoacoustic emissions effectively excludes a diagnosis of otosclerosis. Standard clinical immittance measurements are used to confirm (or exclude) otosclerosis, the typical pattern being a normally shaped tympanogram and absent stapedial reflexes. Multifrequency tympanometry adds little information. Aside from establishing a preoperative diagnosis, audiological evaluation provides quantification of hearing loss, upon which the indication for surgery is based. Moreover, it lays the foundation for evaluation of surgical success and outcome measures. For both of these aims, speech audiometric tests such as a speech reception threshold should be included in the preoperative audiological evaluation of patients with otosclerosis.

Audiological evaluation is essential for stapes surgery in three ways. First, it points to the diagnosis of otosclerosis, even though it cannot establish the diagnosis. Only surgery and possibly imaging can do so. Second, it quantifies hearing loss and thereby helps in making a decision on whether surgery is warranted or not. Finally, it serves as the most important, certainly the best reproducible measure of outcome or success of surgery.

Some audiometric measures can be used for all three of these aims; some may help just for one or two. Tests should be selected in such a way that they provide the necessary information effectively and efficiently.
Diagnostic Audiometry

The audiometric diagnosis of otosclerosis is based largely on interpretation of the air-bone gaps that establish the presence of a conductive component to hearing loss. Other measures such as tuning fork tests or more sophisticated behavioral tests may be used along with objective audiometric measurements for this purpose.

Tuning Fork Tests

Tuning fork tests are a simple means of determining the presence of a conductive hearing loss. They are based on the same physical principles as the audiometric measurements. As such, they are subject to the same limitations and uncertainties, which are discussed in more detail in a later section on pure-tone audiometry.

A multitude of tuning fork tests exists; most were developed before electroacoustic audiometry was available as a routine clinical procedure. The two tuning fork tests still routinely used today by most otologists are the Weber and Rinne tests, both of which are generally well known. Weber described his classical test in 1825 [1]. The test relies on the finding that acoustic energy transmitted to the inner ear by bone rather than air conduction is greater in an ear with a conductive hearing loss. Thus, the Weber test alone detects one-sided or asymmetric conductive hearing loss. An alternative without the need of a tuning fork is the humming test [2], in which lateralization occurs when the patient is asked to hum loudly with the mouth closed.

The Rinne test is helpful when both ears have a conductive hearing loss [3]. It can be interpreted in two ways. First, it can be based on a comparison between bone and air conduction thresholds. Normally, the air conduction threshold is reached about 15 s later than the bone conduction threshold. Alternatively, it can be based on a loudness comparison between the two conduction modes.

The usefulness of the tuning fork tests derives from their being simple, inexpensive and quick. In addition, it is important that the surgeon performs these tests personally. Experienced surgeons can gain quick and useful information not only about the validity of the audiogram or the hearing of the patient, but also about the personality of the patient such as being very clear or hesitant during these tests.

Pure-Tone Audiometry

If an audiometer is calibrated correctly, then air and bone conduction thresholds measured in decibels hearing level should more or less be superimposed when there is no conductive component present. Because both thresholds
will show a slightly skewed distribution with a peak by definition at 0 dB HL in a normal hearing population, the two thresholds should cross one another in individual measurements due to this statistical distribution. Calibration or the measurement procedure may be skewed if bone conduction thresholds are always found to be better than air conduction thresholds on audiograms.

Even though air and bone conduction thresholds are by convention the same decibel hearing level in ears without a conductive component, we should keep in mind that the energy delivered by a vibrator for obtaining bone conduction thresholds is orders of magnitude greater than that needed with headphones used to deliver stimuli for air conduction threshold measures. This fact leads to inherent limitations in threshold tests with bone conduction stimulation. These include a restricted upper level of output (typically 50–70 dB HL, depending upon the equipment and the frequency being tested) and an upper frequency limit of 4 kHz because vibrators generate air-conducted sound at higher frequencies, which may then be heard through air conduction.

The higher energy level of vibrators is also partially responsible for clearly greater variance of bone conduction threshold measurements, besides calibration procedures being less reliable than those for air conduction. Other reasons for the higher variability of bone conduction thresholds include more individual variability in transmission of the vibration to the skull, from the skull to the inner ear, and the critical need of accurate masking of the nontest ear. All of these difficulties can make the measurement of bone conduction threshold challenging.

One difficult test situation involves the hearing sensitivity of an unaffected ear. It is not unusual to have conductive hearing loss from otosclerosis on only one ear with normal hearing on the opposite side. Masking is essential to eliminate participation of the nontest ear, and for reasons just mentioned, measurements may not reach a level of validity that is required as the basis for recommending surgery.

Bone conduction thresholds can be elevated in ears with otosclerosis, particularly in the 2-kHz region. This typical finding is called the Carhart notch, and it reflects the impedance mismatch between the middle and inner ear created by the fixation of the stapes. The Carhart notch is a useful hint for the presence of otosclerosis, but it does not provide definitive proof.

Not every difference between thresholds measured using earphones or bone vibrators for the same ears is invariably due to conductive dysfunction. Figure 1 displays the audiogram of such a case. Unusually low bone conduction thresholds and an air-bone gap in the frequency range below 2 kHz can be noted. The diagnosis of otosclerosis is improbable with such an audiometric pattern. An alternative possibility for such a pattern is pressure equalization between the perilymphatic and cerebrospinal fluid spaces as can occur with a spontaneous dehiscence of the superior semicircular canal. Figure 2 illustrates
Fig. 1. Audiogram of a patient with dehiscent superior semicircular canals demonstrating air-bone gaps in the lower frequency range not due to conductive malfunction of the middle ear.

Fig. 2. CT scan of the superior semicircular canal showing a dehiscence of its bony shell on both sides.
this finding for the ears of the patient with the corresponding audiogram in figure 1. Mikulec et al. [4] have recently described a series of patients with similar findings, many of whom had undergone stapes surgery with a presumed diagnosis of otosclerosis.

Fluid mechanics and the impedance of the system change with such a ‘third’ window of the inner ear leading to increased sensitivity of the so-called bone conduction response [5]. Several hypotheses have been proposed to explain how such an increased sensitivity may occur. These are linked to more general hypotheses about how sound reaches the cochlear fluids in the bone conduction mode. These mechanisms remain controversial; they are complex and not entirely clear.

One explanation of an air-bone gap in such cases has been proposed by Sohmer et al. [6]. They concluded that so-called ‘bone’ conduction is not only due to sound reaching the inner ear by bone vibration. They demonstrated that acoustic energy delivered by a vibrator might reach the inner ear through soft tissues and cerebrospinal fluid without bone actually vibrating. Thus, ‘bone conduction’ may be a misnomer. It cannot and should not be taken literally. The point is that the presence of an air-bone gap in threshold measurements is not reliable enough to use as the sole basis for making a decision about surgery. Conductive components should be verified by other means.

**Objective Audiometric Tests**

Simple and effective methods are available to confirm or exclude a conductive dysfunction. Immittance measurements have proven their clinical value in evaluating the status of the middle ear for decades. This method represents the standard, and it should be included in every audiological evaluation for the differential diagnosis of otosclerosis. The usual pattern in an ear with otosclerosis is a normally shaped tympanogram with absent stapedial muscle reflexes for both ipsilateral and contralateral stimulation. It is essential to include contralaterally induced stapedial reflexes because they are more reliable and less prone to artifacts.

Multifrequency tympanometry provides information on the middle ear resonant frequency, which is higher in ears with otosclerosis due to the fixation of the ossicular chain [7]. However, a large overlap of the resonance frequencies between normal and otosclerotic ears limits the diagnostic usefulness of this testing.

The measurement of otoacoustic emissions (OAEs) can also be helpful in establishing a conductive component to a hearing loss. OAEs are not present in ears with otosclerosis. Their presence effectively excludes not only such a diagnosis, but also a clinically important conductive middle ear component. OAE tests are useful because they are easy, quick and reliable. The measurement of
transiently evoked OAEs may be preferable over distortion product OAEs (DPOAEs) because they are less prone to artifacts. When measuring DPOAEs, the increased stiffness of the ossicular chain in otosclerosis may lead to artifactual distortions at sound levels for which they do not normally occur. Moreover, clinical DPOAE systems cannot differentiate such artifactual distortion products from those biologically generated within the inner ear.

Quantifying Audiometry

An essential part of the audiological assessment is to demonstrate the need for rehabilitative measures, and the need for surgery in the particular case of suspected otosclerosis. A small air-bone gap with little overall hearing loss will not be an indication for surgery, even if the diagnosis of otosclerosis can be established. Three major components are to be considered when recommending surgery for otosclerosis: the overall hearing loss, the amount of the air-bone gap, and the handicap experienced by the patient. While these three components are interrelated, they cannot be predicted from one another. They have to be assessed independently.

The overall effects of the hearing loss are usually inferred from the air conduction thresholds on the audiogram. However, we should keep in mind that any definition of hearing loss on this basis, or for that matter on any other audiometric basis alone, is arbitrary. Air conduction threshold measures provide only an indirect means of determining the hearing difficulties that patients might experience in their daily lives. The inclusion of speech audiometry, usually by measuring the speech reception threshold, will not add information about these effects. The advantage of including speech audiometry relates more to the outcome measures discussed below.

The amount of the air-bone gap can provide an indication of the hearing gain that can be achieved by surgery. However, the derivation of the air-bone gap is limited by the general lack of precision in measuring bone conduction thresholds, as described previously, and by the presence of a Carhart notch, which can change after surgery in an unpredictable way. Thus, the possible gain of hearing thresholds due to surgery may be assessed in more general and intuitive ways rather than by relying strictly upon numeric data.

As a rule, the same thing is generally true for the assessment of hearing handicap in patients with otosclerosis. Surgeons tend to assess the degree of auditory handicap intuitively by talking to their patients. The use of formal questionnaires does not seem to be in widespread use for the purpose of evaluating pre- and postsurgical effects of stapes surgery. Many validated questionnaires have been used in other rehabilitative areas of audiology, and their use
adds significantly to audiometric measures. Therefore, assessing hearing handicap in patients with otosclerosis using such questionnaires would be beneficial not only in evaluating handicaps before surgery, but also outcome and surgical success.

**Outcome Measures**

The Committee on Hearing and Equilibrium of the American Academy of Otolaryngology has published formal recommendations for how to evaluate and report audiometric improvement after surgery for otosclerosis [8]. These recommendations include air conduction threshold measurements from 0.5 to 8 kHz and bone conduction between 0.5 and 4 kHz, both including 3 kHz. It is needless to say that all of these measurements have to be done before and after surgery, including the repetition of the measurement of bone conduction. The postoperative air-bone gap must be determined from these direct measurements because bone conduction thresholds may increase or decrease as a result of the surgery.

Even though these guidelines do not include speech audiometry, there are good reasons to include measures of speech audiometry to evaluate outcome. For example, stapedectomy has been shown to produce better threshold gains for pure tones but worse speech audiometric gains when compared with small fenestration stapedotomy [9]. The reason for such findings may be because of different mechanical properties of the two methods of stapes replacement, favoring the transmission of high frequencies and transient events for stapedotomy because of less mass and less elastic fixation.

Thus, speech audiometry, particularly a threshold for speech (i.e. speech reception threshold) is recommended as an overall audiometric measurement to evaluate surgical outcome after stapes surgery. Improvement of speech reception threshold has been shown to be a reliable measure of postoperative success [10]. It performs as well or better than any averages of pure-tone thresholds.

Overall hearing handicap and quality of life can be assessed using questionnaires, either as a single measurement after surgery, or as a repeated measurement before and after surgery. A multitude of validated questionnaires exists for such purposes, but few results have been reported, indicating that such methods are used rarely.

**References**


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Sofia Profile Plot – A New Graphical Approach to Present the Changes of Hearing Thresholds with Time

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\textbf{Abstract}

After pure-tone audiometry, we have several sequences of threshold values. Usually, a multiple-line plot is used to present and compare data between measurements by overlaying them in a single graph. Calculation of air-bone gap and pure-tone average is widely accepted as an approach to simplify statistical handling of these data. The aim of this report was to introduce the Sofia profile plot using as examples different otosclerotic cases. This plot provides a simple way to visually present several pre- and postoperative hearing thresholds. Individual data points (pure-tone average and some other thresholds) are presented by marks in two-dimensional space. The vertical axis represents the time line and starts with the first threshold evaluation. The horizontal scale is used to mark hearing levels in decibels – the right ear on the left of the vertical axis and the left ear on the right. The Sofia profile plot was developed especially for otosclerotic patients and permits the unambiguous marking of the onset of any individual unilateral or bilateral event (e.g. operation, revision, tinnitus) and thus to visually inspect its impact on hearing levels.

\textbf{Background}

Pure-tone threshold audiometry is a well-established method to check and follow hearing. It has been suggested to present not only summary data (level 1), but also raw audiometric data for each individual patient (level 2) [1]. Usually, a multiple-line plot is used to compare data between measurements by overlaying them in a single graph. There is an international standard with a two-dimensional grid and symbols for a black-and-white data presentation.
Customarily, we plot the frequency/intensity data for the two ears separately and if there are two measurements we can use color coding and/or specific symbols.

**Limitations**

There is a problem if, instead of performing summary statistics, we want to present several threshold sets at different times for a patient or compare both pre- and postoperative data for several patients. It is even more problematic if we try to simultaneously present several measurements for several patients.

We can simplify data manipulation and preserve meaningful personal information by calculating some parameters like the widely accepted pure-tone average (PTA) for speech frequencies or air-bone gap (ABG). Two quite useful graphical approaches based on PTA and scatter plot were proposed to submit individual data for many patients simultaneously.

The first method, known as the Glasgow plot [2], compares the PTA for air conduction between the two ears, both pre- and postoperatively, and is a valuable tool to estimate the effect of middle ear operation on hearing symmetry. (We can use the same approach to follow one patient continuously, but the figure is somewhat confusing and there is a lack of information about bone conduction.) The problem with the absent ‘bone data’ was successfully resolved in the Amsterdam plot [3], with which we can estimate overclosure or iatrogenic cochlear damage. It is possible to compare these data for many patients but not to follow one patient at different times.

**The Principle of the Sofia Profile Plot**

We start with the classical pure-tone threshold data set calculating PTA separately for bone and air conduction. Based on personal preferences, the PTA can be calculated using three or four frequencies with/without 3 kHz.

The plotting space is two-dimensional. The vertical axis represents the time line (fig. 1) and starts with the first threshold evaluation. There is no ‘end point’ and new data can be added manually, when they are available. Presenting data with time allows to have a more or less regular threshold evaluation. It is even possible to have some ‘missing points’ in the data set when there was no audiometric follow-up for a long time. In such a case, the respective values can be ‘interpolated’, or the real situation can be presented on an interrupted axis.

The vertical axis labels can be real dates corresponding to the patients’ records. Most of the popular graphical programs permit the effortless plotting
of real dates on a timeline. The time axis should have a relative dimension when different cases are compared. In figure 2, there was a 6-month interval between two successful operations; therefore, it was reasonable to use a 1-month plotting step. In contrast, there were 2.5 years between the operations in example 2 (fig. 3); thus, a 3-month vertical axis step was chosen.

**Fig. 1.** Schematic presentation of the Sofia profile plot. Pure-tone curves: sequential values for averaged pure-tone thresholds for 0.5 kHz, 1 kHz and 2 kHz (eventually 3 kHz) for air conduction (PTA AC; ⬤) and bone conduction (PTA BC; ●). ‘Free curve’ (▲): any other data set measured in decibels, such as 4 kHz bone conduction, or speech recognition thresholds.

**Fig. 2.** Typical case of symmetrical stapedial otosclerosis with successful postoperative bilateral ABG closure. A slight improvement in postoperative PTA BC as a result of the Carhart effect can be clearly observed. There were two short episodes of central tinnitus. Each step in the time axis presents a month. ▲ = PTA AC; ● = PTA BC.
The horizontal scale is used to mark hearing levels (in decibels) – the right ear on the left of the vertical axis and the left ear on the right (fig. 1). Individual data points are presented by different marks and/or lines and time changes can be followed not only for PTA, but also for a third or a forth continuous variable like bone conduction for 4 kHz (fig. 4), high-frequency air conduction or speech reception threshold. Moreover, some interdependencies like ABG are clearly visible. As with other analytical approaches, it is advisable to measure and plot averaged postoperative bone conduction thresholds, and thus to rule out the problem of ‘overclosure’. Otherwise, there will obviously be an interception of the PTA air conduction (PTA AC) and PTA bone conduction (PTA BC) curves.

Having a time line, unilateral events like trauma and operation, or temporary conditions like appearance and disappearance of tinnitus or stapedius reflex can be clearly marked. It is also possible to notify general events affecting both ears like pregnancy, noise exposure, common infection, barotrauma, or intoxication.

Moreover, several patients may be compared graphically – all data sets can be aligned based on the time of operation or on the first subjective symptom. However, comparing cases with different time intervals between consecutive operations or with distinct follow-up durations is problematic. This can be resolved by sacrificing the time scale and categorizing the data into first

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**Fig. 3.** A case of mixed bilateral otosclerosis with a gradual elevation (both pre- and postoperatively) in BC thresholds. The interval between two operations was 2.5 years; each mark on the time line presents 3 months. There was a slight change after the first operation in the nonoperated (left) ear, probably as a result of masking phenomenon or interassay variability. ♦ = PTA AC; ● = PTA BC.
**Fig. 4.** Asymmetrical mixed otosclerosis – 3 months’ follow-up. There was a marked ABG on the right, which was successfully closed after stapedotomy. The bone conduction thresholds for 4 kHz are also shown and a slight operative damage can be observed in spite of a clear postoperative improvement in bone conduction as a result of the Carhart effect. The left ear shows a small ABG and cochlear involvement. ◆ = PTA AC; ● = PTA BC; ▲ = ‘free curve’ (see figure 1).

**Fig. 5.** Comparison of figures 2, 3 and 4 on a common plot after time data categorization.

preoperative period, interoperative period, and postoperative period (fig. 5). It is also a good idea to horizontally order the two ears and, instead of left and right, designate them as first operated and second operated or treated and nontreated.
Discussion

The proposed chart plot was specially developed for otosclerotic patients and the data presented here were from this group. However, the same approach can also be used for other pathologies. It was initially named ‘vase plot’, or ‘profile plot’, but following the established naming convention for the Glasgow plot and Amsterdam plot, we entitled it the Sofia profile plot.

Natural hearing is binaural and several parameters have been used to address this before and after surgery. Using the proposed method of data presentation, both ears are related and symmetry of the condition for the plotted parameters is obvious. The categorized variant of the Sofia profile plot can easily compare dissimilar conditions or treatment modalities.

All graphs in this paper are monochromatic – different curves and symbols are clearly distinguishable and the proposed plot is useful for black-and-white publication.

There is no universal graphical approach to simultaneously present several measurements of pure-tone thresholds at different frequencies for a group of patients. For the sake of clarity, we ought to omit some data and average others. The proposed plot is designed to follow the time course of averaged threshold data and clearly mark uni- and bilateral events.

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Distortion Product Otoacoustic Emissions in Otosclerosis: Intraoperative Findings

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Abstract

The aim of the study was to investigate changes in middle ear dynamic characteristics caused by both otosclerosis and stapes surgery (platinotomy, prosthesis positioning, ossicular chain maneuver) and to evaluate distortion product otoacoustic emissions (DPOAEs) before and following surgery. The study included 15 patients (12 women, 3 men; mean age 51 years; range 32–69 years) with advanced otosclerosis. All the patients were evaluated with the use of pure-tone audiograms (preoperatively, 5 and 30 days after surgery), stapedial reflexes (preoperatively), and DPOAE recordings (preoperatively, at the end of surgery, and 5 and 30 days after surgery). Changes in the hearing thresholds and in the DPOAE amplitudes were compared. Preoperative tests showed conductive hearing loss, with a mean air-bone gap of 36.6 dB HL ranging from 0.25 to 1 kHz, and no stapedial reflexes were detected. DPOAEs were not measurable preoperatively, and they were detected only in 2 patients at the end of surgery, with low amplitudes in a narrow frequency range. No significant changes occurred in DPOAEs 5 days postoperatively. A month after surgery, improvement in conductive hearing loss was observed; the mean air-bone gap from 0.25 to 1 kHz was 12.9 dB HL, whereas the higher frequencies were still affected by the disease. DPOAEs increased in amplitude in 4 patients, but this was not significant. It remains unclear why DPOAEs are not detected despite a subjective hearing improvement and a sufficiently closed air-bone gap at least in middle and low frequencies. The results of our study show that DPOAEs cannot replace behavioral threshold tests; they may only be included in a battery of tests for a complete clinical follow-up for efficiency monitoring after stapes surgery.

Otoacustic emissions (OAEs) are objective, noninvasive measures for cochlear outer hair cell function. OAEs are the product of biomechanical motility of hair cells; they are divided into spontaneous and evoked emission [1].
Distortion product otoacoustic emissions (DPOAEs) occur because of the nonlinear nature of outer hair cells. DPOAEs are produced when two tones of different, but related, frequencies (F₁ and F₂) are presented to the cochlea simultaneously; in response to these two tones, a normal cochlea will generate tones related to F₁ and F₂.

OAEs are usually used to evaluate, analyze and check several diseases that may involve the cochlea, including otosclerosis [2].

Otosclerosis is a primary localized disease of the bony otic capsule. It has a predilection for the oval window and fixes the stapedial footplate, but it can also involve the whole otic capsule, causing conductive or sensorineural hearing loss. Usually stapes surgery, and particularly stapedotomy, is the first-choice treatment. The aim of the study was to investigate changes in middle ear dynamic characteristics caused both by the disease and the surgical steps (platinotomy, prosthesis positioning, ossicular chain maneuver) and to evaluate their influence on DPOAE responses in patients with otosclerosis [3, 4].

A group of 15 patients (12 women and 3 men) affected by advanced otosclerosis was included in the present study. The patients were admitted to the ENT clinic and candidates for stapedotomy. Preoperatively, pure-tone audiograms, stapedial reflexes and DPOAEs were recorded. At the end of surgery, after piston prosthesis insertion and tympanomeatal flap repositioning, DPOAEs were recorded. Five days thereafter, before patient discharge, DPOAEs were measured again. The patients were asked to come back to the clinic 30 days after surgery and they underwent pure-tone audiogram and DPOAE measurements.

Regarding DPOAEs, stimulus presentation, data recording and spectrum analysis were carried out using a Labat Otoacoustic Emission Test Instrument Model Eclipse. The F₁ and F₂ levels were both 75 dB SPL, they were constant at all frequencies tested and DPOAEs were plotted for different frequencies (DP-gram). DP-grams were collected in 1-octave steps from 500 Hz to 1 kHz and in 1/3-octave steps from 1 to 8 kHz.

Preoperative tests showed conductive hearing loss, with a mean air-bone gap of 36.6 dB HL ranging from 0.25 to and 1 kHz; no stapedial reflexes were detected. DPOAEs were not measurable preoperatively and they were evident only in 2 patients in the intraoperative test, with low amplitudes in a narrow frequency range. No significant changes were observed 5 days postoperatively. A month after surgery, conductive hearing loss had improved; the mean air-bone gap from 0.25 to and 1 kHz was 12.9 dB HL. The DPOAE amplitude increased in 4 patients, but it was not significant. Figures 1 and 2 show the mean audiometric and DP-gram results.

Air-bone gaps in pure-tone audiograms were reduced in all operated patients limited to the frequency range from 0.25 to 1 kHz, while the higher frequencies were still affected by the disease.
The results of the present study showed that despite a subjective hearing improvement and the fact that the air-bone gap is sufficiently closed, at least in middle and low frequencies, OAEs cannot be recorded in most cases. However, it could be observed that the surgical maneuvers in the middle ear and around the oval window do not significantly affect the outer hair cell physiology even at the level of the basal cochlear turn.

References


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Superior Semicircular Canal Dehiscence Mimicking Otosclerotic Hearing Loss

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Abstract

A puzzling aspect of middle ear surgery is the presence of an air-bone gap in a small number of cases with no apparent cause. We believe that some of these cases are due to unrecognized superior semicircular canal dehiscence (SSCD). We have now gathered experience from 20 patients with SSCD presenting with apparent conductive hearing loss without vestibular symptoms. All affected ears had SSCD on high-resolution CT scan. The common findings in these patients were: (1) the air-bone gaps occurred in the lower frequencies below 2,000 Hz, and ranged from 10 to 60 dB; (2) bone conduction thresholds below 2,000 Hz were sometimes negative (−5 dB to −15 dB); (3) the acoustic (stapedial) reflex was present; (4) measurement of umbo velocity by laser Doppler vibrometry showed slight hypermobility of umbo motion; (5) the vestibular-evoked myogenic potential response was present, with thresholds that were abnormally low, and (6) the middle ear was normal at exploratory tympanotomy, including normal mobility of the ossicles and a patent round window niche. We have investigated the mechanism of the air-bone gap due to SSCD using a theoretical framework, clinical research data and an animal model (chinchilla). Our research supports the hypothesis that SSCD introduces a ‘third’ window into the inner ear which produces the air-bone gap by (1) shunting air-conducted sound away from the cochlea, thus elevating air conduction thresholds, and (2) increasing the difference in impedance between the scala tympani and scala vestibuli, thus improving thresholds for bone-conducted sound.

Superior semicircular canal dehiscence (SSCD) syndrome is a recently described clinical entity associated with vestibular symptoms typically evoked by sound and pressure stimuli [1, 2]. As experience with this syndrome has accrued, it has become apparent that some patients with SSCD can present with
apparent conductive hearing loss without vestibular symptoms [3–5]. In many cases, the clinical presentation so closely mimics that of otosclerosis that exploratory tympanotomy and even stapedectomy has been performed on some of these patients without benefit to the hearing [3–5]. In this paper, we describe our experience with this condition, report on our research to understand the mechanisms of the hearing loss, and point out methods that may enable the clinician to make an accurate diagnosis.

**Clinical Presentation of SSCD with Conductive Hearing Loss**

In the 3 years between 2001 and 2004, we have made the diagnosis of SSCD as a cause of apparent conductive hearing loss without vertigo in 20 cases. These patients have ranged from 20 to 70 years in age, equally divided between males and females. The typical clinical presentation is that of an adult patient complaining of a unilateral or bilateral progressive hearing loss. Some patients also complain of autophony, aural blockage or distortion of sounds. When asked specifically about vestibular complaints, about 20% volunteered a history of mild disequilibrium or imbalance. Otoscopy typically reveals a normal tympanic membrane with an aerated middle ear. The Rinne test is negative and the Weber test lateralizes to the affected ear. In our series, only 20% of patients had sound-induced or pressure-induced nystagmus when tested with video Frenzel lenses.

Audiologic testing reveals an air-bone gap which is greater in the lower frequencies (fig. 1). The air-bone gaps can be quite large, up to 40–50 dB. Bone conduction thresholds are often negative (−5 dB to −15 dB) below 2,000 Hz in many cases. However, in some patients in our series, the bone thresholds were not negative and even a Carhart notch was observed. The acoustic (stapedial) reflex is generally present in SSCD cases, whereas it is absent in middle ear diseases such as otosclerosis. The vestibular-evoked myogenic potential (VEMP) response is generally present in SSCD with thresholds that are abnormally low [5, 6] (in contrast, the VEMP response is usually absent in otosclerotic hearing loss). Measurement of umbo velocity by laser Doppler vibrometry shows the velocity to be in the high normal range in SSCD, approximately one standard deviation above mean normal [7, 8]. In otosclerotic hearing loss, the umbo velocity is usually one standard deviation below mean normal [9]. Exploratory tympanotomy is negative, with normal mobility of all ossicles and a patent round window. The diagnosis is made by high-resolution computed tomographic (CT) scanning with reformatting of the images in planes parallel to and perpendicular to that of the superior canal [1, 2, 5, 10].
Evidence that SSCD Can Cause a Conductive Hearing Loss

Direct evidence that SSCD can result in an air-bone gap is the improvement of hearing and resolution of the gap after surgical closure of an SSCD. We have experience with one patient, a 50-year-old man who had a low-frequency air-bone gap of 25 dB and chronic disequilibrium due to SSCD (fig. 2). He underwent a

*Fig. 1.* Audiogram of 4 of our cases with SSCD presenting as conductive hearing loss without vertigo. The air-bone gaps are larger in the lower frequencies. Note that the bone conduction thresholds are sometimes better than 0 dB (−5 to −15 dB) in the lower frequencies.

Evidence that SSCD Can Cause a Conductive Hearing Loss

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Fig. 2. A case of a 50-year-old man with conductive hearing loss and chronic disequilibrium due to SSCD. The preoperative audiogram shows a low-frequency air-bone gap of up to 25 dB. The CT scan image shows the dehiscence (arrow). Middle fossa plugging was done with bone wax and temporalis fascia. The audiogram 2 weeks after surgery shows resolution of the air-bone gap, with a high-frequency sensorineural loss at 8 kHz.

middle fossa procedure with plugging of the SSCD using bone wax and temporalis fascia. His vestibular complaints resolved and a postoperative audiogram showed closure of the air-bone gap. Minor et al. [3] described a patient with a significant conductive hearing loss and oscillopsia who underwent resurfacing of a dehiscent superior canal, and who experienced improvement of the air conduction.
thresholds by 20 dB. In addition, it has been noted that patients with SSCD and
the typical vestibular complaints often have a small, low-frequency air-bone gap
of 5–10 dB [1, 2, 5]. This small conductive loss usually resolves after surgical
repair of the SSCD [5].

There are indirect lines of evidence to support the hypothesis that SSCD
can cause a conductive hearing loss: (1) middle ear exploratory surgery in these
cases does not reveal any abnormality to explain the conductive hearing loss,
and (2) diagnostic tests such as the acoustic reflex, VEMP response and laser
Doppler vibrometry of the umbo show results that are the opposite of what is
expected in the presence of middle ear pathology.

**Mechanisms of Conductive Hearing Loss Resulting from SSCD**

We have initiated a series of studies to investigate the mechanism by which
an air-bone gap could arise as a result of an SSCD, including mathematical
model analyses, experiments in a chinchilla model of SSCD, and measurements
of middle ear function using clinical research tools such as laser Doppler
vibrometry in patients with SSCD [7]. The evidence to date from our investiga-
tions supports the hypothesis that SSCD can cause a conductive hearing loss by
acting as a ‘third’ window in the inner ear [3, 5, 7] that results in elevation of
thresholds for air-conducted sounds and reduction of thresholds for bone-
conducted sounds. As shown in figure 3, air-conducted sound stimuli enter the

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**Fig. 3.** Proposed mechanism of hearing loss by air conduction due to SSCD. Acoustic
energy is shunted through the dehiscence away from the cochlea.
vestibule through motion of the stapes. Our data support the hypothesis that the SSCD shunts a portion of this acoustic energy through the dehiscence away from the cochlea, thus resulting in a hearing loss by air conduction. In our model calculations, the physical constraints imposed by the anatomical dimensions of the human labyrinth indicate that such hearing loss will be greatest at the lower frequencies. The effect of an SSCD on bone conduction can be understood based on the compressional mechanism of bone conduction. As shown in figure 4a, in the normal ear, compression of inner ear fluid by a bone-conducted sound stimulates the cochlea because of an inequality in the impedance on the two sides of the cochlear partition, where the scala tympani impedance is dominated by the round window and the scala vestibuli impedance is dominated by the stapes and oval window. This inequality leads to a pressure difference across the cochlear partition, resulting in motion of the basilar membrane which leads to perception of bone-conducted sound. As shown in figure 4b, we hypothesize that the SSCD, acting as a shunt at low frequencies, increases the inequality in the impedance between the two scalae, thereby increasing the cochlea’s response to compressional bone conduction. Such a mechanism can explain the ‘negative’ bone conduction thresholds observed in our patients. Again, the physical dimensions of the human labyrinth would constrain the improvement in bone conduction thresholds to frequencies below 2,000 Hz, which is consistent with our clinical observations. We believe that a ‘third’ window hypothesis as described above can also explain the occurrence of a low-frequency air-bone gap in other types of inner ear pathologies such as an enlarged vestibular aqueduct [11] or dehiscence of other semicircular canals.

**Differentiation of Conductive Hearing Loss due to SSCD from Otosclerosis**

The typical features of conductive hearing loss in SSCD are a low-frequency air-bone gap with bone conduction thresholds that are better than 0 dB in the lower frequencies. It is important to accurately determine the audiometric bone conduction thresholds by testing at levels below 0 dB HL, if necessary. Acoustic reflexes are generally present in SSCD but absent in otosclerotic stapes fixation. If available, VEMP testing and laser Doppler vibrometry testing can also assist in the diagnosis, as previously described. In suspected cases of SSCD, the diagnosis can be made by high-resolution CT scanning in the first week of initial hearing loss in the auditory canal. The recognition and characterization of conductive hearing loss in SSCD combined with a heightened awareness of its diagnostic possibility should serve to reduce the number of patients who undergo unnecessary middle ear surgery in the future.
Fig. 4.  a Normal bone conduction by the compressional mechanism. Bone-conducted sound causes compression of inner ear fluids. This results in a pressure difference across the cochlear partition because of unequal impedance between the scala tympani and scala vestibuli. In the normal ear, the scala tympani impedance is controlled by the round window, while the scala vestibuli impedance is controlled by the stapes and oval window. b Proposed mechanism of improved bone conduction thresholds in SSCD. SSCD acts as a third window and increases the inequality in impedance between the scalae. Hence, the pressure difference across the cochlear partition is increased compared to normal, resulting in improved thresholds for bone-conducted sound.
Future Directions

So far, we have not performed surgical repair of SSCD in patients with conductive hearing losses without disabling vertigo because of the risk of sensorineural deafness as well as the potential risks of middle fossa surgery. We have repaired SSCD for relief of vestibular complaints via a middle fossa approach in 12 patients. Although no case developed a severe or profound hearing loss in our series, a mild to moderate high-frequency sensorineural hearing loss at 4 and 8 kHz occurred in 2 of our 12 cases. Our philosophy and recommendations may change as we accumulate more experience with surgical management of this condition.

The natural history and etiology of SSCD remain uncertain. It is interesting to note that 2 cases in our series with conductive hearing loss without vertigo are brothers, each with bilateral SSCD, raising the possibility of a genetic predisposition to SSCD. We also do not understand why some patients with SSCD become symptomatic with primarily vestibular complaints, whereas others present with both auditory and vestibular symptoms, and a third group has only auditory symptoms. We are hopeful that ongoing clinical and basic research will clarify some of these issues in the future.

Acknowledgement

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Clinical Significance of Stapedioplasty
Biomechanics: Swimming, Diving, Flying after Stapes Surgery

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Abstract

A piston prosthesis in stapedioplasty significantly modifies the function of the normal ossicular chain. Due to the fact that the ear works as a pressure receptor, a piston prosthesis will be displaced at ambient air pressure changes in a different way than the normal stapes. Our ear is constantly exposed to these pressure changes in daily life, for example during swallowing, with tubal opening, with wind gusts at the external ear, during flying, or diving. Temporal bone experiments showed that elevated static pressures, like in tympanometry, can displace a piston up to 0.5 mm in the vestibule. These large movements, which are caused by the missing attachment of the piston to the annual ligament, may explain why a short piston can be lifted out of the footplate perforation (e.g. after sneezing) or a piston with excessive length might come into contact with the membranous labyrinth, causing vertigo with an inward movement. Flying or diving can be performed by the patients after stapedioplasty, provided that a test with tympanometry is tolerated without evoking vertigo.

The middle ear, working as a highly sensitive pressure receptor, not only transmits the acoustic sound pressure to the inner ear, but is also exposed to enormous changes of ambient atmospheric pressures: the sound pressure at the pain threshold (114 dB) reaches 10 million μPa, which corresponds to a static pressure of 1 mm water column (daPa). However, atmospheric pressures of several 100 mm water column are tolerated by the ear without any problem. Our ear is constantly exposed to these pressure changes in daily life, for example during swallowing, with tubal opening, with wind gusts at the external ear, in tympanometry or pneumatic otoscopy, during flying, or diving.

A pressure change of ±400 mm H₂O (daPa) displaces the tympanic membrane and the malleus inwards and outwards up to 1 mm. In the normal ossicular
chain, these forces induce a gliding motion in the malleus-incus joint, and due to additional gliding in the incudostapedial joint, the stapes and consequently the inner ear are uncoupled due to the extensive displacement of the tympanic membrane. The maximal piston-like inwards and outwards movement of the stapes in the normal middle ear never exceeds 10–30 μm, regardless of the pressure in the external ear canal. This limited displacement is also due to the construction of the tympanic membrane with its prearranged radial collagen fibers. With increasing pressure, these fibers with a high tensile strength stretch and limit further bulging of the tympanic membrane. This results in a decrease of displacement of the tympanic membrane even with increasing pressure: the tympanic membrane behaves like a solid wall at pressures above 500–600 mm water column (daPa) [1].

**Displacements of a Stapes Piston in Atmospheric Pressure Changes**

Contrary to the normal middle ear with the stapes solidly attached in the annual ligament, the replacement of the stapes by a piston eliminates this anchoring. Atmospheric pressure changes, which induce displacements of the tympanic membrane, can now move a piston practically unrestrictedly in the vestibule (fig. 1). In experiments with 9 fresh temporal bones, pressures of 400 mm H₂O, like in tympanometry, displaced the pistons an average of 232 μm inwards and outwards. In cases of an impaired gliding capacity of the ossicular joints, which is often found in histological studies in otosclerotic middle ears, this displacement...
reached an average of 407 µm. In 2 temporal bones, this movement even exceeded 0.5 mm (fig. 2).

This comparatively large displacement is the reason why a very short piston may be lifted out of the perforation by simply sneezing or with a valsalva maneuver. It will resettle on the fixed footplate, a finding that is often reported in revision surgeries for recurrent air-bone gap [2]. A very long piston can come into contact with or even pierce the underlying structures of the membranous labyrinth (utricle, saccule) at increased pressure in the external ear canal or with a retraction of the tympanic membrane and cause vertigo.

Considering these excessive displacements and the proximity of the piston to the inner ear structures, surgery under local anesthe sia is recommended. If the insertion depth of the piston is 0.5 mm, as has often been proposed in order to prevent its outward dislocation with sneezing, a test with a gentle pressure downward of the long process of the incus after positioning of the piston can identify the maximal inward movement of the piston. Shortening of the piston is necessary, if the patient reports vertigo with this movement. This contact of the lower end of the piston with the inner ear structures may explain, why in cases of postoperative vertigo, even with nystagmus, removing of the tamponade of the external ear canal can immediately result in a disappearance of the symptoms by lateralizing an inwardly displaced tympanic membrane together with a piston. Such an irritation by an impaling piston is confirmed, if the feeling of vertigo disappears instantly after a cautious valsalva maneuver.

Considering these excessive movements, the scraps of connective tissue that are often placed around the piston in the oval window niche not only serve as a seal to prevent a perilymphatic leakage, but they can also attenuate the pressure-induced displacement of the piston after healing and scarring due to
their frictional resistance. The same applies to the venous or connective tissue grafts under the piston in the fenestration [3].

Therefore, flying can be permitted approx. 2 weeks after stapedioplasty, when this connective tissue seal has matured.

Modern passenger jets, flying at an altitude of 12,000 m, keep the pressure differential relative to sea level in the cabin at 2,000 mm H$_2$O (daPa). This pressure induces excessive displacements of the tympanic membrane even with repeated tubal openings.

A test applying tympanometric pressures of $\pm$400 mm H$_2$O (daPa) to the external ear with simultaneous recording of nystagmus can reveal, whether flying or diving may be hazardous to patients after stapedioplasty. If no vertigo nor a pathologic eye movement is evoked with pressures of 400 mm H$_2$O, even larger pressures should not cause an inner ear irritation, as the stiffening of the radial collagen fibers in the tympanic membrane prevents an increase of the displacement. Therefore, a prosthesis will not be displaced significantly with further increasing pressure. These experimental results are confirmed by experience with military jet pilots who continued to fly without problems after stapedioplasty [4]. Stapedioplasty patients even performed diving, which causes much larger pressure changes, without any problem.

Therefore, it does not seem justified to generally ban pilots, divers, parachuters or other people who are exposed to excessive pressure variations from performing their work or sport after stapedioplasty. A prerequisite for a safe exposure to excessive pressure variations is, however, a pressure test with tympanometry without symptoms.

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Finite Element Model of the Stapes-Inner Ear Interface

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Abstract

Since 1958, stapedotomy has been the method of choice for middle ear surgeons who operate on patients suffering from otosclerosis, especially stiffening of the interface between the stapes footplate of the middle ear and the oval window, which is a part of the cochlea of the inner ear. Later, many surgeons started to use the Schuknecht prosthesis, which consists of cartilage and is inserted into the complete opened oval window during stapedectomy. Our study shows that basilar membrane (BM) displacement is increased with an increasing stapes footplate area by a numerical simulation including the different geometries. An increase in the footplate area leads to an increase in BM displacement equivalent to 13 dB. Therefore, we recommend prostheses with areas as big as the normal stapes footplate area.

In the year 1958, a new surgical technique for the middle ear, i.e. stapedotomy, was introduced [1]. It was suggested to be used in patients who suffer from otosclerosis, which is a disease impeding the normally most efficient movement of the structures of the healthy ear. It is caused by fixation of formerly movable elastic or hinged connections of middle and inner ear structures. During the following years up to now, the surgeons who used stapedotomy developed a surgical procedure where a small hole is drilled into the stapes footplate and a small piston (0.6 mm in diameter) is placed into the hole. Although clinical studies show improvements of hearing results with pistons of a larger diameter (0.6 mm compared to 0.4 mm [2, 3]), ear surgeons prefer small prostheses either for practical reasons or because they are used to them (fig. 1).
Methods

To study the differences between a small piston and a prosthesis with an area similar to the area of a normal stapes footplate (3.6 mm²), an existing finite element model of the cochlea was used and enlarged (fig. 2).

At first, an external pressure of 1 Pa [94 dB (SPL)] was applied to the small piston area of only 0.28 mm². Then, the same pressure was also applied to the large footplate area of 3.6 mm², as it was done in one of our former studies [4]. However, because this configuration is not realistic, neither for the healthy ear nor for any case of middle ear reconstruction, the loading (1 Pa) was applied to a newly suggested stapes prosthesis shown in figure 3.

In this case, the external pressure (1 Pa) was applied to the small area (0.28 mm²) on top of the prosthesis, as it would be connected to the long process of the incus of the middle ear. At first, only one harmonic signal of frequency (f = 2,500 Hz) was used. Former studies had shown the maximum increase in basilar membrane (BM) displacement and therefore maximum improvement of hearing for this frequency.

Fig. 1. a Normal. b Stapedotomy. c Stapedectomy.
Results

Figure 4 shows the BM displacement in the case of a small piston area such as that shown in figure 1. The maximum displacement occurs at approximately 12 mm from the base of the cochlea and reaches a (very small) maximum value of only 7.15 pm.

Figure 5 shows the BM displacement in the case of a large-area prosthesis such as that in figure 3. The maximum BM displacement increases to 0.0328 nm, which is equivalent to a gain of 13 dB compared to the small piston case. Another interesting fact is the basal shift of the maximum BM displacement in the cochlea (approx. 1 mm). We point out that the cochlear model is linear and basal shift has formerly been found in experiments with increased excitation levels at the eardrum.

Discussion

Our study shows the dependence of the BM displacement on the area of the stapes footplate by modelling the cochlea and numerical evaluation. At first, the examination was limited to one frequency (f = 2,500 Hz). The consequence of our results is the recommendation of stapes footplate prostheses which are as similar to the normal stapes footplate as possible. Of course, there are practical limitations to this, i.e. the prosthesis might be tilted during the insertion, and its unavoidable removal would cause a severe acoustic trauma to the patient.
An interesting result is the basal shift of the maximum BM displacement with increasing footplate area. Therefore, an enlargement of the stapes footplate is equivalent to an increase in the excitation level applied at the tympanic membrane, because this also leads to a basal shift of the maximum BM displacement. This was proven by direct measurements of BM displacement with the Mössbauer technique [6]. Another possibility to verify this result is by psychoacoustic examinations. These should not only verify the decrease in the pure-tone threshold level with increasing footplate areas, but might additionally show differing sensation of tone heights with varying size of the prostheses.

Fig. 3. Stapes prosthesis with a large footplate area.

Fig. 4. BM displacement with a small-area (0.28 mm²) piston.
Further studies should include all parts of the middle ear, which were omitted in this study for simplification. These are the tympanic membrane, the three ossicles (malleus, incus, stapes), the three tendons of the malleus, the two tendons of the incus and two middle ear muscles (musculus tensor tympani and musculus stapedius). Of course, these studies should include the whole frequency spectrum of hearing and the nonlinear properties of the signal transmission of the middle ear.

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The Influence of the Footplate-Perilymph Interface on Postoperative Bone Conduction

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Abstract

In a prospective study, 165 total stapedectomies and 152 small fenestra stapedotomies were performed by three experienced surgeons between 2001 and 2003. In total stapedectomy, a self-made Schuknecht steel wire connective tissue prosthesis, and in stapedotomy, a 0.6-mm platinum wire Teflon piston was used. The pre- and postoperative bone conduction thresholds were compared at the frequencies 250 Hz, 500 Hz, 1 kHz, 1.5 kHz, 2 kHz, 3 kHz and 4 kHz. The postoperative bone conduction between 250 Hz and 3 kHz was significantly better in the total stapedectomy group than in the stapedotomy group. At 4 kHz, both groups showed a slight decrease in bone conduction but the difference was not statistically significant. Therefore, especially in cases with preoperative moderate sensorineural hearing loss, we recommend total stapedectomy using a Schuknecht steel wire connective tissue prosthesis, which offers a stapes-perilymph interface similar to the normal stapes.

Smyth and Hassard [1] reviewed 800 stapedectomies and reported that in terms of hearing the small fenestra technique and the total footplate removal were virtually the same concerning results for air conduction. Persson et al. [2] compared the findings in 437 ears from patients with otosclerosis who had undergone partial stapedectomy, total stapedectomy and stapedotomy. Partial stapedectomy was performed on 70 ears (16%) and total stapedectomy was performed on 205 ears (47%). In both groups, the House steel wire prosthesis on fascia was used. On the remaining 262 ears (37%), stapedotomy was performed using the Fisch 0.4-mm Teflon platinum piston. Persson et al. [2] reported that none of these patients in these series presented with sensorineural hearing loss.
 (>15 dB). The comparison between the three groups postoperatively showed that the air-bone gap was smaller for partial and total stapedectomy than for stapedotomy for all frequencies except at 4 kHz. Partial and total stapedectomy also showed a larger improvement in bone conduction thresholds compared with stapedotomy for all frequencies except 4 kHz. At the 3-year follow-up, the hearing gain for all frequencies (250 Hz to 8 kHz) was larger for partial and total stapedectomy than for stapedotomy. In 2002, House et al. [3] stated that the success in stapes surgery depends more on the experience and skill of the surgeon than on the type of prosthesis used.

Since the age of the patients which undergo stapes surgery is increasing worldwide, we have more and more patients who additionally to the loss of air conduction have a moderate to severe sensorineural hearing loss. According to the investigation of Böhnke and Arnold (pp 150–154), there is a rational proof that the size of contact between the prosthesis and the perilymph has an important influence on bone conduction.

**Methods**

In a prospective study, the first author performed 165 total stapedectomies using a Schuknecht steel wire connective tissue prosthesis. The other authors performed 152 stapedotomies using a 0.6-mm Teflon platinum piston. Six weeks and 3 months after surgery, the postoperative values of bone conduction were measured at the frequencies 250 Hz, 500 Hz, 1 kHz, 1.5 kHz, 2 kHz, 3 kHz and 4 kHz. The pre- and postoperative bone conduction data were collected from both groups and a statistical analysis was performed by the Institute of Medical Statistics of the Technical University of Munich.

**Results**

The statistical analysis of pre- and postoperative bone conduction thresholds from 165 patients with total stapedectomy and 152 patients with stapedotomy reveals a significantly better outcome of the total stapedectomy group. The difference of postoperative gain of bone conduction is demonstrated in figure 1.

**Discussion**

Our study shows that the size of the footplate-perilymph interface has an influence on the gain of bone conduction. Since the size of the footplate has a direct influence on sound pressure in the inner ear and on the extension of the basilar membrane movement, it is obvious that the larger the footplate-perilymph
interface the larger the gain in bone conduction. This effect has also been shown by à Wengen [4] and Persson et al. [2].

We therefore recommend a total stapedectomy using a prosthesis with an interface to the perilymph similar to the normal stapes. At the moment, this is given with the ‘old’ Schuknecht wire connective tissue prosthesis.

**Fig. 1.** Difference of postoperative gain of bone conduction. *Statistically significant.

References


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A Checklist for Surgical Exposure in Stapes Surgery: How to Avoid Misapprehension

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Abstract

The goal of middle ear exploration in stapes surgery is to identify impairments of function along the entire ossicular chain. The endaural approach with an extended tympanomeatal flap and an almost routinely performed anterosuperior canalplasty allow adequate exposure to identify the anterior malleal ligament and process (1), the inferior incudomalleal joint (2), the entire stapes including the pyramidal process (3), and the round window niche (4). With this checklist at hand the otologic surgeon can define the exact location of the hearing impairment and choose the proper technique for hearing reconstruction in primary and revision surgeries.

A variety of surgical approaches to the middle ear have been proposed to perform ossiculoplasties. Whereas the retroauricular approach is nowadays rarely employed, most otologists either use an endaural approach or a transcanal approach through the ear speculum. In a typical otosclerosis patient with a wide external ear canal, a straightforward endaural or transcanal procedure may provide sufficient exposure to perform conventional stapes surgery. However, a thorough appreciation of the normal or impaired mobility of the entire ossicular chain and rare middle ear abnormalities may be overlooked or misinterpreted and their correction remain impossible if the exposure is limited to the oval window niche. High-resolution CT scans prior to surgery may already provide information on the size and location of the otosclerotic focus and careful analysis of each section in the axial and coronal plane can rule out further middle and/or inner ear malformations (e.g. dehiscence of the superior semicircular
canal). The surgeon’s appreciation of the intraoperative situs remains the ‘gold standard’ for evaluating the functional impairment within the middle ear. The analysis depends on his expertise and the appropriate surgical exposure. Whereas the surgeon’s experience develops over time and increases with his caseload, the proper exposure is a matter of technique.

In stapes surgery, we have adopted a checklist which is routinely used in all middle ear explorations to appreciate the function or impairment of ossicular movements. Based on this checklist, the senior author (U.F.) has modified the endaural approach for stapes surgery as outlined below.

**Checklist in Stapes Surgery**

The following steps are key elements in the evaluation of middle ear function and are explored and tested routinely in all cases of suspected otosclerosis.

(1) *The Anterior Malleal Process and Ligament*

The learning experience from revision stapes surgeries has led to the recognition of total or partial fixation of the anterior malleal ligament. This clinical entity has been neglected for many years, but has gained attention only recently [1, 2]. Histology of temporal bone specimens confirmed its presence in patients with otosclerosis and it was estimated that in up to 30% of primary stapes surgeries for otosclerosis we may also observe a fixation of the malleus towards the anterior tympanic spine [3]. Whereas a total fixation of the anterior malleal ligament is easily appreciated, a partial fixation is difficult to verify. The only way to test its mobility is visualizing the movements within the ligament upon palpation of the malleus in an anteroposterior and mediolateral direction. Normal mobility or total fixation is a straightforward decision. Once partial impairment of its movements is suggested, separation of the incudostapedial joint is performed (see next checklist steps) and the mobility is reevaluated. In the presence of a partial or total fixation of the anterior malleal ligament in combination with an otosclerotic stapes fixation, a malleostapedectomy procedure is performed. The analysis of 80 patients undergoing revision surgery after stapes surgery demonstrated that partial malleus fixation was present in 38% [4], indicating that this entity was most likely overlooked at the time of primary surgery.

A perfect view is mandatory to visualize and palpate the anterior malleal ligament. In the majority of the ear canals in western countries (e.g. far more frequently than in India), the anterior tympanosquamous suture is a prominent bony wall and groove where the skin of the ear canal is tightly attached and the height of the bone regularly impairs the surgeon’s view onto the anterior
tympanic spine. Therefore, a partial canalplasty using the drill and/or curettes is required to gain access to the anterior malleal ligament.

(2) **Incudomalleal Joint**

A fixation of the incus along its superior and posterior ligaments cannot be inspected through the ear canal. However, discrepancies of the mobility of the malleus and incus can be appreciated upon careful analysis of the incudomalleal joint. This is even more important if a subluxation of the joint is suspected before or after fixation of the piston onto the incus. We routinely advocate the exposure of the inferior third of the joint to visualize any luxations within this joint. The reversal of the steps of stapes surgeries as proposed by the senior author [5] – leaving the stapes suprastructure in place until the crimping of the prosthesis has been completed – also limits the risk of an incus subluxation.

The partial exposure of the incudomalleal joint is achieved by removing enough bony overhangs between the short process of the malleus and the posterior tympanic spine. This can be performed with different sizes of sharp curettes or a small drill.

(3) **Exposure of the Stapes and the Pyramidal Process**

Visualization of the entire oval window niche requires bone removal of the posterosuperior canal wall, extending anteriorly to the exposure of the lower third of the incudomalleal joint and inferiorly to the entrance of the chorda tympani into the tympanic bone. Sufficient bone removal is achieved once the entire stapes tendon and the pyramidal process are identified. This canal enlargement not only provides space to illuminate the oval window niche using the microscope light source, but also allows enough room to insert the crurotomy scissors to cut through the posterior crus once the stapes piston is fixed to the incus.

(4) **Visualization of the Round Window**

The final point on the checklist is the identification of the round window niche and membrane. The anteroinferior displacement of the tympanomeatal flap allows access to the round window area. If possible, the chorda tympani nerve is left attached to the flap in order to keep the chorda away from the surgical field until the piston is firmly attached to the incus. When removing the stapes suprastructure, the chorda may be separated from the flap to introduce the 2.5-mm hook to fracture the anterior crus. The brief identification of the round window niche allows to exclude obliterative otosclerosis reaching the round window membrane and to rule out the rare instance of a congenital round window atresia [6].
The checklist is summarized in figure 1. The goal of the surgical approach is to see all 4 elements with only one position of the operating microscope, centered on the stapes footplate. To achieve this goal, an enlarged tympanomeatal flap is required and ample bone removal of the antero- and posterosuperior external canal wall becomes necessary. The endaural approach with an extended tympanomeatal flap and a partial canalplasty is therefore our technique of choice in stapes surgery.

**The Endaural Approach**

The endaural approach requires only a minimal helicotragal skin incision which becomes almost invisible over time [7]. Separating the soft tissue from the underlying bone enables the placement of two endaural retractors and allows the surgeon to work with both hands without stabilizing any speculum with his fingers. The tympanomeatal flap consists of two parts: the meatal skin flap is elevated before the tympanic membrane is lifted from the sulcus. Any subsequent bony work is finished before entering the middle ear space to avoid contamination from debris within the external ear canal. The meatal skin flap has been modified to enable access to the anterior malleal ligament (fig. 2). The anterior limb is incised using a No. 11 blade anteriorly to the anterior tympanic spine (at 3 o’clock in a right ear, 9 o’clock in a left ear), then medially and courses in a spiral way laterally over the tympanosquamous suture to end in the endaural incision at the lateral end of the tympanic bone at the 12 o’clock position (fig. 3). The posterior limb of the triangular flap begins at 8 o’clock (right ear) ascending spirally from the tympanic sulcus to the lateral edge of the external ear canal. Once the skin is separated from the bone, any bony overhang

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which may impair the visualization of the anterior tympanic spine is removed with the drill (or curette). This partial canalplasty has become almost a routine even in primary stapes surgeries. The elevation of the tympanic annulus from the sulcus begins at the posterior tympanic spine and includes the pars flaccida until the anterior tympanic spine is identified. Exposing the short process of the malleus keeps the extended tympanomeatal flap away and allows early determination of the mobility of the ossicles. Further removal of bone covering the oval window niche and inferior third of the incudomalleal joint using curettes or diamond burrs provides the necessary exposure of the middle ear to follow the checklist before proceeding with the stapes surgery.

**Conclusion**

The endaural approach with an extended tympanomeatal flap and an almost routinely performed anterosuperior canalplasty allows sufficient expo-
sure to identify the anterior malleal ligament and process, the inferior incudomalleal joint, the entire stapes including the pyramidal process, and the round window niche with one position of the operating microscope. With this checklist at hand, the otologic surgeon is able to identify impairments of function along the ossicular chain in primary and revision surgeries which is the basic requirement to choose the proper technique for hearing reconstruction.

References


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Microtraumatic Stapedotomy

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Abstract

Several modifications have been introduced during the 35 years following the first stapedectomy. The size of the footplate fenestration into the vestibule defines the type of the surgical technique, varying from total stapedectomy to partial stapedectomy or small fenestra stapedotomy. This paper presents a new microtraumatic modification of stapedotomy. After the incudostapedial joint is separated and following the fracture of the stapes crura, the stapes superstructure with the stapes tendon intact is left lying or bending on the promontory. Then, a 4.5-mm-long Schuknecht prosthesis is inserted and the oval window is sealed with small pieces of connective tissue filling the oval window niche and the area between the stapes crura. The results of the new microtraumatic technique with regard to hearing were similar to the standard small fenestra stapedotomy (closure of the air-bone gap). However, multifrequency tympanometry revealed that the new technique provides the patient with a complete physiological middle ear function postoperatively, which was not the case when the other stapedotomy techniques were used. This was reflected in a better hearing quality and less loud-noise intolerance reported by the patients who had been operated on with the new microtraumatic technique.

Otosclerosis is a disease of the bone that is unique to the otic capsule. It may cause a conductive hearing loss, a mixed conductive-sensorineural hearing loss, or occasionally a purely sensorineural hearing loss.

The most common area of stapedial fixation in otosclerosis is the anterior crus. The process may progress to involve the entire footplate or may continue anteriorly towards the cochlea causing a sensorineural hearing loss [1].

Otomicroscopy and physical examination of the ear are usually normal in otosclerosis and in many other ear diseases conductive in nature. Therefore, the differential diagnosis of any conductive hearing loss is very important, especially when there is an intact tympanic membrane, and should include otitis media with...
effusion, tympanosclerosis, incus fixation and ossicular discontinuity [2–5]. Moreover, a systemic disease such as Paget’s disease and osteogenesis imperfecta may fix the stapes or the ossicular chain and also cause conductive hearing loss.

Today, the differential diagnosis in such cases may be achieved using modern diagnostic procedures such as multiple-frequency tympanometry that has shown very encouraging results during the last 10 years [6, 7].

The surgical management of otosclerosis was the first successful microsurgical operation and played an important role in the development of modern otology. Several modifications have been introduced during the 35 years following the first stapedectomy. The size of the footplate fenestration into the vestibule defines the type of the surgical technique, varying from total stapedectomy to partial stapedectomy or small fenestra stapedotomy. All of these variations have the common objective to allow the sound energy to reach the cochlea and close the air-bone gap, as physiologically and efficiently as possible, with long-term results and minimal complications [8].

The present paper presents a new microtraumatic modification of stapedotomy that provides a sound energy transfer through the middle ear very close to the physiological function of the normal tympano-ossicular system.

**Methods**

After an endaural incision, the tympanomeatal flap is elevated between 6 and 12 o’clock to allow a good access to the middle ear. Then, a small part of the posterior canal wall is removed using a drill or House curette in order to have adequate access to the oval window and the stapedius muscle. The chorda tympani is preserved intact if possible. Then, a small (0.7 mm in diameter) fenestra is opened in the stapes footplate (preferably in the posterior part) using a hand microdrill or a needle. After that, the incudostapedial joint is separated and following the fracture of the stapes crura with crura crushers or a needle, the stapes superstructure with the stapes tendon intact is left lying or bending on the promontory (fig. 1). After the insertion of a 4.5-mm-long Schuknecht prosthesis, the oval window is sealed with small pieces of connective tissue around the prosthesis filling the oval window niche and the area between the stapes crura.

**Results and Discussion**

The results of the new microtraumatic technique with regard to hearing were similar to the standard small fenestra stapedotomy (closure of the air-bone gap). However, multifrequency tympanometry revealed that the new technique provides the patient with a complete physiological middle ear function postoperatively, which was not the case when the other stapedotomy techniques were
used. This was reflected in a better hearing quality and less loud-noise intolerance reported by the patients who had been operated on with the new microtraumatic technique.

There has been a long debate among otologists with regard to the size of the fenestra in the footplate and whether a stapedectomy (total or partial) or a small fenestra stapedotomy should be performed. Aarnisalo et al. [9] compared the long-term results (up to 20 years following surgery) of large fenestra versus small fenestra stapedotomy. The pure-tone average improvement did not differ significantly between the techniques compared with the preoperative values. The air-bone gap tended to enlarge as a function of time. In conclusion, the authors did not find any statistically significant differences between the techniques regarding hearing results. Both techniques were found safe and effective in restoring hearing and improving the quality of life, although some of the patients continued to have some problems such as vertigo, tinnitus, and loud-noise intolerance [9].

However, Fisch [10] found a highly statistically significant difference between stapedectomy and stapedotomy with regard to the rate of sensorineural hearing loss that occurred 6 months to 5 years following surgery. Among 444 stapedectomy patients, 27 (6.1%) had a severe sensorineural hearing loss

Fig. 1. Microtraumatic stapedotomy: the stapes superstructure with the stapes tendon intact is left lying or bending on the promontory.
(20 dB or greater for 0.5–2 kHz, 20% discrimination or greater), whereas among 233 stapedotomy patients, only 1 patient (0.4%) had a similar problem.

Irrespective of the results of the studies in the literature, for the last 10 years, there has been a general trend in surgery towards minimally invasive and microtraumatic procedures [11]. Moreover, postoperative quality of life is of high priority in otology and skull base surgery [12, 13]. The new microtraumatic stapedotomy technique gives excellent hearing results, comparable to the standard small fenestra stapedotomy. In addition, it provides the patients with a better (more normal) hearing quality and less loud-noise intolerance. Multiple-frequency tympanometry (a method that evaluates middle ear function in an accurate and objective way) was used postoperatively in order to compare the new technique to the standard small fenestra stapedotomy. In ears operated with the standard techniques, the middle ear vibration patterns (susceptance and conductance) measured on the surface of the tympanic membrane with different frequencies were found enormously increased and the resonant frequency enormously decreased. In other words, the operated ears showed a superflaccidity, a nonphysiological condition, similar to ossicular chain discontinuity. This may very well explain some of the unusual complaints with regard to the hearing quality that patients had following a successful stapedotomy, despite the excellent closure of the air-bone gap. On the contrary, the ears operated with the new microtraumatic technique showed normal vibration and normal susceptance and conductance with a resonance frequency within the normal range. This is the main advantage of the new method and explains the better hearing quality that patients enjoy following microtraumatic stapedotomy.

References

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Abstract

Four hundred and twelve consecutive stapes operations for otosclerosis performed by the author were analyzed. A fat wire stapedectomy prosthesis (Schuknecht) was used in 160 cases and a Fisch Teflon wire piston in 252 ears. Ninety-four percent of the patients with a fat wire prosthesis had a closure within 10 dB and the remaining 6% one within 10–20 dB. As for patients with a Fisch Teflon wire piston, 85% had a closure within 10 dB, and 98–100% within 0–20 dB. Speech reception was better after the operation in 97% of patients with the fat wire prosthesis and in 99% of patients having the Teflon wire piston. There was a significantly different improvement in speech reception (p < 0.02) at the 20-dB level in favor of the Teflon wire piston. Our results show that the small fenestra technique with a 0.4-mm piston causes better speech reception at high frequencies.

Surgery for otosclerosis has been performed at our department since the beginning of the 1960s. The modern surgery with removal of the stapes footplate and replacement with a prosthesis connected to the long process of the incus has proved to be a reliable and secure procedure in most ears. The development of many different prostheses to replace the fixed stapes has undergone a certain refinement.

Reports have advocated the use of small fenestra techniques to avoid damage to the inner ear and provide better hearing at high frequencies [1–4]. It has been argued that small fenestra or stapedotomy techniques are safer, with more predictable and better long-term results. In a previous study [5], we compared the fat wire prosthesis to the Fisch 0.4-mm piston and found better hearing at high frequencies with the piston technique.

Most will agree that 8 or 9 out of every ten patients should have a postoperative improvement in the air-bone gap within 10–20 dB, with only a low percentage of risk for sensorineural hearing loss [6]. From our department, Gundersen
reported that 93% of 753 cases with a conductive hearing loss had a closure within 10 dB and earlier material from this author showed the same results. The rate of grave sensorineural hearing loss was 1.7% in Gundersen’s series and even less in Møller’s series [5].

**Materials and Methods**

Four hundred and twelve consecutive stapes operations performed by the author were analyzed. A fat wire stapedectomy prosthesis was used in 160 cases and a Fisch Teflon wire piston in 252 ears. The last 190 pistons were made of Teflon platinum while the others were made of Teflon-stainless steel (n = 62). In stapedotomy, the whole stapes including the plate was removed, fat was taken from the ear lobe and the prosthesis was made in the operating room. The Fisch piston was 0.4 mm in diameter (Richards) and cut to length. A hole was handmade in the plate in the first 62 piston cases with the Teflon-stainless steel wire. A Causse Skeeter low-rotation drill was used to drill a hole of 5 mm in the posterior central part of the footplate in the last 252 stapedotomy cases. The oval window niche was closed with a piece of fat from the ear lobe to prevent a perilymphatic fistula.

The operations were done under local anesthesia in the first 220 patients, thereafter under general anesthesia. Only ears with pure otosclerosis are included in the material. The mean preoperative pure-tone average was 53 dB in the stapedectomy group and 57 dB in the stapedotomy group. The mean conductive hearing loss (pure-tone average of 500, 1,000, 2,000 Hz) was 30 dB in the stapedectomy group and 35 dB in the stapedotomy group. The follow-up was at least 1 year and the results reported are the audiograms 3–6 months postoperatively.

**Results**

Hearing improvement is considered as a gain in air conduction hearing level, as postoperative closure of the air-bone gap using the postoperative bone and air conduction and as a gain in speech reception. The use of preoperative bone conduction will in some cases mark overclosure and will not be reported. Preoperative hearing loss and age were comparable in the two groups. In the fat wire group (n = 160), 2 ears had to be reoperated to achieve a satisfactory result, while in the piston group, 11 ears were reoperated and 10 had improved hearing.

Ninety-four percent of the patients with a fat wire prosthesis had a closure within 10 dB and the remaining 6% one within 10–20 dB. As for patients with a Fisch Teflon wire piston, 85% had a closure within 10 dB, and 98–100% within 0–20 dB (table 1).

The high-tone gain was calculated as PTA (pure-tone air conduction as; mean of 2, 4, and 6 kHz) and changes in speech reception thresholds were
registered at 50% reception of monosyllables. The mean gain was 15 dB for the fat wire group and 17.5 dB for the piston group. Two patients experienced no gain at the high frequencies in the fat wire group and 5 in the piston group. Hearing loss was seen in 2 cases in the piston group, and in none in the fat wire group, but high tone sensorineural losses were seen in 20 patients in the fat wire group and in 12 patients in the piston group (table 2).

Two patients of the 160 with stapedectomy had to be reoperated due to incus necrosis and a malleus-fixed prosthesis was placed with success. As mentioned, 11 cases had to be reoperated in the piston group, and they all were from the first series having a piston of Teflon-stainless steel (n = 62), with difficulties in crimping. Reasons for reoperations were: piston out of the hole (n = 4), piston slipped off the incus (n = 2), incus necrosis (n = 2), reossification of the footplate (n = 1), ossification in the epitympanum (n = 1), and anterior crus interposition (n = 1). Most problems were solved by using a Skeeter drill and with the new platinum wire piston.

The chorda tympani was cut in 35 of the 160 cases with the fat wire prosthesis and in 17 of the 252 cases with a piston. The permanent complaints of taste disturbances were less than 1%. Four patients had permanent dizziness after piston operation, none after the fat wire procedure. All patients experienced

Table 1. Stapedectomy versus stapedotomy: postoperative closure of the air-bone gap (n = 412 with postoperative conductive hearing loss)

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Closure within 10 dB, %</th>
<th>Closure within 0–20 dB, %</th>
<th>Reoperations, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stapedectomy, fat wire (n = 160)</td>
<td>94</td>
<td>100</td>
<td>2</td>
</tr>
<tr>
<td>Fisch 0.4 mm, Teflon-stainless steel (n = 62)</td>
<td>85</td>
<td>100</td>
<td>13</td>
</tr>
<tr>
<td>Fisch 0.4 mm, Teflon platinum (n = 190)</td>
<td>85</td>
<td>98</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Table 2. Stapedectomy versus stapedotomy (n = 412): hearing gain and hearing loss at high frequencies

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Hearing gain, n</th>
<th>Median gain, dB</th>
<th>Hearing loss, at 2, 4, 6 KHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stapedectomy, fat wire (n = 160)</td>
<td>140</td>
<td>15</td>
<td>20 (12.5%)</td>
</tr>
<tr>
<td>Fisch 0.4 mm, Teflon-stainless steel (n = 62)</td>
<td>57</td>
<td>18.3</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Fisch 0.4 mm, Teflon platinum (n = 190)</td>
<td>183</td>
<td>16.7</td>
<td>7 (2.6%)</td>
</tr>
</tbody>
</table>

Figures in parentheses incident percentages.
satisfactory hearing gain after surgery. Of the 3 who agreed to be reoperated, we found that 2 of them had a perilymphatic fistula closed with fat. Only the one that was not reoperated continued to have vertigo. In 2 ears, the tympanic membrane had to be closed at the primary operation. One patient had a granulation formation after a piston operation with a resulting dead ear. Antibiotics were not given in the last 260 cases. The infection rate was less than 1% in total.

Discussion

Our results show that the small fenestra technique with a 0.4-mm piston could give better speech reception and better hearing at high frequencies. The conclusion is based on the fact that among the authors’ first series of 160 stapedectomies, 94% had a closure within 10 dB after surgery, which compares well with Gundersen’s [7] series of 753 procedures. It is probably safer not to remove the whole footplate to avoid injury to the inner ear during surgery [8], but the differences are marginal. The results with the small fenestra technique are predictable in that it produces stable hearing results and better hearing at higher frequencies. We found, however, that the conductive gap at the middle and low frequencies remained larger in the stapedotomy cases compared to the stapedectomy ones. The difference in this aspect in favor of stapedectomy is in contrast to data presented by Fisch [3].

The size of the piston could influence the results, but most data do not support that size matters [9].

It has been shown that good results in otosclerosis surgery depend on the training of the surgeon. It has been argued that less than 8 operations per year are too little to maintain adequate skills. A dramatic drop in good results could be observed by Shah [10] showing a decrease from 84 to 58% of patients with an air-bone closure within 10 dB postoperatively when one surgeon did 50 stapedectomies in 1966 compared to 22 operations in 1977. The concern about the lack of the surgeons’ experience when too few operations are performed will tend to centralize this sort of surgery [11].

The hearing loss at the high-tone frequencies shown by Mair [12] is probably due to damage of the basal turn of the cochlear duct during surgery. The differences in the results concerning speech improvement probably have many aspects like surgery, technique, age and mother tongue. Many of the patients had used a hearing aid before the operation and most could do well without after.

The high rate of reoperations we experienced with the first Fisch Teflon-stainless steel piston may be due to at least 2 reasons. It was a new technique with special difficulties in preparing the hole in the footplate with perforators.
and hooks. About 10% of the plates were fractured so it was decided to have them removed and a fat wire prosthesis was used instead. The stainless steel was a bit difficult to crimp around the long process of the incus. It became obvious as a result of reoperations that the crimps had to be tighter than with the fat wire prostheses. With more experience, with the Skeeter low-rotation drill and platinum wire, better results were obtained.

In conclusion, we agree that in stapes surgery the surgeons’ experience and skills might be more important than the small differences between different holes and pistons [13, 14].

References


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Evolution of Stapedectomy Prostheses over Time

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Abstract
The history of stapedectomy prostheses started in 1956, when John J. Shea first described the microsurgical technique of the stapedectomy procedure in which an otosclerotic stapes was replaced with a prosthesis made of Teflon. Over the years, the evolution of the prostheses was influenced by the changes in the microsurgical technique, materials used and technical properties. The materials evolved from Teflon, metal, to plastic, and most recently to gold and titanium. While initially the diameter of the pistons used was 0.8 and 0.6 mm, from the 1970s onwards, it has been becoming even smaller in order to ease the procedure and reduce the risk of inner ear damage. Improvement was made in the way the prosthesis is fixed to the long incus process, resulting in different solutions like Teflon memory effect, platinum and gold band, titanium-gold clip prostheses or nickel-titanium alloy. Eventually, the most decisive factor for successful surgery is surgical experience with a specific type of prostheses and the expertise in the microsurgery technique.

The history of stapedectomy prostheses started when John J. Shea [1, 2], who was a clinical fellow with Novotny and Burian in Vienna, first described the microsurgical technique of stapedectomy in 1956. After replacing an otosclerotic stapes with a prosthesis made of a newly discovered biocompatible material – Teflon – and covering the oval window with a vein, Shea achieved a great hearing improvement in a female patient with otosclerosis (fig. 1). After the Teflon stapes, he used a hollow polyethylene tube for a certain period of time, but its use was stopped because of inner ear fistulae and purulent labyrinthitis. Stapedectomy was a great success enabling correction of the otosclerotic conductive hearing loss and improving the patient’s social and professional ability, which made it very popular among otologists. Over the years, otological microsurgeons made new improvements to this surgical technique.
In 1960, Schuknecht [3] developed a steel wire-adipose tissue prosthesis made directly during the operation, which was used more often than the other types of prostheses. Those were tantalum wire prostheses with a loop at the end resting on the fragments of the fractured footplate to reconstruct the sound-conducting mechanism of the middle ear. The soft tissue graft was about 2–3 mm in size and the shaft of the prosthesis was 4–5 mm in length, while the opposite end of the prosthesis was fashioned into an ‘incus hook’. The main disadvantage was potential lateral displacement of the wire and adhesions in the vestibulum, which represented a risk to the inner ear during revision surgery.

The era of limited manipulations of the footplate, as opposed to stapedectomy, started with Plester [4], who removed only the posterior third of the footplate in the so-called partial stapedectomy (or partial platinectomy) technique. His idea was soon followed by Shea et al. [5] and Marquet [6], who made a small opening in the middle of the footplate into which fitted a special type of prostheses – the piston prosthesis. It was the beginning of stapedotomy, a procedure that was supposed to further decrease the inner ear risk. Also described as ‘minimal invasive high-success surgery’, it showed to: (a) decrease the risk of inner ear damage, (b) improve high-frequency gain, (c) improve overclosure of low/middle-frequency gain, (d) reduce the risk of lateral prosthesis dislocation, and (e) reduce the incidence of inner ear infections and perilymph fistulae.

Increased interest in the technique of stapedotomy was followed by the development of piston prostheses made of various materials (fig. 2). Shea’s prosthesis is made entirely of Teflon and its ring tightens around the incus virtually by itself thanks to the ‘memory effect’. The combination of a Teflon shaft in the vestibulum with metal wire for attachment to the incus resulted in a new wire-Teflon prosthesis, which is still routinely used in many centers over the world. Initially they had a wire loop made of stainless steel, tantalum or molybdenum or later of fine platinum band. The platinum band is quite soft so it can be easily closed around the incus process. Robinson’s [9] prosthesis is made...
entirely of stainless steel and fastened to the incus process at the top with a handle. The prefabricated, commercially available piston prostheses replaced the intraoperatively prepared wire prostheses which were made individually by the surgeon at the operating table, in order to simplify the operation, save time and ensure a standard quality.

Marquet [7], in his stapedotomy review article, pointed out that there are many factors that influence the success of the procedure. It is very important that nonwettable materials (like Teflon) should be used for prostheses due to the phenomenon of surface tension. Furthermore, the prosthesis should protrude a little into the vestibule because otherwise a fibrous layer from the graft can involve the extremity of the prosthesis and cause bad functional results. The piston penetration should not exceed 400 μm. He also refers to the footplate hole diameter, which should be 0.7 mm, so it would not touch the annular ligament but is not too small to transmit sufficient energy either. While initially the diameter of pistons used was 0.8 and 0.6 mm, from the 1970s onwards, it has been becoming even smaller, i.e. 0.3–0.4 mm. Thanks to the small diameter of a piston, it became possible to reverse the classic stapedotomy steps in the way that the footplate was perforated first and the fine piston was inserted while the stapes structure was still present and fixed to the incus process. Since these piston prostheses fitted the small footplate perforation exactly, some surgeons also dispensed the use of a vein, fascia or adipose tissue graft to cover the fenestra. The possible gap around the prosthesis was filled by blood clots, Gelfoam, connective or adipose tissue. Particularly popular among ear surgeons is the stapedotomy technique developed by Fisch [8], who was using the fine 0.4-mm metal wire-Teflon piston, and later platinum band-Teflon piston.

Fig. 2. From left to right: Fisch Teflon platinum 0.4-mm piston, Teflon wire 0.6-mm piston, gold piston, wire prosthesis.
Steinbach in the 1990s introduced pistons made of pure gold that have a soft band that can easily be pressed onto the incus process. Although the initial results were encouraging, gold pistons showed in some reports to have caused damage to the inner ear due to material intolerance, which resulted in granulomatous reactions and progressive postoperative sensorineural hearing loss [9]. Another inconvenience is a relatively high percentage of implant extrusions seen in some studies [10].

A promising new material seems to be titanium due to its particularly good biocompatibility. Important advantages of titanium implants are their low weight (approximately 4 mg), ease of handling, none or low instance of extrusion, and minimal tissue reaction, leading to a good audiometric result [11]. Nevertheless, it should be taken into consideration that since titanium is not a noble material, it should not come into contact with steel and other materials for its ability to absorb toxic substances.

Recent refinements in the technique of stapes surgery consider the fixation of the prostheses to the incus. If the transmission of movement between the incus and prosthesis is imperfect, it can lead to incus erosion with loosening of the prosthesis and conductive hearing loss. This is the most frequent reason for revision surgery. Rigid steel wire prostheses had many disadvantages in the way of fixation and were replaced with platinum and gold band – these small soft bands can be fitted with gentle pressure around the long incus process without the spring tension inherent in steel. The titanium-gold clip prostheses, introduced by à Wengen [12], have an automatic fixation to the incus process through spring tension. Titanium has a shape memory, and a clip was constructed which uses this memory for fixation onto the incus (fig. 3). The combination of a Teflon shaft and a nickel-titanium alloy loop resulted in a new
piston in which the crimping of the loop is activated by thermal energy, 45°C or less, using low-intensity Erbium laser or bipolar current [13]. Some authors tend to use a drop of glass ionomer cement for additional consolidation of the piston. It is particularly useful in stapes revision operations, when the prosthesis has to be fixed again to a broken incus, as well as in malleus handle stapedectomy, where additional consolidation of the metal loop around the conical malleus handle facilitates optimal positioning of a prosthesis.

References


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Autogenic and Xenogenic Materials in Stapes Surgery – Retrospective Analysis of 350 Cases

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Abstract

Aim of the Study: Retrospective analysis of the postoperative hearing results in stapes surgery using autogenic materials versus xenogenic materials at the 12-month follow-up. Materials and Methods: A total number of 350 otosclerosis patients who had undergone surgical treatment at the Otosurgery Department, Medical University of Lodz, Poland, from 1980 to 2002 were included in the study. All patients were divided into four groups: group 1 (n = 54): interposition using Portmann’s method; group 2 (n = 160): stapes replaced with the Shea-type prosthesis; group 3 (n = 60): platinum wire prosthesis (Zini-type), and group 4 (n = 76): Teflon piston operation (Fisch-type). The mean air-bone gap was analyzed using pure-tone audiometry (for 3 frequencies: 500, 1,000, and 2,000 Hz) before and 12 months after surgery. Results: The preoperative mean air-bone gaps (500, 1,000, and 2,000 Hz) were 35.6 dB for group 1, 33.2 dB for group 2, 34.7 dB for group 3, and 33.6 dB for group 4. The 12-month postoperative mean air-bone gaps (500, 1,000, and 2,000 Hz) were 19 dB for group 1, 15.9 dB for group 2, 18.4 dB for group 3, and 13.5 dB for group 4. The percentages of patients with a mean air-bone gap of 15 dB or less (500, 1,000, and 2,000 Hz) were 75% for group 1, 81.3% for group 2, 83% for group 3, and 85% for group 4. Conclusions: 12-month postoperative hearing results (mean air-bone gap for 3 frequencies) – compared between the four studied groups – showed statistically nonsignificant differences. According to our experience, Teflon piston prosthesis shows the lowest postoperative mean air-bone gap.

The first documented attempts to establish a surgical technique for stapes mobilization date back to 1876 when Kessel published his description of the direct mobilization of the stapedial footplate [1]. Shea, in 1956, performed total stapedectomy covering the oval window with a vein graft, starting the era of modern stapes surgery [2]. The following years were devoted to the improvement of surgical techniques and materials [3–5].
The pioneers of stapes surgery in the early 1960s in Poland were: Miodoński [4], Lewenfisz and Bardadin (see Bardadin [1] and Latkowski et al. [5]) who used the stapes interposition technique.

At the Otosurgery Department of the Medical University of Lodz, Poland, total stapedectomy was the main surgical technique in the otosclerosis treatment from 1980 till 1995. Fat tissue or perichondrium harvested from the tragus were commonly used to cover the oval window. Starting from 1996 till the present day, the most frequent procedure has been stapedotomy using a Teflon piston (0.5 mm).

The aim of the study was the retrospective analysis of the postoperative hearing results in stapes surgery using autogenic materials versus xenogenic materials at the 12-month follow-up.

**Materials and Methods**

A total number of 350 otosclerosis patients treated at the Otosurgery Department of the Medical University of Lodz from 1980 to 2002 were included in the study.

From 1980 to 1995, there were 274 patients who underwent total stapedectomy. Beginning from 1996 till the present day, Teflon piston stapedotomy has become the procedure of choice in the surgical treatment of otosclerosis (76 patients enrolled in the study). All the patients included in the study were divided into four groups according to the applied material for the stapes reconstruction as well as the surgical procedure performed. The first three studied groups included patients after total stapedectomy with various materials and the last group consisted of subjects after Teflon piston stapedotomy. These groups were as follows: group 1 (n = 54): interposition with Portmann’s method (using the posterior crus of stapes or both crura; oval window sealed with fat tissue); group 2 (n = 160): stapes replaced with the Shea-type prosthesis (sealed with fat tissue or tragal perichondrium); group 3 (n = 60): Zini-type platinum wire prosthesis (sealed with tragal perichondrium), and group 4 (n = 76): Fisch-type Teflon piston operation (0.5 mm, sealed with fibrin clot).

The mean air-bone gap was analyzed (for 3 frequencies: 500, 1,000, and 2,000 Hz) using pure-tone audiometry before and 12 months after surgery.

**Results**

The preoperative mean air-bone gaps (500, 1,000, and 2,000 Hz) were 35.6 dB for group 1, 33.2 dB for group 2, 34.7 dB for group 3, and 33.6 dB for group 4. The 12-month postoperative mean air-bone gaps (500, 1,000, and 2,000 Hz) were 19 dB for group 1, 15.9 dB for group 2, 18.4 dB for group 3, and 13.5 dB for group 4. The differences in the 12-month postoperative mean air-bone gaps between the four studied groups appeared to be statistically nonsignificant. A summary of these results is presented in table 1.
Table 1. Analysis of the mean air-bone gap before and 12 months after surgery (total group: n = 350)

<table>
<thead>
<tr>
<th></th>
<th>Mean air-bone gap before surgery, dB</th>
<th>Mean air-bone gap 12 months after surgery, dB</th>
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<tr>
<td>Total stapedectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>group 1</td>
<td>35.6</td>
<td>19.0</td>
</tr>
<tr>
<td>(n = 54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>group 2</td>
<td>33.2</td>
<td>15.9</td>
</tr>
<tr>
<td>(n = 160)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>group 3</td>
<td>34.7</td>
<td>18.4</td>
</tr>
<tr>
<td>(n = 60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stapedotomy (Teflon piston)</td>
<td>33.6</td>
<td>13.5</td>
</tr>
<tr>
<td>(n = 76)</td>
<td></td>
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Fig. 1. The percentage of patients with a mean air-bone gap (ABG) of <15 dB or >15 dB at the 12-month follow-up.

Postoperative hearing improvement was considered when patients showed a mean air-bone gap of 15 dB or less on pure-tone audiometry 12 months after surgery.

The percentages of patients with improved hearing after surgery were 75% for group 1, 81.3% for group 2, 83% for group 3, and 85% for group 4 (fig. 1).
Discussion

We have not observed statistically significant differences between the groups while analyzing the mean air-bone gap. This fact may lead to the conclusion that during the first 12 months of the postoperative course, autogenic materials like adipose tissue and perichondrium are equally efficient in substituting the stapes footplate. A small number of the complications were mainly due to prosthesis displacement or inadequate prosthesis length causing conductive hearing loss. This can easily be eliminated during stapes revision surgery.

Teflon piston operation is considered to reduce surgical risk because performing an opening in the stapes footplate greatly decreases the risk of iatrogenic perceptive hearing loss due to the membranaceous labyrinth injury.

Although all studied materials used in stapes surgery show statistically nonsignificant differences on postoperative hearing evaluation, based on our experience and the literature, Teflon piston operation compared to total stapedectomy seems to be safer and give better hearing results on the longer than 12-month follow-up [6–8].

Another vital issue that should be considered before choosing the surgical technique in stapes reconstruction is the surgeon’s experience [6, 7].

Conclusions

The following conclusions could be found: (1) 12-month postoperative hearing results (mean air-bone gap for 3 frequencies) – compared between the four studied groups – showed statistically nonsignificant differences, and (2) according to our experience, Teflon piston prosthesis shows the lowest postoperative mean air-bone gap.

Acknowledgements

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A New Self-Retaining Titanium Clip Stapes Prosthesis

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Abstract

Objective: Crimping of the stapes prosthesis might result in injury to the incus. Attachment is often not tight. Facilitated fixation of a stapes prosthesis could improve surgery and provide more stable results. Materials and Methods: After the development of a unique titanium clip over a 6-year period (Kurz AG, Dusslingen, Germany) and reception of a CE mark, the first implantation was performed in September 2000. Full FDA approval was received in June 2002. Results: Only 60% of the circumference of the incus is touched by the clip permitting adequate mucosal blood supply to the lenticular process. Application of the prosthesis is quick and stable. Discussion: This new stapes prosthesis facilitates surgery and reduces operation time. There is no need for crimping anymore. Acoustic coupling is ideal due to the spring action of the self-retaining clip. Most surgeons have switched entirely to this prosthesis. Long-term results will be needed to prove the reduction of incus necrosis.

Since the era of modern stapes surgery started with Shea [1, 2] in 1956, many improvements of the surgical technique [3] as well as of new materials have shown to provide increased safety [4] and to speed up the procedure [5].

Fixation of the stapes prosthesis remains one of the most difficult steps in stapes surgery. Repeated crimping might injure the mucosal lining of the long process of the incus. Furthermore, strangulation of mucosal blood vessels (fig. 1) by the prosthesis might lead to incus necrosis [6–10]. Adequate fixation with ideal acoustic coupling is often not possible [11] and audiometric results remain unpredictable [12]. A standardized and facilitated fixation might reduce these difficulties. Titanium remains the metal of choice after long-term complications have been found using gold [13].
Materials and Methods

The diameter of the piston is 0.4 or 0.6 mm depending on the surgeon’s choice, and the width of the clip is 0.25 mm (fig. 2). The length of the prosthesis is decided after measurement in the ear. The prosthesis is ordered in various lengths and the piston should not be

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**Fig. 3.** Structure and function of the clip prothesis.

**Fig. 4.** Transport of the clip prosthesis onto the incus: in first position of double arch.
shortened during surgery. Application onto the long process is possible with various instruments (figs. 3–5). The clip is patented internationally.

A 0.5-mm right-angled hook or a sickle knife are preferred. If the stapes superstructure or the stapedial tendon are still intact at the time of application, push-on of the prosthesis is easy. Otherwise, the long process of the incus should be stabilized with a 45-degree hook. The contact area of the clip is only about 60% of the incus circumference (fig. 6).

**Results**

In a multicenter study, the use of this clip prosthesis was judged to be easy and intuitive. Surgery is significantly facilitated and most otologists have switched completely to this new prosthesis. Audiometric results are excellent and more predictable.

**Discussion**

The aims of developing this prosthesis were: (1) standardization of prosthesis fixation: no more crimping; (2) optimal acoustic transfer due to close fixation in the main axis of movement and thus less conductive hearing loss;
(3) reliable results independent of the surgeon’s experience; (4) reduced risk for incus necrosis due to minimal trauma to the mucosal lining and absence of strangulation, and (5) shorter surgery time.

In fact, the use of this clip prosthesis is spreading fast. The judgement of its usefulness, however, lies with the otologic surgeons. Long-term results will be needed to prove the reduction of incus necrosis.

Acknowledgement

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The Heat-Activated Stapes Prosthesis ‘SMart’ Piston

Technique and Preliminary Results

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Abstract

Since 2003 we are using in our stapedotomies the Nitinol® ‘Smart’ Piston. This prosthesis has a Teflon® ‘vestibular’ end and a wire shaft made by Nitinol®, with a heat activated self-crimping loop. Nitinol® is an alloy of Nickel + Titanium, belonging to the class of the so-called smart materials, i.e. materials with shape-memory and superelastic properties. Nitinol® is lightweight and highly biocompatible thanks to the thin layer of Titanium oxide covering the Nickel surface. The special advantage of this piston is that the loop grips by itself very uniformly and quite tightly around the incudal process or the malleus handle when a minimal heating (about 60°C) is applied using a disposable heater (‘Thermal Tip’). This piston was successfully used in our Department between 2003 and 2004 in a first group of 42 cases of stapedotomy and in 7 cases of malleostapedotomy. The shape and the uniformity of the loop grip was controlled by examining fresh temporal bone specimens by S.E.M. (×21 ÷ 166) and in all specimens the loop was uniformly surrounding the ossicle, without ‘dead’ spaces. It is our feeling that this prosthesis is very useful in stapes surgery for at least two reasons: 1. because it improves the quality of the interface ‘piston loop/long process of incus’; 2. because the duration of the procedure is reduced.

Stapes surgery aims at improving the hearing function by rearranging the anatomy of the ear, particularly the impaired functionality of the ossicular chain.

Occasionally, as stated by Schuknecht [1], these aims are ‘skewed by… maladroit surgery’, and a faulty technique possibly hinders the achievement of the optimum audiological outcome, the so-called air-bone gap (ABG) closure. Among the subjects undergoing revision surgery (63/1,920 patients between
1992 and 2001, i.e. 3.3%), 19 individuals showed prosthesis displacement or slippage and 14 had an incus erosion (22%).

In accordance with other authors [2–4], these findings can be referred to the so-called loose wire syndrome (LWS), an often unsuspected drawback of an uneventful surgery.

The LWS, reported by McGee in 1981 [5], is characterized by a prosthesis loosely attached to the vibrating incus, thus leading to an unexpectedly incomplete ABG closure, to distortion of sound and to poor speech discrimination. This triad of symptoms may be alleviated temporarily by a Valsalva maneuver [6, 7].

The design and size of the prosthesis (piston) connecting the mobile incus to the labyrinthine fluids, and specially the loop and its grip, were felt to play a significant role in the LWS, which was reported in a nonnegligible number of revisions, i.e. in 6.6–23% of patients [8–10]. Consequently, an effort was made to create loops that can be handled more easily, and that can be more effectively attached and tightened to the incus [11] (fig. 1).

Overcrimping, previously considered to be one of the main causes of incus erosion, was shown to lack a firm anatomical proof [3, 4, 8–10].

Recently, two papers [7, 12] have suggested reappraising the technical quality of stapedotomy, stapedoplasty and ossiculoplasty, paying special attention...
to the interface prosthesis/ossicles because of the loss of energy in the case of a weak contact.

In fact, as shown by Huber et al. [13], tight crimping of the piston at the incus consistently improves the transfer of sound energy and the residual loss remains as small as 2 dB. With loose crimping or no crimping, the amount of the loss largely varies, possibly reaching as much as 28 dB. The loop of the prosthesis must be closely connected to the incus in at least two opposite points, independent of the remaining opening(s) of the loop: ‘unfavourable sound transmission . . .’ is likely to result from ‘ . . . major gaps and poor loop contact to the incus on non-opposite sides . . . ’ [13]. Note that if motion is allowed between the piston and the incus (i.e. if they are not vibrating as a whole), notching will develop in the latter, gradually leading to erosion (fig. 2); therefore, tight crimping is needed. On the other hand, in case of bony closure of the oval window (5–25% of the cases), the ossicle is very likely to be eroded due to its vibration against the ‘fixed’ piston [6, 8–10].

Also, the crimping tool (either the straight alligator or the McGee forceps) has been shown to be a critical factor depending on the type (band-shaped loop, wire loop, broad-spiral-shaped loop) and the material (gold, steel, platinum, titanium) of the loop [13, 14].

We believe that for both these problems, the LWS and the quality of crimping, a sound solution may be achieved by using the Nitinol® heat-activated piston.

Since 2003, we started using the Nitinol ‘SMart’ piston (as manufactured by Gyrus ENT, Gyrus Int’l Ltd., Workingham, Berkshire, UK) in a number of cases of stapedotomy (fig. 3). This piston has a Teflon® vestibular end and a wire, heat-activated self-crimping loop made by Nitinol. The piston weighs 1.35 mg.
Nitinol is an alloy of nickel + titanium, belonging to the class of the so-called SMart materials, i.e. materials with shape memory and superelastic properties. The name Nitinol comes from the acronym Nickel + Titanium + naval ordnance laboratory, where the alloy was discovered in the USA. The shape memory is based on a reversible solid-state phase transformation from austenite to martensite and vice versa.

**Fig. 3.** a The SMart stapes prosthesis is a Teflon piston with a Nitinol shaft (courtesy of Gyrus Ltd.). b Self-crimping to the incus is heat-activated by a temperature of 45–60°C administered for <1 s on top of the loop by means of a special tool, the ‘Thermal Tip®’.

**Fig. 4.** A thin layer of titanium oxide completely and uniformly covers the nickel surface. NiTi is highly stable in the body (courtesy of Gyrus Ltd.).
Nitinol is lightweight and highly biocompatible thanks to the thin layer of titanium oxide completely and uniformly covering the nickel surface (fig. 4). In addition, most studies have shown that NiTi is highly stable in the body [15], and it is also compatible with imaging techniques (CT, MRI).

Its elastic modulus is closer to that of bone than other metal implant materials. The piston loop grip by itself is uniformly and tightly attached around the process of the incus or the malleus handle when minimal heating is applied. Crimping is instantaneously activated by a temperature of 45–60°C obtained by means of a 10-watt bipolar current delivered on top of the loop with a bayonet microforceps, or using the Smart Heating Device®, the tip of which reaches 60°C in 1 s at a 0.5-mm air gap, cooling down again in 3 s.

The quality of the grip had previously been investigated in our Department by attaching the SMart piston to the incus in a number of fresh temporal bone specimens and by examining the interface loop/incus with scanning electron microscopy (Philips XL 30 ESEM TMP) at magnifications of ×21 to ×166.

In all specimens, the loop was found to uniformly surround the ossicle, with no, or very few, minimal gaps (fig. 5a, b).

This piston had successfully been used in our Department during the last 10 months in 49 cases of stapedotomy. Patients were adult men (n = 20) and women (n = 29), with bilateral otosclerosis. Subjects reporting, or suspected of, Ni sensitivity were excluded from the present study. The operation was carried out under local (n = 42 patients) or general anesthesia (n = 7 patients) with either a transcanal or an endaural approach. The average duration of surgery was 17 min (12–32 min). The piston diameter was 0.5 mm in all cases, and the length

![Fig. 5. The loop of the SMart piston uniformly and tightly surrounds the incus apophysis.](image)

- SEM magnification ×166.
- SEM magnification ×79 (same specimen).
was 4.25–4.50 mm. The diameter of the footplate fenestration was 0.6–0.7 mm in all cases, and fibrous tissue pledgets (endaural approach) or small autologous blood clots (transcanal approach) were applied at the piston/footplate interface.

The following are the very preliminary, short-term auditory status outcomes: a mean ABG of ≤10 dB [16] was achieved in 44 (90%) stapedotomy cases at the 3rd month of follow-up, and it was unchanged at the 6th postoperative month. We did not notice any complication; in particular, no case of sensorineural deafness was observed.

Despite the limited number of cases and the short follow-up, our pilot study clearly shows that the SMart piston might be considered an advanced stapes prosthesis likely to effectively improve the quality and duration of the procedure, as well as the learning curve of junior surgeons.

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A New Self-Fixing and Articulated Malleus Grip Stapedectomy Prosthesis

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Abstract

A new prosthesis for malleus-grip stapedectomy is presented: the Clip\textsuperscript{®} Piston MVP according to Häusler. The titanium piston is equipped with a self-fixing clip mechanism for automatic fixation of the prosthesis on the proximal malleus handle as well as a ball and socket articulation allowing easy introduction of the piston at an optimal angle into the oval window as well as adjustment of the insertion depth. A first series of malleus-grip stapedectomies performed with the Clip\textsuperscript{®} Piston MVP shows a hearing gain of 20 to 50 dB and a residual air-bone gap of $\leq 20$ dB in all cases. In one patient, revision surgery was necessary because of piston ejection from the oval window. It appears that with the new Clip\textsuperscript{®} Piston MVP the previously difficult surgery of malleus-grip stapedectomy has become straightforward and technically simpler.

Malleus-grip stapedectomy (malleo-vestibulopexy) is an effective treatment of conductive hearing loss due to an ankylosed or missing stapes combined with an absent, luxated or fixed incus or a fixed malleus head. Malleus-grip stapedectomy is technically more demanding than the usual stapedotomy with prosthesis fixation on the incus. Several surgical techniques using extra long wire loop piston prosthesis types have been proposed over the last 40 years [1–6]. The delicate steps of malleus-grip stapedectomy include the fixation of the wire loop around the proximal part of the malleus handle and the oblique insertion with positioning and bending the extra long prosthesis into the oval window. Published results of malleus-grip stapedectomy using conventional extra-long prostheses are generally good but nevertheless slightly poorer than those obtained with primary incus stapedotomy. Significant post-operative hearing gains are reported in 80 to 93% of patients [2–13]. At the Department
of ENT in Bern, malleus grip stapedectomy is realized in about 10% of all stapedectomies/stapedotomies. This rate has remained roughly constant during the last 10 years. The Bernese statistics of 112 malleus grip stapedectomies performed between 1992 and 2003 show postoperative hearing gain in 92% with residual air bone gaps of ≤20 dB [10, 11].

In order to overcome several technical difficulties, a new self-fixing and articulated malleus grip prosthesis with a ball and socket articulation has been developed and has been in use in Bern since 2003. The piston has been inserted in a first series of patients, so that clinical short-term results with a follow-up of up to 1 year are available.

**Patients and Methods**

*Description of the Prosthesis*

Particular features of the new malleus grip prosthesis, commercially used under the name Clip® Piston MVP according to Häuster by Kurz GmbH, Germany, are the self-fixing clip mechanism which was developed analogous to the àWengen self-fixing clip piston for classical stapedotomy on the long incus process [14] and a ball and socket articulation for easy bending as shown on figure 1. The prosthesis material is ASTM F67 medical grade titanium. The piston diameter is either 0.4 or 0.6 mm; the prostheses lengths were initially restricted to 5.75, 6 and 6.25 mm. Since the beginning of 2005, for reasons explained below, additional lengths of 5, 5.2, 5 and 5.5 mm have been added.

*Patients*

Thus far, the Clip Piston MVP has been inserted in 10 patients, 6 men and 4 women, ages ranging from 36 to 68 years. Two were primary procedures with a high degree conductive hearing loss due to an ankylosed malleus head and incus body in addition to a stapes fixation, probably of congenital origin. Eight were revision surgeries following classical incus stapedotomy with necrosis of the long incus process and prosthesis extrusion.

*Technique of Malleus Grip Stapedectomy using the New Self-Fixing and Articulated Clip Piston MVP*

Surgery was performed under local anesthesia by the transcanal approach through a fixed aural speculum as described in Häusler [10, 11] with a technique which has evolved out of the trans-canal method described initially by Schuknecht [15]. A posterior tympanomeatal flap was elevated. In revision cases, the previously displaced stapedotomy prosthesis was extracted as was the body of the incus. In the two primary cases, the incus was mobilized and taken out and the fixed malleus head was cut and also extracted. The stapes footplate was either totally removed or largely perforated. The tympanic membrane was detached from the proximal part of the malleus handle with a tip. The articulated MVP clip piston was introduced with micro-forceps and gently pushed onto the proximal malleus handle until the self-fixing mechanism snapped into place as shown in figure 2a and b. The piston was then positioned progressively into the oval window by carefully bending the articulation by using a tip in the
right hand and a 1 mm hook in the other (fig. 2c and d). This maneuver was easy and fast due to the mobile articulation of the piston. The oval window was sealed with small pledgets of adipose tissue harvested at the posterior face of the earlobe. The clip on the malleus was also covered by small bits of adipose tissue. Next, the tympano-meatal flap was replaced and the hearing improvement was immediately measured with the Rinne tuning fork test and the whispered voice prior to the closing of the ear canal with a dressing.

**Post-Operative Evaluation**

Patients were evaluated clinically and with classical pure tone audiometry 2 and 12 months following surgery, basically according to the guidelines of the Committee on Hearing and Equilibrium [16].
Results

Surgical Techniques
Malleus-grip stapedectomy with Clip Piston MVP was technically easy and fast in all 10 patients with operation times varying between 14 to 35 minutes, in spite of the fact that most cases were quite complex middle ear malformations or surgical revisions. Several patients had mild vertiginous sensations in the immediate post-operative period, other surgical complications did not occur. Post-operative follow-up was uneventful in 9 patients. In one early operated patient with a shallow middle ear cavity where a long 6.25 mm piston was inserted, the articulation came into contact with a posterior part of the tympanic membrane and, eventually, an extrusion occurred. For this reason, revision surgery was performed, and the extruded 6.25 mm piston was replaced by a 5.25 mm piston without further problems and with stable postoperative hearing gain.1

Post-Operative Hearing Results
All 10 patients, including the patient following clip-piston MVP malleus grip stapedectomy revision had significant post-operative hearing gains between 20 and 50 dB with air-bone gap closures of 20 dB or less. Five patients had over closures of 10 to 15 dB and 2 patients had high-tone frequency losses of maximally 20 dB at 4,000 Hz. There were no significant sensorineural hearing impairments.

Discussion and Conclusion

It appears that the insertion and positioning of the new articulated self-fixing malleus grip piston is considerably easier and faster than was the case with the previously used classical wire-loop malleus grip prosthesis. Several advantages can be enumerated: First, the self-fixing clip mechanisms makes fixation of the prosthesis on the proximal malleus grip easier than the previous wrapping of the wire loop around the handle of the malleus. Second, the ball and socket articulation allows an easy and progressive insertion of the prosthesis into the oval window, until an optimal position is reached without the previous necessity of oblique insertion and bending of the piston. Finally, there is no more need for a complicated pre-operative measurement of the variable piston lengths because the articulation allows easy intra-operative adjustments. Nevertheless, as shown

1Because of this event, shorter MVP Clip Pistons with lengths of 5, 5.25 and 5.5 mm were developed. Currently the most frequently used prosthesis lengths are 5.25 and 5.5 mm.
by the single case with extrusion of a 6.25 mm clip MVP piston in a shallow tympanic cavity, one should use shorter pistons, e.g. 5 to 5.5 mm lengths if the distance between malleus grip and the oval window is short.

In conclusion, the new self-fixing and articulated prosthesis has made the previously difficult surgery of malleus grip stapedectomy straight forward and technically simpler. This has also been confirmed by several other stapes surgeons around the world who have performed first malleus grip stapedectomy trials with this new prosthesis (e.g. H. Hamersma, Pretoria, P.P. Singh, New Delhi, P. Van de Heyning, Antwerp).

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The Crimping Problem in Stapes Surgery

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Abstract

\textbf{Aim of the Study:} The goal of this study was to compare the attachment of stapes prostheses with differently shaped loops to the long process of the incus. \textbf{Method:} Gold, steel/Teflon, platinum/Teflon, and two different titanium stapes prostheses were inserted in 30 specially prepared temporal bones by three experienced surgeons using the Fisch technique with the McGee crimper and straight alligator forceps for the crimping of the loops. \textbf{Results:} In all prostheses, a sufficiently firm attachment of the long process of the incus was achieved. The band-shaped loops showed a better contact with the incus than did the wire loops. However, the broad spiral-shaped loops led to a loss of the perpendicular axis of the piston to the long incus process. \textbf{Conclusion:} The geometry of the loop affects the final length of the piston in the vestibule and its angle to the long process of the incus.

In order to study the effect of the crimping process in stapes surgery, the attachment of five different stapes prostheses (fig. 1) made of titanium, gold, steel and platinum was compared in 30 especially prepared temporal bones. For the crimping of the loops to the long process of the incus, two different instruments (McGee and straight alligator forceps) were used by three experienced surgeons. The Fisch technique was used and photographs were taken with 0- and 70-degree rod lens telescopes at defined views.

All prostheses showed a sufficiently firm attachment to the long process of the incus.

The results depended on the instrument used for crimping and the material of the stapes prosthesis but not on the surgeon. Band-shaped loops had a better contact to the bone than wire loops. The steel wire showed an S-shaped deformation in one case when crimped with the McGee crimper (fig. 2a).

The spirally shaped loops (titanium and gold from Kurz, Dusslingen, Germany) demonstrated very good contact with the bone of the long process of the incus, but resulted in a deviation of the perpendicular axis of the stapes piston to the long process of the incus (fig. 2b). If the spiral was pointed towards the end of the long process of the incus, a more perpendicular angle could be achieved (fig. 2c).
Regarding the instrument, a McGee crimper should not be used for crimping the spirally band-shaped loops, as this resulted in a loss of the spiral shape. The long hook of the spirally shaped loops thus prevented a complete closure of the loop around the long process of the incus (fig. 3a, b).

Concerning the material, the gold loop proved to be too soft and resulted in deformations not visible in the surgical view (fig. 4a). This also led to a functional elongation of the piston, protruding further into the vestibule than desired (fig. 4b). Titanium showed a constant good attachment and less changes in the functional length of the piston than the other materials (fig. 3c).
In conclusion, a medium-sized band-shaped nonspirally formed titanium loop with a short hook, like the titanium-Leibinger prosthesis, is found to be most suitable to be crimped to the incus. Gold is too soft causing deviations invisible during surgery. Titanium is harder than gold, preventing undesirable deviations of the loop, but malleable enough to achieve a good connection with the long process of the incus.

For band-shaped loops crimping with straight alligator forceps results in a better attachment to the incus compared with the McGee crimper.

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Advantages and Risks of Various Sealing Procedures of the Oval Window: Vein Graft, Adipose Tissue, Gelfoam, Merogel

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Abstract
An overview of various proposed sealing procedures of the oval window proposed for stapedectomy or stapedotomy are presented. These include vein graft, adipose tissue and substances like Gelfoam or Merogel. The advantages and pitfalls with these materials are discussed.

In 1876, Kessel showed that stapedectomy, followed by carefully sealing the oval window with connective tissue, did not necessarily result in damage to the inner ear. In 1956, Shea started the era of modern stapes surgery by replacing an ankylosed stapes with a Teflon prosthesis after having sealed the oval window with a thin vein graft. Since then, various autologous and heterologous materials have been proposed for sealing the oval window following stapedectomy and stapedotomy, including vein, fascia, perichondrium, adipose tissue, and blood, as well as a heterologous gelatin sponge (Gelfoam\textsuperscript{®}), and more recently, esterified hyaluronic acid (Merogel\textsuperscript{®}). For the small-fenestra stapedotomy technique, Teflon and metal pistons often are in direct contact with inner ear fluids and only the narrow gap around the prosthesis is still covered with some blood, adipose or connective tissue, or is even left open.

Though experimental studies on methods of sealing the oval window are relatively rare and not uniform, many clinical reports have described the
advantages and disadvantages of the various sealing materials. Thin vein walls seem to have a good protective effect for the inner ear, but veins may produce fibrous reactions that sometimes result in lifting of the prosthesis and reossification of the footplate below the graft. Lippy et al. [1] reported 3% of vein lateralization in 63 revision cases with conductive hearing loss and 10% in 29 revision cases with sensorineural hearing loss. Fibrous reactions have also been reported for perichondrium and fascia grafts. Adipose tissue, mostly harvested from the back of the earlobe, is known to be resistant to infections and to remain stable over years. Moreover, adipose tissue adapts well to the oval window niche. It has been observed that adipose tissue, harvested with high concentrations of local anesthetics, may lead to postoperative vertigo and possibly to inner ear damage in some cases. Blood is easily applied with a syringe, and small amounts have been shown not to be toxic to the labyrinth. Larger amounts of blood, however, may produce hemosiderosis, which has been reported to cause hearing loss and vertigo [2].

For a period of time, it was fashionable to seal the oval window with Gelfoam, which is a gelatin sponge consisting of purified peptides from porcine skin. Opinions regarding Gelfoam varied. There were several reports in the literature comparing the result of Gelfoam with the result of different sealing materials as well as indicating a high incidence of labyrinthine fistula with Gelfoam [3–5]. An oval window fistula was found more frequently with Gelfoam than with fascia in several stapedectomy series [6–9]. Early reports of the toxic effects of Gelfoam on the inner ear were recognized to be due to sterilization using formaldehyde. Shenoi [10] conducted an experiment on the cat to evaluate the toxic effect of varying quantities of formaldehyde on the inner ear and found that the organ of Corti started to degenerate at a concentration of 20–60 μg formaldehyde; however, it was more marked with 50–60 μg formaldehyde. After changing the sterilization procedure, the toxic effect of Gelfoam could be avoided. Sheehy and Perkins [6] compared Gelfoam pad, fat graft and fascia graft techniques in a primary stapedectomy group. They found that there was no difference regarding air-bone gap closure in the short term. On the other hand, in the long term, the hearing results were better with the tissue graft technique than with the Gelfoam technique. According to Sheehy and Perkins, causes of failure with the wire loop-Gelfoam pad stapedectomy technique were wire loop displacement, high membrane formation and window fibrosis.

It was shown in some studies that Gelfoam gave a thinner membrane than viable grafts [11, 12]. The thickness of the oval window sealing material might be important to prevent perilymphatic fistula formation. However, the original thickness of the graft material could be thick, and atrophic changes might have occurred later. So, it is not easy to estimate the importance of the thickness of graft materials to protect the inner ear.
Merogel, an esterified hyaluronic acid extracted from rooster combs, has recently been introduced in otological surgery. In contrast to Gelfoam, it dissolves spontaneously without fibrous reaction. This is generally considered to be a major advantage in middle ear surgery. As a sealing material of the overall window in stapes surgery, this characteristic might, however, be rather disadvantageous.

Sealing materials are not necessary using the stapedotomy technique according to some authors [13, 14]. It was concluded that in a well-calibrated stapedotomy opening, there is no risk of perilymphatic fistula formation. Moreover, Goldman et al. [15] showed in cats that after stapedectomy, the oval window sealed itself with a two-layer membrane derived from the tympanic mucoperiosteum of the middle ear and the vestibular endosteum, if there was no infection.

Still, the question remains which of the following is most important if one wishes to avoid perilymphatic fistula formation and possible inner ear trauma: technique, prosthesis or sealing materials? There is a greater area of contact between the sealing materials and the perilymph in the total stapedectomy cases. If a sealing material does carry some risk, it would be more dangerous for the inner ear. Therefore, we may categorize the techniques and sealing materials as follows to get uniform results: total stapedectomy + sealing materials, partial stapedectomy + sealing materials, stapedotomy + sealing materials, stapedotomy + materials around the prosthesis.

As the numerous clinical reports on stapedotomy performed with various sealing procedures seem to give rather similar results, no uniform recommendation can be given (table 1). A careful sealing of the inner ear with autologous tissue seems clearly indicated in the case of large footplate openings. Tight sealing of the oval window with autologous tissue and additional packing of the

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Material</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kessel</td>
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<td>vein</td>
</tr>
<tr>
<td>Shea</td>
<td>1956</td>
<td>vein</td>
</tr>
<tr>
<td>Schuknecht</td>
<td>1960</td>
<td>fat</td>
</tr>
<tr>
<td>Goodhill</td>
<td>1961</td>
<td>perichondrium</td>
</tr>
<tr>
<td>House</td>
<td>1962</td>
<td>Gelfoam</td>
</tr>
<tr>
<td>Marquet</td>
<td>1994</td>
<td>vein (total stapedectomy), no sealing (small fenestra)</td>
</tr>
<tr>
<td>Fisch</td>
<td>1994</td>
<td>blood, small piece of Gelfoam if necessary</td>
</tr>
<tr>
<td>Paparella</td>
<td>1994</td>
<td>Gelfoam + blood [pers. commun.]</td>
</tr>
<tr>
<td>Fraysee</td>
<td>1994</td>
<td>fat [pers. commun.]</td>
</tr>
<tr>
<td>Babaghian</td>
<td>1994</td>
<td>blood [pers. commun.]</td>
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</tbody>
</table>

Table 1. Sealing procedures proposed by various authors
middle ear with Gelfoam or Merogel is obligatory in gushers and oozers. It might be advisable for persons who wish to pilot aircrafts or want to continue scuba diving following stapedectomy to get additional protection against baro-trauma through a solid tissue graft sealing the oval window, placed between the piston prosthesis and the inner ear fluid.

References


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Audiological Long-Term Results following Stapedotomy with Stapedial Tendon Preservation

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Abstract

Various functions are attributed to the stapedial reflex: as a low-frequency filter, it improves hearing in noise and serves in the protection against acoustic trauma. Our study analyzed 25 patients who had undergone argon laser stapedotomy with preservation of the stapedial tendon compared to patients without tendon preservation. Long-term audiological results are presented. Seventy-six percent of the patients had a residual postoperative air-bone gap of 10 dB or better and 97% of the patients 20 dB or better following stapedotomy with preservation of the stapedial tendon; these results are equal to those of patients without tendon preservation. The comparison of the uncomfortable threshold level showed no statistical difference between patients with and without tendon preservation, but patients with tendon preservation showed a tendency to better results in the sound-noise ratio. These favorable results remained constant in long-term controls.

Various functions are attributed to the stapedial reflex. Reger et al. [1] showed a low-frequency threshold shift during contraction of the stapedial muscle, which indicates a low-frequency filter function of the stapedial reflex. This could be a protection against acoustic trauma and serve for a better hearing in noise. Additionally, the tendon of the stapedial muscle attributes to the blood flow to the distal part of the incus [1–5]. In stapes surgery, the stapedial tendon is normally transected in order to remove the stapes crura before insertion of the prosthesis. This presentation reviews the technique of preserving the stapedial tendon and demonstrates long-term audiological results.
Patients and Methods

Twenty-five patients (17 women, 8 men) underwent argon laser stapedotomy with tendon preservation in our clinic between August 1999 and March 2001. Age ranged from 18 to 70 years (average 44 years). After elevation of a posterior tympanomeatal flap, the crura of the stapes were dissected using an argon laser microhandpiece with 0.1-second pulses of 2.5 W. The footplate was perforated using the laser. The piston was inserted and attached to the long process of the incus (fig. 1). Finally, the oval window was sealed using ear lobe fat. The stapedial reflex was triggered at the end of the procedure. We compared these patients to a group without tendon preservation. For follow-up, our audiological setup included pure-tone audiometry, the average uncomfortable level and the acoustic stapedial reflex measurement. In order to assess postoperative subjective hyperacusis and problems with hearing in noise, a questionnaire derived from the Abbreviated Profile of Hearing Aid Benefit [6] was evaluated. The first follow-up examination was done after 3–21 months. To evaluate the long-term result, we conducted a second follow-up after 15–51 months. For statistics, we performed ordinary one-way analyses of variance using standard parametric methods.

Results

The postoperative residual air-bone gap in pure-tone audiometry in patients with preserved stapedial tendon was found to be 10 dB or better in
76% in the first and 74% in the second follow-up and 20 dB or better in 96% in both follow-up examinations. The postoperative hearing results were very similar to those in patients without tendon preservation (79 and 97%, respectively) [7]. The comparison of the average uncomfortable threshold at 0.5, 1, 2, and 3 kHz was 99.3 dB in the first and 100 dB in the second follow-up in patients with preserved stapedial tendon. These findings showed no statistical difference (p = 0.2296) compared to one another and to the group of patients without tendon preservation (103.4 dB). The stapedial reflex in impedance measurements was positive postoperatively in 8 patients with preserved stapedial tendon (fig. 2). Our questionnaire revealed similar occurrence of subjective problems in a noisy environment in both groups (19.1 and 19.2%, respectively).

Fig. 2. Tympanogram and stapedial reflex measurement in a patient with otosclerosis in both ears 4 months after stapedotomy with stapedial tendon preservation on the left side. The reflex can only be triggered in the operated ear.
**Discussion**

In theory, the stapedial reflex has a protective function to restrict damage occurring with strong acoustic stimuli. Preserving the stapedial tendon should therefore reduce postoperative problems with hearing in noise and hyperacusis [8, 9]. In stapedotomy with mechanical microinstruments, the preservation of the stapedial tendon is a technically delicate procedure [10–12]. The introduction of fiber-optic laser microinstruments facilitated the dissection of the stapedial crura while preserving the stapedial tendon. In our study, we found no statistical difference in the audiological results with or without stapedial tendon preservation. This corresponds to findings of different other authors [5, 13–16]. The long-term control of patients with preserved stapedial tendon showed constant good postoperative results. Interestingly, 3 patients in whom stapedotomy was performed with tendon preservation in one ear and without tendon preservation in the other ear claimed to experience less hyperacusis in the ear with tendon preservation.

**Conclusion**

Preserving the stapedial tendon can be done with the argon laser. Hearing results are equal compared to patients without preserved tendon. Although some findings indicate better hearing in noise and less intolerance to noise, there is no statistical significance.

**References**


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Malleostapedotomy – The Marburg Experience

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Abstract

Background: The surgical procedure for patients with otosclerosis routinely is incus stapedotomy. In case of otosclerosis with incus necrosis or a bony fixation of the malleus and incus, malleostapedotomy is performed. Patients and Methods: Between May 2002 and September 2003, malleostapedotomy was performed in 6 out of 34 patients with otosclerosis. In 2 primary cases, a middle ear dysplasia was found. The malleus was fixed in 2 further primary cases. Two revision surgeries were performed with incus necrosis present. A titanium piston was used, which was fixed at the malleus handle and introduced into an opening of the footplate. Results: The preoperative air-bone gap was reduced from 36 dB(A) to 13 dB(A) after surgery for an average checkup time of 3 months. The length of the prostheses varied from 6.3 to 7.5 mm. No patient showed a hearing loss or vertigo after surgery. Conclusion: Malleostapedotomy is the technique of choice in case of an additional pathology of the ossicular chain in patients with otosclerosis. Larger numbers of patients and long-term investigations need to compare the results of malleostapedotomy with those of a conventional incus stapedotomy.

The technique of stapedioplasty introduced by Shea for patients with otosclerosis has been changed in the last decades [1, 2]. Despite the development of new operating microscopes, instrumentation, and implant materials, the principle has remained unchanged. Many discussions and publications have dealt with successful results obtained by numerous surgeons. Hence, the search for possible reasons for a persistent conductive hearing loss after stapedioplasty has become more and more acknowledged. Beside a prosthesis dislocation following incus necrosis, a possible incus or malleus fixation became more evident. By focusing on the anterior malleal process and ligament, the identification
of additional fixations of the ossicular chain increased [3]. For patients with a recurrent or persistent conductive hearing loss after stapes surgery, various techniques for revision surgery are described [4–6]. Presently, malleostapedotomy is used more frequently with the introduction of new prosthesis material and design [7]. The purpose of this article was to describe the results of otosclerosis patients, in whom malleostapedotomy with a titanium piston was performed.

**Patients and Methods**

Thirty-four patients with otosclerosis and conductive hearing loss were treated at the ENT Department of the Philipps University, Marburg, Germany, between May 2002 and September 2003. Malleostapedotomy was performed in 6 out of 34 patients (18%; n = 34). The age of the 1 male and 5 female patients ranged from 30 to 48 years (mean age, 35 years). Two primary cases presented a middle ear dysplasia class 2 [8]. The malleus was fixed in 2 further primary cases. Two revision surgeries were performed with incus necrosis present.

The operations were performed under local anesthesia in 50% of cases using an endaural or transcanal approach. With a circular incision, a large transmeatal flap was developed and the external ear canal widened with a diamond burr or curette, when necessary. Then, the tympanomeatal flap was elevated from the identified posterior tympanic spine in an anterior direction, remaining above the level of the chorda tympani until the lateral malleal process and ligament became visible, and the preparation continued until the anterior tympanic spine could be identified. To obtain a good view of the oval window niche, pyramidal process, and facial nerve canal, parts of the scutum were removed with a curette.

In revision surgery, where incus necrosis was evident, the incus body, malleus head and anterior malleal ligament were dissected. The malleus handle remained attached to the ligament of the tensor tympani muscle while preserving the chorda tympani. Both dislocated gold pistons were removed.

Fixation of the complete ossicular chain was detected in all four primary cases after disruption of the incudostapedial joint by gentle palpation with a hook. A middle ear dysplasia class 2 was identified in 2 cases as classified by Teunissen and Cremers [8]. The incus, malleus and anterior malleal ligament were dissected, preserving the chorda tympani, and leaving the malleus handle attached to the tensor tympani muscle ligament.

After removing the stapes arch with the erbium YAG laser (Carl Zeiss, Oberkochen, Germany), the distance between the stapes footplate and malleus handle was achieved with a measuring rod (Storz, Tuttingen, Germany). A titanium piston with a diameter of 0.4 mm (Storz) was then trimmed to the desired length (6.3–7.5 mm; mean 6.8) using a special cutting block. The piston was inserted into an opening of the footplate, the loop then placed on the malleus handle anteriorly to the lateral process and crimped with an alligator forceps (fig. 1a). Finally the stapedotomy opening was sealed with adipose tissue and drops of the patient’s blood before repositioning of the tympanomeatal flap.

All patients were counseled before, 1 and 3 months after surgery. Otoscopic checks with an operating microscope (Carl Zeiss) and pure-tone audiograms were performed. Only 1 patient could not be examined after a month. The mean air-bone gap was documented for the frequencies of 0.5, 1, 2, and 4 kHz.
Results

In both revision cases, the type of prosthesis used in primary surgery could be identified. A 5.5 mm × 0.6 mm gold piston was removed in 1 case, while the second case presented an angular gold piston attached to a rudimentary incus. Both prostheses were dislocated, with no visible perforation of the footplate. Malleostapedotomy was performed, reducing the preoperative mean air-bone gap for the measured frequencies of 0.5, 1, 2, and 4 kHz from the initial 40 dB(A) to 8 dB(A) 3 months after surgery. The otoscopic checkup after 3 months presented an inflammation-free status of the drum. The loop of the prosthesis was located at the malleus handle and underneath the tympanic membrane (fig. 1b).

In 2 out of 4 primary cases, the complete ossicular chain was immobile, including the anterior malleal ligament. After disrupting the incudostapedial joint, removing of the incus and malleus head, the malleus handle was mobile. By malleostapedotomy, the mean preoperative air-bone gap was reduced from 34 dB(A) to 10 dB(A) 3 months after surgery. The follow-up, including otoscopic checks, revealed a normal status of the tympanic membrane 3 months postoperatively.

Two other patients presented a stapes ankylosis in combination with a congenital anomaly of the ossicular chain classified as a middle ear dysplasia class 2. In both cases, malleostapedotomy could be performed. One patient presented a wide malleus handle where the prosthesis could be fixed only after major widening of the loop. A 7.5-mm titanium piston was used with a larger angulation than usual. The conductive hearing loss of this patient could not be

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Fig. 1. a Intraoperative situs after insertion of a titanium piston into an opening of the footplate (white arrow). b Otoscopic view 3 months after surgery with the prosthesis loop attached to the malleus handle (black arrow).
The mean air-bone gap for all patients could be reduced from 36 dB(A) to 13 dB(A) as summarized in table 1. No dead ears occurred in this series and no patient reported a persistent vertigo.

**Fig. 2.** *a* Radiographic visualization of the intact ossicular chain (white arrow) with digital volume tomography (Accuitomo, Morita, Japan). The vestibulum (black arrow) and facial nerve (grey arrow) are identified. *b* A gold piston (5.5 × 0.6 mm) is shown with the loop attached to the long process after incus stapedotomy (arrow). *c* Another examination presents a titanium piston (7.5 × 0.4 mm) attached to the malleus handle and introduced into an opening of the footplate after malleostapedotomy (arrows).
**Discussion**

The surgical technique for patients with otosclerosis introduced by Shea has been used throughout the world by numerous surgeons with great success. The principle of stapedioplasty has remained unchanged, with only aspects of the technique changing over the years. Meanwhile, a less traumatic operation technique with new prosthesis materials has been established. Instead of the retroauricular approach, an endaural or transmeatal approach is frequently used, as stapedectomy has been replaced by stapedotomy. The introduction of titanium in 1994 with its overriding qualities, i.e. high biocompatibility and stability, high stiffness but low weight, set a new standard for middle ear prostheses [9–11].

Titanium middle ear implants were first successfully used for chronic otitis media until a titanium piston was introduced for patients with otosclerosis [12]. The filigree and lightweight piston is now routinely used with good functional results and a low complication rate. Several groups have already shown its qualities compared to different alloplastic materials [13, 14]. However, not only the implant material itself is crucial for sound transmission and long-term outcome, the surgical technique, especially the crimping process, is also highly important to prevent a degeneration of the long process of the incus, which often led to prosthesis dislocation [15].

Revision surgeries often revealed incus process necrosis, massive ossification of the footplate or fixation of the complete ossicular chain. Various techniques have been described to replace missing or fixed ossicles reestablishing sound transmission [4]. In 2001, Fisch et al. [7] described malleostapedotomy in revision surgery for otosclerosis. In their study, they compared 82 consecutive revision stapes surgery cases over 5 years; in 56 of them, malleostapedotomy was performed using a titanium piston and in 15, incus stapedotomy was performed with a platinum ribbon Teflon piston. Both prostheses with a diameter of 0.4 mm were trimmed to the desired length with a special cutting block. Comparing postoperative air-bone gaps, malleostapedotomy showed better

---

**Table 1.** Pre- and postoperative air-bone gap after malleostapedotomy (n = 6)

<table>
<thead>
<tr>
<th>Air-bone gap, dB</th>
<th>Patients before surgery</th>
<th>Patients 1 month after surgery</th>
<th>Patients 3 months after surgery</th>
</tr>
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<tbody>
<tr>
<td>≤10</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>11–20</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>21–30</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>&gt;31</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
functional hearing results than incus stapedotomy. Eighteen percent of the patients had a postoperative air-bone gap within 0–10 dB(A), 59% within 11–20 dB(A), 14% within 21–30 dB(A) and 9% had an air-bone gap higher than 31 dB(A) (measured frequencies 0.5, 1, 2, and 4 kHz; n = 56).

Histopathological investigation of otosclerotic temporal bones confirmed the presence of severe hyalinization of the anterior malleal ligament sufficient enough to reduce the mobility of the malleus in 30% of specimen [3].

In our series, only 4 out of 34 patients with otosclerosis presented a fixation of the malleus. This is a rate of 11% of patients, which is lower than reported by Fisch et al. Our postoperative hearing results after malleostapedotomy showed a closure of the air-bone gap within 0–10 dB(A) in 4 of 6 patients for a follow-up time of 3 months after surgery. One patient presented an air-bone gap of 13 dB(A), another of 30 dB(A). No displacement of the prosthesis loop next to the lateral malleal process could be identified; the position can be checked by an otoscope through the tympanic membrane when no cartilage is used (fig. 1b). No total deafness and no persistent vertigo occurred in our series. Only 1 patient reported slight temporary dizziness. A radiographic check of the prosthesis with digital volume tomography identified the titanium piston in the normal position in the middle ear and vestibulum (fig. 2c).

Conclusion

Malleostapedotomy is the technique of choice in case of an additional pathology of the ossicular chain in patients with otosclerosis. Larger numbers of patients and long-term investigations are needed to compare the results of malleostapedotomy with those of conventional incus stapedotomy in primary and revision cases.

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Stapes Surgery in Osteogenesis Imperfecta

A Clinical Study of 16 Patients

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Abstract

Osteogenesis Imperfecta (OI), an autosomal disease of connective tissue, with the main feature of bone fractures, accompanied by blue sclerae and hearing loss. Hearing loss affects about 50% of the patients, beginning in the second and third decade of life. The hearing loss is progressive, starting with a conductive loss, then a mixed and later on a sensorineural loss. There are similarities between otosclerosis, although OI is a distinct entity. The diseases are treated in the same surgical way. The result is, however, not as good in OI as in otosclerosis according to different reports. A screening study of 15 patients with OI at the Karolinska Hospital, Sweden, has been performed, differing in age from 25–60. Audiometric examinations have been measured of both air and bone conduction. About 50% of the included patients had hearing loss. Three of the patients wore hearing aids. Of these 15 patients, only 4 had been operated on with stapes surgery. One of these patients needs a new operation. An indication for stapes surgery was found in about 50% of the investigated OI patients.

Osteogenesis imperfecta (OI) is a genetic disease involving connective tissue and localized to chromosome 17, with both autosomal dominant and recessive inheritance. It is due to a mutation in genes that encode for procollagen, forming the fibrils and fibers in collagen, which gives structural support to bone, ligaments, and tendons. The prevalence varies in the Nordic countries between 3.3–5.7/100,000. The main features are bone fractures, accompanied by blue sclerae and hearing loss. Hearing loss affects about 50% of the patients, beginning in the second and third decades of life. The hearing loss is progressive,
usually starting with a conductive loss, followed by a mixed and later a sensorineural loss. There are similarities between otosclerosis and OI, although OI is a distinct entity. The diseases are treated surgically in the same way, but the results are not as good in OI as in otosclerosis.

OI has been classified into 6 different types according to severity, discussed at the International Conference on OI, Annecy, 2002.

(1) Type I A/B: mild to severe bone fragility, blue sclerae, dentinogenesis imperfecta
(2) Type II: lethal
(3) Type III: severe bone fragility (long bones affected), blue sclerae
(4) Type IV A/B: bone fragility, mild to moderate deformity
(5) Type V: hyperplastic callus formation, white sclerae
(6) Type VI: vertebral fractures, bone fragility, light blue sclerae

Types I and III are the most common. The typical features of the disease are:

(a) Bone fragility
(b) Short stature
(c) Secondary deformities (bowed limbs, kyphoscoliosis)
(d) Other manifestations of collagen-containing tissue
(e) Blue sclerae
(f) Dentinogenesis imperfecta (fragility of teeth due to poor mineralization of dentine)
(g) Hearing loss (>50%, mostly OI types I and III)
(h) Vertigo

This pathology often results in a phenotype with short stature and skeletal deformities. The diagnosis is often set by a medical history (family history), clinical examination and skeletal radiographs. Treatment today is trying to prevent fractures and reduce deformities with a beneficial addition of medication such as bisphosphonates and growth hormones.

Connected to the disease is a progressive hearing loss, starting at a mean age of 28 years. Most common is a mixed hearing loss, followed by a sensorineural loss and a conductive loss (younger patients). A bilateral loss is seen in almost 90%.

The hearing loss in OI is age related with an estimated annual increase of 1–1.7 dB [1]. It has an earlier onset, a severer middle ear involvement and a higher incidence of sensorineural hearing loss compared to otosclerosis.

The middle ear involvement in the hearing loss is due either to fractures of the stapes superstructures, ossicular discontinuity, or a fixed or thick stapes footplate. The sensorineural hearing loss may be due to hair cell loss, atrophy and calcification of the stria vascularis and tectorial membrane distortion. In a study by Kuurila et al. [2], consisting of 137 adults, hearing loss was identified
in 58% of the patients, less pronounced among OI type IV patients. Hearing loss was classified due to the calculation of the mean value at 0.5, 1 and 2 kHz: (1) conductive loss: air-bone gap >15 dB, (2) sensorineural loss: air conduction >15 dB and air-bone gap <15 dB, (3) mixed hearing loss: air-bone gap >15 dB and bone conduction >15 dB.

The surgical treatment of choice in OI is stapedotomy. Often, in patients with OI type I without fractures, the diagnosis might not even have been established, which is why the anatomical challenges suddenly appear. The surgery is delicate and typical findings can be a thick, fixated or obliterated stapes footplate, thick and vascular mucosa with extensive bleeding and elastic, fractured or atrophic crura that have to be taken into account. It has been reported that satisfying surgical results can be found in these patients, despite being poorer than in otosclerosis patients, taking into account that better results are seen when the procedures are centralized [3]. The progressive sensorineural hearing loss found as a result of the disease has a negative influence on the final surgical outcome [4].

In the present Stockholm study, 16 adult patients with OI (OI type I: 81%, OI type IV: 19%) were evaluated. Of these, 62% were females and their mean age was 40.6 years (range 24–69 years). Normal hearing was found in 8 patients and hearing loss was noted in the remaining 8 patients (50%). Four patients had a mixed hearing loss bilaterally (25%), 2 a sensorineural loss bilaterally (12.5%), 1 a mixed unilateral loss (6.25%) and 1 a conductive unilateral loss (6.25%). Four patients (50% of hearing impaired) used hearing aids. Tinnitus was declared by 2 patients (12.5% totally).

This group of OI patients has just been collected and only 3 ears have so far been operated with stapes surgery. Of these, 2 were performed in 1 patient, in 1999 and 2004. Further reports will follow when the number of operations has increased.

In summary, when treating patients with OI, it is recommended to first establish a diagnosis of the disease, which makes the planned surgery more efficient and successful; moreover, the anatomical variations can more easily be dealt with. Often, when it comes to more rare diseases, a centralization and a reduced number of surgeons are beneficial.

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Stapes Surgery in Japanese Patients with Osteogenesis Imperfecta

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Graduate School of Medicine, Osaka, Japan

Abstract

Osteogenesis imperfecta (OI) is a heterogenous connective tissue disorder. The classical triad of symptoms involves a conductive and/or sensorineural hearing impairment together with a tendency to spontaneous bone fractures and blue sclerae. Between 1993–2004, primary stapes surgery was performed on 14 ears of 11 OI patients who presented with conductive and/or mixed hearing loss. Pathological findings included atrophy and/or fractures of the stapedial crura in combination with thickening and fixation of the stapes footplate and hypervascularity of the promontory mucosa. All the patients with stapes surgery had significant hearing gain and bone conduction thresholds did not differ significantly in any of the cases; the mean postoperative air-bone gap at the main speech frequency range was within 10 dB in 13/14 (93%) and within 20 dB in 14/14 (100%). Hearing results following stapes surgery in patients with otosclerosis during the same time interval (n = 132) did not differ significantly. These data indicate that stapes surgery in OI can be performed safely with comparable functional predictability as in otosclerosis.

Osteogenesis imperfecta (OI) is a heterogenous connective tissue disorder characterized by osseous fragility, blue sclerae and progressive hearing loss. OI is caused by a defect in the synthesis of type I collagen molecules due to point mutations in two related genes, COLIA1 on chromosome 17 and COLAIA2 on chromosome 7. The first to report on the clinical triad were Van der Hoeve and De Kley in 1917 [1]. A classification of OI into types I–IV was proposed by Sillence et al. [2] and a further subdivision has been made based on clinical, biochemical, radiographic and genetic features [3].

In the most common form, i.e. OI type I, approximately half of the cases show conductive or mixed hearing loss, which usually appears in the late second
to early third decades of life. Since the conductive component in hearing loss usually results from pathological changes involving stapes (i.e. fixation of stapes footplate as in otosclerosis, atrophy and/or fractures of stapedial crura), it has been accepted that stapes surgery could be effective and successfully and safely improve the hearing of OI cases [4–8].

The present study was conducted to examine intraoperative findings of the middle ear in Japanese OI cases, evaluate the short- and long-term effectiveness of stapes surgery among them, and compare the success rate of stapes surgery in OI cases to that in patients with otosclerosis.

**Materials and Methods**

Between 1993–2004, a small fenestration stapedectomy was performed on 15 ears (14 with primary procedure and 1 with revision procedure) of 11 patients (8 females and 3 males) from 9 independent families with OI. The mean age at the surgery was 32.6 years (ranged 14–53). The diagnosis of OI was based on the phenotype appearance. During the same period, stapes surgery was performed on 132 ears with conductive and mixed hearing loss due to otosclerosis.

All the surgical procedures were performed by the same surgeon (K.D.) using the standardized technique to improve hearing loss in OI cases with an air-bone gap on pure-tone audiometry of >20 dB in the main speech frequency range (table 1). In all cases, the surgery was performed under local anesthesia with a retroauricular approach. After elevation of a tympanomeatal flap, pathological changes in the middle ear were carefully confirmed. In most cases, a Teflon wire piston prosthesis with a 0.6-mm diameter and a length of 3.5–4.5 mm was used for ossicular chain reconstruction.

Preoperative pure-tone audiograms and the latest available audiogram from the clinical records (mean follow-up period 77.6 months) were evaluated. The air and bone conduction values at 0.5, 1, and 2 kHz were used to calculate the mean air-bone gap and the prevalence of postoperative air-bone gap within 10 dB and 20 dB was evaluated.

**Results**

Intraoperative findings of the middle ear (n = 14) and hearing results (n = 14) are summarized in table 2. The most frequently observed pathological changes were atrophy and/or fractures of the stapedial crura in combination with thickening and fixation of the stapes footplate: fixed stapes footplate was confirmed in 14/14 (100%), atrophy and/or fractures of stapedial crura in 8/14 (57%), thickened promontory mucosa in 9/14 (64%), remarkably hemorrhagic mucosa covering stapes footplate in 8/14 (57%), thickened and brittle stapes footplate in 6/14 (43%), and fixations of the malleus and incus in 2/14 (14%).
Immediate postoperative results showed a marked hearing improvement in all OI cases. A significant closure of the mean air-bone gap within 10 dB was achieved in 13/14 (93%) and within 20 dB in 14/14 (100%). Postoperative bone conduction thresholds did not change significantly in any of the OI cases.

A significant closure of the mean air-bone gap within 10 dB was achieved in 122/132 (92%) and within 20 dB in 126/132 (96%).

**Discussion**

Between 1993–2004, approximately 10% (15/147) of all stapes surgeries were performed on OI cases at the Department of Otolaryngology and Sensory Organ Surgery, Osaka University Graduate School of Medicine. There is a relatively high incidence of OI cases since one of the authors (K.D.) is the otological adviser to the Japanese OI Patient Association.

The most frequently observed pathological changes in the middle ear were atrophy and/or fractures of the stapedial crura in combination with thickening.

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Name</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Pedigree</th>
<th>Operation date</th>
<th>Side</th>
<th>Surgery</th>
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<td>14</td>
<td>female</td>
<td>VDH</td>
<td>2</td>
<td>3/03/1995</td>
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</tbody>
</table>

p. stapedectomy = partial stapedectomy; VDH = Van der Hoere syndrome.
### Table 2. Findings during stapes surgery in 14 ears with OI (one revision case excluded)

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Malleus, incus</th>
<th>Stapes crura</th>
<th>Stapes footplate</th>
<th>Middle ear m.m.</th>
<th>Bleeding</th>
<th>Facial n.</th>
<th>Hear gain</th>
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<td>normal</td>
<td>–</td>
<td>normal</td>
<td>succ.</td>
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Facial n. = Facial nerve; imp. = improved; middle ear m.m. = mucous membrane; NE = not evaluated; succ. = successful.
and fixation of the stapes footplate in Japanese OI cases. These findings were almost consistent with the findings in previous reports.

Following stapes surgery, the mean postoperative air-bone gap at the main speech frequency range was within 10 dB in 13/14 (93%) and within 20 dB in 14/14 (100%). Bone conduction thresholds did not change in any of the OI cases. The functional results following stapes surgery in patients with otosclerosis during the same time interval were comparable.

These encouraging results indicate that stapes surgery in OI cases can be performed safely and successfully by an experienced otologic surgeon with the same functional predictability as in those patients with otosclerosis, even though the underlying etiology is considerably different.

References


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Stapes Surgery in the Elderly

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Abstract

Thirty-eight patients aged 70 years and older submitted to stapedectomy by the same surgeon were identified and their clinical records retrospectively reviewed. The comparison group consisted of 38 patients belonging to a younger age group (less than 70 years old) who were randomly selected from patients operated with the same technique in or around the same period. Although the success rate, defined as a postoperative air-bone gap within 10 dB, was lower in the older group (71\%) than in the younger group (92\%), stapedectomy remains an effective surgical procedure also in the elderly.

Materials and Methods

Patients aged 70 and older submitted to stapedectomy by the same surgeon (S.I.) were identified and their clinical files retrospectively reviewed. Out of 1,518 patients operated between 1973 and 2003 for otosclerosis, 38 were in this age group. The average age at the time of surgery was 73 years and 2 of these patients were older than 80. The comparison group consisted of 38 patients who were younger than 70 years, randomly selected from patients operated in the same period as the corresponding older patients and using the same technique.
The average age of the patients in the comparison group at the time of surgery was 44 years. Hearing data were recorded in the database following the guidelines of the Committee on Hearing and Equilibrium [6]. Hearing at 3 kHz was not tested in all cases; when thresholds at 3 kHz were not available, they were estimated as the mean of thresholds at 2 and 4 kHz, as suggested by Monsell [7]. The results from 2 patients with a very far-advanced otosclerosis were registered separately.

Statistical analysis was performed with Microsoft® Excel 2000 (Redmond, Wash., USA).

**Results**

The mean preoperative air conduction level was 80.4 dB for patients aged 70 years and older and 62.6 dB for patients younger than 70 years. The mean postoperative air conduction level was 53.6 dB for the older group and 34.7 dB for the younger group. The median pure-tone average hearing improvement after stapedectomy was 28.3 dB for the older group and 28.4 dB for the control group.

To comply with level 1 of the Committee on Hearing and Equilibrium guidelines, the hearing results of the 38 patients aged 70 and older and of the 38 patients younger than 70 years are presented as follows.

**Postoperative Air-Bone Gap**

The preoperative mean air-bone gap was 33 dB for patients aged 70 and older and 30 dB for the younger patients. The postoperative mean air-bone gap was 10 dB for the older group and 8 dB for the younger group (tables 2 and 3).

When a successful surgical result was defined as a postoperative air-bone gap within 10 dB, the success rate was 71% in the older group and 92% in the younger group (table 4). In our study, the air-bone gap was reported using air and bone conduction values determined at the same time. When using the former practice of comparing the postoperative air conduction thresholds with the preoperative bone conduction thresholds, 74% in the older group and 90% in the control group had an air-bone closure within 10 dB.

| Table 1. Successful hearing results for stapedectomy (≤10 dB air-bone gap) |
|---------------------------------|-----------------|-----------------|
| Age, years | Older group, % | Younger group, % |
| à Wengen et al. [1] | 60+ | 61 | 83 |
| Vartiainen [3] | 60+ | 61.4 | 66.9 |
| Lippy et al. [4] | 70+ | 90.9 | 90 |
| Albera et al. [5] | 60+ | 73 | 67 |
### Table 2. Patients aged 70+: pre- and postoperative air-bone gap (dB)

<table>
<thead>
<tr>
<th>Frequency, kHz</th>
<th>Preoperative air-bone gap</th>
<th>Postoperative air-bone gap</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean ± SD</td>
<td>range</td>
<td>mean ± SD</td>
</tr>
<tr>
<td>0.5</td>
<td>44.3 ± 2.9</td>
<td>65</td>
<td>10.7 ± 2.5</td>
</tr>
<tr>
<td>1</td>
<td>35.8 ± 4.6</td>
<td>60</td>
<td>7.4 ± 3.3</td>
</tr>
<tr>
<td>2</td>
<td>26.2 ± 2.6</td>
<td>60</td>
<td>9.2 ± 1.1</td>
</tr>
<tr>
<td>3</td>
<td>27.7 ± 3.2</td>
<td>60</td>
<td>11.2 ± 1.9</td>
</tr>
<tr>
<td>4</td>
<td>29.2 ± 4.4</td>
<td>65</td>
<td>13.9 ± 2.3</td>
</tr>
<tr>
<td>0.5, 1, 2, 3</td>
<td>33.5 ± 3.3</td>
<td>60</td>
<td>9.6 ± 1.9</td>
</tr>
</tbody>
</table>

### Table 3. Patients younger than 70 years: pre- and postoperative air-bone gap (dB)

<table>
<thead>
<tr>
<th>Frequency, kHz</th>
<th>Preoperative air-bone gap</th>
<th>Postoperative air-bone gap</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean ± SD</td>
<td>range</td>
<td>mean ± SD</td>
</tr>
<tr>
<td>0.5</td>
<td>40.5 ± 2.3</td>
<td>45</td>
<td>10.7 ± 4.0</td>
</tr>
<tr>
<td>1</td>
<td>32.4 ± 3.1</td>
<td>45</td>
<td>7.6 ± 1.7</td>
</tr>
<tr>
<td>2</td>
<td>29.0 ± 5.3</td>
<td>55</td>
<td>6.1 ± 2.7</td>
</tr>
<tr>
<td>3</td>
<td>23.1 ± 4.8</td>
<td>60</td>
<td>6.8 ± 2.5</td>
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<td>4</td>
<td>23.2 ± 5.2</td>
<td>70</td>
<td>8.8 ± 2.1</td>
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<tr>
<td>0.5, 1, 2, 3</td>
<td>29.8 ± 3.3</td>
<td>37.5</td>
<td>7.8 ± 1.7</td>
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</tbody>
</table>

### Table 4. Postoperative air-bone gap in 10-dB bins

<table>
<thead>
<tr>
<th>Frequency, kHz</th>
<th>Age group years</th>
<th>Patients</th>
<th>0–10 dB</th>
<th>11–20 dB</th>
<th>21–30 dB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5, 1, 2, 3</td>
<td>≥70 38</td>
<td>27 (71)</td>
<td>9 (24)</td>
<td>2 (5)</td>
<td></td>
</tr>
<tr>
<td>0.5, 1, 2, 3</td>
<td>&lt;70 38</td>
<td>35 (92)</td>
<td>1 (3)</td>
<td>2 (5)</td>
<td></td>
</tr>
</tbody>
</table>

Figures in parentheses indicate percentages.
Table 5. Closure of the air-bone gap (dB)

<table>
<thead>
<tr>
<th>Frequency, kHz</th>
<th>Patients aged 70+</th>
<th>Patients younger than 70</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>SD</td>
<td>range</td>
</tr>
<tr>
<td>0.5</td>
<td>33.7</td>
<td>12.6</td>
<td>60</td>
</tr>
<tr>
<td>1</td>
<td>28.4</td>
<td>11.4</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>17.0</td>
<td>10.9</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>16.5</td>
<td>11.0</td>
<td>37.5</td>
</tr>
<tr>
<td>4</td>
<td>15.3</td>
<td>13.0</td>
<td>45</td>
</tr>
<tr>
<td>0.5, 1, 2, 3</td>
<td>23.9</td>
<td>9.7</td>
<td>32.5</td>
</tr>
</tbody>
</table>

Table 6. Patients aged 70+: pre- and postoperative bone conduction threshold (dB)

<table>
<thead>
<tr>
<th>Frequency kHz</th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>Mean difference</th>
<th>p value</th>
</tr>
</thead>
<tbody>
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<td>mean</td>
<td>SD</td>
<td>range</td>
<td>mean</td>
</tr>
<tr>
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<td>12.4</td>
<td>45</td>
<td>34.1</td>
</tr>
<tr>
<td>1</td>
<td>42.5</td>
<td>11.0</td>
<td>45</td>
<td>38.4</td>
</tr>
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<td>53.3</td>
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<td>3</td>
<td>56.2</td>
<td>12.0</td>
<td>55</td>
<td>50.9</td>
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<td>59.1</td>
<td>12.1</td>
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<td>55.4</td>
</tr>
<tr>
<td>1, 2, 4</td>
<td>51.6</td>
<td>10.9</td>
<td>46.7</td>
<td>46.7</td>
</tr>
</tbody>
</table>

Closure of Air-Bone Gap

The closure of the air-bone gap was determined as the preoperative minus the postoperative air-bone gap (table 5). There was no significant difference in mean air-bone gap hearing results between the more than 70-year-old group (24 dB) and the younger group (22 dB).

Change in High-Frequency Pure-Tone Bone Conduction Thresholds

The preoperative minus the postoperative high-frequency pure-tone bone conduction average at 1, 2, and 4 kHz is a measure of overclosure or operative hearing damage [7]. Overclosure/damage results are presented in tables 6 and 7. The mean improvement of high-frequency pure-tone average (1, 2, and 4 kHz) in bone conduction scores after stapedectomy were 4.9 dB for patients aged 70 years and older and 6.8 dB for patient younger than 70 years. This difference was not significant (p < 0.005).
Far-Advanced Otosclerosis

The term far-advanced otosclerosis indicates clinical otosclerosis with an air conduction level in excess of 85 dB, and with bone conduction nonmeasurable in any of the speech-hearing frequencies on a standard clinical audiometer [8].

One of our patients, a 71-year-old female, falls into this category. Another patient, a 73-year-old, had a fragmentary bone conduction. Preoperatively, both patients had a negative Rinne test at 512 Hz and were able to hear the numbers 1 to 10 shouted through a speaking tube on both sides. Both considered their operation to be a success as they could use a hearing aid much more effectively after than before surgery.

Discussion

Although the success rate, defined as a postoperative air-bone gap within 10 dB, was lower in the older group (71%) than in the younger group (92%), stapedectomy may be considered as an effective surgical procedure also in the elderly. After surgery, half of our patients eliminated the need for amplification and the other half reduced that need. Similar conclusions were reached by other authors [4, 9]. The different success rate between the younger group (92%) and the older group (71%) may be explained by the stiffness of the anterior malleal ligament which is reported to develop in otosclerosis after many years of stapes fixation [10]. Cochlear sensitivity to surgical trauma does not increase with age. Overclosure defined as an apparent postoperative improvement in bone conduction due to the Carhart phenomenon was the same in the two groups, which does not support the idea that in older ears the cochlea is less protected against the potential risks of surgery.
Stapedotomy instead of stapedectomy is recommended in the elderly as following surgery the vestibular disturbances are less in stapedotomy than in stapedectomy.

Finally, the elderly with a biological age greater than their anagraphic age are better off using a hearing aid.

Acknowledgements

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References


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Physical Characteristics of Various Lasers Used in Stapes Surgery

Martin Frenz

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Abstract

The invention of modern small-fenestra stapedotomy procedures using a piston-type prosthesis resulted in a remarkable hearing improvement and at the same time in a reduction of complications compared to conventionally performed stapedectomies. These procedures, however, still contain unpredictable risks such as uncontrolled stapes fracturing, luxation of the stapes or creating a floating footplate, which all can cause hearing loss or even deafness. The worldwide use of the small-fenestration techniques led to the observation that most cases of sensorineural hearing loss occurring after surgery were due to intraoperative trauma to the inner ear, most commonly during footplate manipulation. This led to the use of lasers in otological surgery as a possible tool for precise noncontact cutting of bone without any drill vibration. Today, argon, KTP, CO\textsubscript{2} and Er:YAG lasers are clinically used in middle ear surgery. Each laser has its characteristic interaction process with bone with its specific advantages and disadvantages. Therefore, it is not surprising that there are conflicting and controversially discussed experimental and clinical reports. The purpose of this study was to comprehensively compare the physical processes underlying the laser-tissue interaction of the different laser systems in view of safety and efficacy in order to enhance the ability to perform safe minimally invasive surgery on the stapes footplate.
prosthesis. To further reduce the risk of an inner ear damage, Shea et al. [4] and Marquet [5] performed the first procedures where only a small hole was drilled in the center of the stapes footplate in which the size of the piston exactly fits. This novel technique marked the beginning of the era of stapedotomy. The small-fenestration techniques resulted in an improvement in hearing in the higher frequencies compared to conventional stapedectomy. These techniques, however, were difficult to perform and required a high level of surgical skill. Nevertheless, there still remained unpredictable risks such as uncontrolled stapes fracturing, luxation of the stapes or creating a floating footplate, which all can cause hearing loss or even deafness [6–8]. Most problems causing sensorineural hearing loss appeared during footplate manipulation. Lasers are capable of precisely ablating tissue without any mechanical contact and seem therefore to be the ideal instrument to circumvent all the mechanical manipulations. Besides the possibility of precise noncontact ablation, the ideal laser should have a high bone ablation efficiency, should not penetrate deeply into the perilymph nor increase its temperature, should not cause undesired thermal or acoustical side effects, and its radiation should preferably be conducted through optical fibers.

**Basics of Laser-Tissue Interaction**

Nowadays, a large number of different medical laser sources is available covering a wide spectral range, from the ultraviolet in excimer lasers to the far-infrared (IR) range in carbon dioxide lasers, and with pulse durations in femtoseconds as well as continuous-wave radiation. The diversity of their physical properties leads to manifold laser-induced tissue effects. The main parameters influencing the laser-tissue interaction are the wavelength, irradiation time or pulse duration and radiant exposure or irradiance in case of a continuous-wave laser. Depending on the chosen laser settings, a wide range of tissue reactions and medical outcomes can be achieved. Tissue can be cut either leaving an extended lateral zone of thermally damaged tissue behind, which guarantees good hemostasis, or highly precisely with minimal damage as required for example in cutting cartilage or bone. In general, the process of light interaction with tissue is complex since it involves, besides the laser parameters, a large number of different mutually dependent and often dynamically changing tissue variables, such as optical, thermal and mechanical properties, rate of temperature increase, or heat transfer. To optimize the laser parameters for stapes surgery, the physical processes underlying the laser-tissue interaction must therefore be well understood.

When light hits tissue, it is either scattered, absorbed or transmitted. The light distribution in the tissue is mainly governed by the absorption coefficient
μ_s, the scattering coefficient μ_s and the anisotropy factor g of that tissue [9]. Of course, laser-based treatment is only achieved when radiation is absorbed. Absorption occurs due to coupling photon energy of a particular frequency with the energy of electronic or vibrational transitions in the molecules. At short wavelengths (190–400 nm), absorption occurs mainly by proteins, lipids and nucleic acids of the cells. The most attractive laser in the medical field is the ArF (λ = 193 nm) excimer laser. Unfortunately, reliable fiber delivery systems are not yet available for the 193-nm wavelength [10]. In the visible and near-IR spectrum, strong absorption is due to hemoglobin and melanin. The main medical lasers are the argon laser at wavelengths of λ = 488 nm and 514 nm, the Nd:YAG laser (λ = 1.064 μm), the KTP laser (a frequency-doubled Nd:YAG laser) at 532 nm and the AlGaAs diode laser at around λ = 810 nm. In the IR region, water is the main absorbing chromophore in the tissue. The absorption peaks at 1.9, 2.9 and 6 μm are caused by the fundamental symmetric and asymmetric vibrational stretching and bending modes of OH bonds in water molecules. Typical lasers in the IR region are the CO_2 laser (λ = 9.6 and 10.6 μm), the erbium laser (Er:YAG, λ = 2.94 μm and Er:YSGG, λ = 2.79 μm), the Ho:YAG (λ = 2.1 μm) and the Tm:YAG (λ = 2.01 μm) laser. In addition, there is strong absorption at 6.45 μm due to vibrational interaction with the amide II protein band from collagen, a wavelength which can be obtained by a free electron laser [11]. Figure 1 shows the absorption coefficient of water, blood and melanin as a function of wavelength.

Absorption means conversion of laser energy into heat, which, depending on the thermal tissue properties and the irradiation time, diffuses into the tissue leading to coagulation, vaporization, carbonization or, in the case of hard tissues like bone or tooth, even to melting of the tissue sample [12]. The laser wavelength determines the optical penetration depth (fig. 1), and hence, the volume in which heat is deposited. With increasing temperature, the major mechanisms by which tissue is affected are hyperthermia (approx. 40–45°C), reduction of enzyme activity (approx. 50°C) and denaturation of proteins and collagen (approx. 60–80°C). Further increasing the temperature causes coagulation and/or necrosis, which may be useful if hemostasis is required, dehydration, vacuolization, carbonization and finally pyrolysis and vaporization of tissue. In case of total surface desiccation, strong carbonization takes place, which leads to a rapid increase of the absorption coefficient. As a result, the surface temperature exceeds several hundred degrees Celsius causing organic tissue material to burn. For example, if the laser parameters are chosen such that the beam intensity is high enough to vaporize tissue in its path and the irradiation time long enough so that heat can diffuse out of the irradiated volume heating the adjacent tissue to denaturation temperature, then a surgical cut can be made with no or minimal bleeding [13].
The dynamics of heating and tissue ablation depends on the pulse duration. The ablation mechanism using a pulsed IR laser (CO$_2$, erbium or holmium) is believed to be a process of explosive water vaporization and photothermal disruption of tissue [14]. Fast deposition of optical energy leads to vaporization of tissue water, resulting in an explosive removal of tissue structures. The drilling process is therefore explained by a combination of a thermal contribution due to vaporization and a mechanical one that originates from the recoil pressure-driven expulsion of the tissue matrix. Therefore, concerns exist that laser-induced pressure transients can cause possible unwanted side effects such as mechanical rupture of tissue structures far away from the irradiated area [15].

The explosive vaporization is especially apparent when pulsed IR laser radiation is delivered into water. Due to the high absorption of water in the IR range, an explosive phase transition from liquid to vapor takes place. As a result, a fast-expanding vapor bubble is formed. Since water vapor has a much lower absorption coefficient than water in the liquid state, the laser radiation passes through it, once the steam is formed, drilling a deep channel into the...
water. Fast vapor condensation at the channel wall causes the collapse of the bubble, which generates, similar to the collapse of a cavitation bubble, shock and pressure waves [16–18].

Simple thermal models suggest that suitable short laser pulses can ablate tissue leaving only a minimal zone of thermal damage [19–21]. These models require thermal confinement. This is the case where the laser pulse duration is shorter than the thermal relaxation time: no heat diffusion takes place during the pulse duration and the tissue heated above the ablation threshold is ejected before heat diffusion to the surrounding tissue can take place. The width of the damage zone will then be determined mainly by the optical penetration depth of the incident radiation. If the laser pulse duration is longer than the heat diffusion time, the thermal energy diffuses into the tissue already during the laser pulse causing lateral thermal damage [22].

Laser ablation is always a trade-off between thermal damage to surrounding tissue, caused by heat diffusion during long pulses, and mechanical damage, caused by short pulses. The goal is to control and predict the zone of tissue damage by varying laser parameters. Optimal therapeutic results require a balanced mixture of both appropriate wavelength selection and precise exposure time.

An important point in any minimally invasive medical application of lasers is the availability of an appropriate delivery system. The best laser delivery systems are based on optical fibers that have the desirable properties of flexibility, high power transmission with minimal loss, and nontoxicity. In the spectral range from about 300 nm up to 2,000 nm, quartz fibers show performance of high transmittance, flexibility and user-friendliness. Whereas radiation in the ultraviolet range can only be transmitted through hollow waveguides, different fibers are nowadays available to transmit IR radiation at least up to a wavelength of about 4 μm.

Heavy-metal fluoride glasses based on zirconium fluoride (ZrF₄) are considered to be prime candidates for transmitting IR radiation beyond 2 μm owing to their superior glass-forming ability with respect to halide glasses. ZrF₄ fibers can be fabricated with excellent performance at 2.94 μm. The fibers have diameter cores of 100–600 μm, bending radii of less than 1 cm, and losses of less than 0.2 dB/m. The only drawback is their brittleness and hygroscopic property. A clinical use therefore requires protection against mechanical destruction and contamination of tissue material ejected out of the operation area [23, 24]. IR fibers based on germanium oxide (attenuation <1 dB/m, bending radius <4 cm), although being much less brittle than ZrF₄ fibers, cannot be used either without protecting the distal end by an endpiece [25]. An alternative to the fiber materials mentioned above is sapphire, which has a slightly higher attenuation at 3 μm but excellent thermal and mechanical properties [26, 27].
Use of Lasers in Stapes Surgery

The use of lasers in otology goes back to Escudero [28], who in 1979 was the first to employ an argon laser in patients undergoing tympanoplasty. In the same year, Palva [29] and Perkins [30] were the first to use the argon laser in combination with a micromanipulator adapted to an operating microscope for perforation of the stapes footplate. The results of their clinical observations were promising and the postoperative hearing gains good. In subsequent experiments and clinical observations, the safety of the argon laser for otological applications was questioned with respect to possible inner ear damage. The main disadvantage of the argon laser is its low absorption in bone leading to thermal damage of the footplate and even to a possible damage of inner ear structures (saccule and utricle) due to direct irradiation. Vollrath and Schreiner [31, 32] and Schreiner and Vollrath [33] found a temperature elevation of up to 10°C in the perilymph after using an argon laser at power settings of 2 W and pulse durations of 0.5 s. In 1990, Horn et al. [35] published a new method for performing argon laser stapedotomy by using a fiber-optic microhandpiece (see also Gherini et al. [34, 36]). Due to the divergent beam at the fiber tip, this approach appeared to be considerably safer than the conventional micromanipulator-operated argon laser beam. Increasing the fiber-bone distance from 100 μm to 500 μm reduces the radiant exposure by almost a factor of three when using a fiber with a numerical aperture of NA = 0.2. Using a fiber-optic microhandpiece instead of a micromanipulator reduces the temperature increase in the perilymph measured in an inner ear model to about 2–3°C or less [37]. In addition, the fiber optics allows access to structures out of direct sight, as it is quite often the case for the anterior crus of stapes. Also, if good hemostasis is required, the argon laser is particularly suitable.

The search for an ideal otological laser has been directed towards the development of lasers with good water absorption characteristics in order to precisely and efficiently ablate bone tissue. Possible laser sources are the Ho:YAG at a wavelength of λ = 2.1 μm, the Er:YAG (λ = 2.94 μm) or the CO₂ laser at λ = 10.6 or 9.6 μm.

Out of these, the Ho:YAG laser is the one with the lowest absorption coefficient in bone. Assuming an optical penetration in bone of δ = 700 μm, temperatures of up to 1,500°C have been measured on the bone surface when applying consecutive laser pulses [38, 39]. This high temperature is also confirmed by scanning electron microscopy images showing melted and recrystallized surface structures and residuals of carbonization. Besides the high temperature, the ablation process is accompanied by an acoustic phenomenon, which led to strong irreversible alterations in the compound action potential or even to a total loss of hearing after perforation of the basal convolution of
guinea pig cochlea [40]. Therefore, the holmium laser cannot be recommended for middle ear surgery.

Considering its optical properties, the CO\textsubscript{2} laser seems to be favorable for stapes surgery, which was also confirmed by good clinical results [41–43]. The drawback is that no optical fiber is available, with the exception of waveguides that are rather rigid and have a bending-dependent transmission [44], or silver halide fibers, which are toxic to tissue [45]. Surgical CO\textsubscript{2} lasers have an articulated arm connected to a micromanipulator for guiding the radiation from the laser to the narrow operation site. In addition, a coaxially guiding visible laser beam is necessary to visualize the spot of interaction.

In contrast, the radiation of the Er:YAG laser seems to be suitable for middle ear surgery. Erbium laser radiation shows an excellent ablation efficiency of soft and hard tissue by virtue of its high absorption in water. Moreover, the perilymph therefore acts as a natural backstop for the erbium laser radiation. In addition, special optical fibers are available through which the radiation can be transmitted. The good ablation of bone means that the majority of the laser energy is used to remove tissue, leaving minimal residual energy to cause collateral thermal damage of the adjacent tissue [46, 47]. Histological examinations on a perforated stapes footplate with erbium laser pulses showed a lateral thermal damage zone restricted to 5–10 \textmu m [48]. Such small and very locally restricted thermal damage leads to the assumption that erbium laser stapedotomy is not accompanied by undesired thermal side effects in the inner ear. The main drawback associated with the pulsed near-IR lasers has been found to be the unavoidable generation of pressure waves during bone ablation indicated by a loud pop.

In order to set guidelines for the erbium laser parameters suitable for ear surgery, a number of experiments were performed on an inner ear model [48]. These experiments confirmed that there is virtually no temperature increase in the inner ear liquid. However, as a result of the explosive ablation of tissue, erbium laser pulses produce considerable acoustic waves. A particularly strong pressure wave was measured when the stapes footplate was already perforated and the laser radiation directly evaporated the perilymph resulting in the formation of a vapor channel (fig. 2). The depth of the vapor channel is proportional to the amount of laser energy applied. Schlieren images taken of the perilymph just below the footplate of the perforated stapes revealed that this strong pressure transient is due to the collapse of the vapor channel created in the perilymph. The experiments showed that the higher the radiant exposure of the laser radiation, the stronger the pressure transient [49]. However, the amplitude of the pressure transients was found to be independent of whether a micromanipulator-controlled erbium laser or a laser applied through a fiber-optic microhandpiece was used, but only when the fiber tip was applied in the noncontact mode. In the contact mode where the space between the distal fiber tip and bone surface is
Fig. 2. Schematics of the experimental inner ear model to measure temperature rise, pressure transients and to capture images of the vapor channel formation underneath the stapes footplate during and after laser fenestration. The images taken in the perilymph underneath the footplate clearly demonstrate that the perilymph acts as a backstop for erbium laser radiation while forming a vapor channel (see left picture taken at $t = 145 \mu s$). The strong pressure transient of 9 bar measured after perforation is a result of the vapor channel collapse visualized as a dark shadow (marked by 4 arrows) in the Schlieren technique picture taken 240 $\mu s$ after the beginning of the 200-$\mu$s-long laser pulse. The pressure transients were measured using a 9-$\mu$m-thick PVDF pressure transducer foil [48]. Time-resolved temperature measurements were performed using a fluorescent film [39].
bridged by tissue water or blood, the laser-induced pressure amplitude was found to be about thirty times higher. If limiting the radiant exposure in the noncontact mode to below 17 J/cm², the amplitudes of the generated pressure transients measured at a distance equivalent to the path from the footplate to the position of the nearest hair cells were found to be less than 600 mbar both during the bone ablation process (recoil pressure) as well as after the collapse of the vapor bubble formed in the inner ear after complete perforation of the footplate. An acoustic stress of this magnitude in a frequency range between 20 Hz and 20 kHz should not lead to a permanent hearing loss according to the limit graph to avoid hearing defects published by Pfander [50]. These findings were confirmed by in vivo experiments on the inner ear of a guinea pig [51, 52]. The experimental setup allowed the measurement of the postsynaptic inner hair cell receptor activity. Radiant exposures below 17 J/cm² only produced a transitory increase in activity, suggesting that the cochlear function was not irreversibly damaged. However, a radiant exposure of 40 J/cm² directly applied to the inner ear liquid was able to destroy the cochlea. Based on these results, we concluded that the maximum erbium laser radiant exposure allowed for use in stapes surgery was 10–17 J/cm².

Erbium laser stapedotomies were performed on patients under local anesthesia through a fixed ear speculum using either a fiber-optic microhandpiece or a micromanipulator-controlled system (Opmi®TwinER) [49].

The patients reported postoperatively that they perceived the erbium laser pulses as loud acoustic events such as bangs, the striking of a hammer on iron, or as gun shots. All patients indicated improved hearing in a postoperative qualitative whispered number test. Quantitative hearing gains were evaluated by comparing the preoperative pure-tone audiogram with a postoperative audiogram performed 2 and 12 months following stapedotomy. The postoperative hearing gain was evaluated by comparing the preoperative mean air-bone gap with the postoperative gap measured at 0.5, 1, 2 and 3 kHz. Inner ear function was monitored by comparing preoperative with postoperative bone conduction thresholds at 0.5, 1, 2, 3, as well as at 4 and 6 kHz. In addition, the bone conduction threshold of the operated ear was measured 2, 6 and 24 h after surgery and compared with the preoperative values.

The audiometric studies performed postoperatively revealed that all patients had improved hearing after stapedotomy independent of the beam delivery system used. Four months after stapedotomy, the air-bone gap was closed in 87% of the patients to within 10 dB and in all patients to within 20 dB (between 0.5 and 2 kHz). There was no long-lasting sensorineural hearing loss in the low and middle frequencies. These results compare well with other reports on stapes surgery [53–56]. The bone conduction threshold measurements performed 2, 6 and 24 h after stapedotomy revealed for one patient a moderate to severe high-frequency sensorineural impairment up to
75 dB, which, however, returned to preoperative values within 6 h after the operation.

The most significant and longest-lasting threshold shift was observed when high numbers of erbium laser pulses had been applied for perforation of thick footplates. Concerns about possible high-frequency hearing loss after erbium laser stapedotomy had already been published by Varvares et al. [57] who found a 10- to 30-dB hearing loss between 1 kHz and 10 kHz when measuring compound action potential auditory thresholds in guinea pigs during precise ablation of stapes. They reported that no threshold shift was found when the footplate perforation was incomplete. These findings agree well with experimental studies on the inner ear model that clearly showed that the acoustic noise in the perilymph was significantly higher when laser radiation was directly absorbed by the perilymph. Although the frequency spectrum of the pressure transients is broad, the injury was restricted to the high frequencies, since they are closest to the site of generation of the transients lying at the basal turn of the cochlea. Damage of the lower frequencies is strongly reduced due to the rapid attenuation of the pressure waves with increasing distance of propagation.

The latest laser applied in middle ear surgery was an ultrafast Ti:sapphire laser running at a pulse duration of 180 fs [58]. The authors concluded that femtosecond laser pulses seem to be ideally suited since the radiant exposure for ablation is only in the range of 1 J/cm². Due to this low energy level, no thermal damage to the surrounding tissue was found. However, the problem of pressure wave generation using such short laser pulses has not yet been addressed.

**Conclusion**

Laser technology permits nontactile, mechanically atraumatic and very precise cutting and thus offers excellent prerequisites for use in microsurgery of the ear. The main problem is that none of the clinically used lasers has ideal characteristics. Argon laser radiation is poorly absorbed in bone and perilymph but can be transmitted through optical fibers; CO₂ lasers, although having a strong absorption in both, bone and perilymph, cannot be transmitted through optical fibers, which makes their use somehow cumbersome, and the holmium laser leads to carbonization of the ablation site, which can cause thermal inner ear injury. Because of the restricted penetration depth into tissue and bone when using erbium laser pulses, there is virtually no heat effect on the surrounding structures. The deposited erbium laser energy remains limited to a restricted volume, which makes this laser an outstandingly precise microsurgical instrument. On the other hand, the explosion-like ablation of tissue, when using the
pulsed erbium laser, causes the formation of pressure waves with high acoustical energy.

In summary, lasers seem to have a high potential in ENT surgery, especially in middle ear surgery. Particularly in revision surgery, the laser often allows operations which are not possible with conventional surgical techniques. However, it has to be mentioned that in order to gain maximum hearing, the physical processes underlying the laser-tissue interaction must fully be understood to be able to optimize the laser parameters. In general, when using pulsed laser sources, the laser pulse energy should be kept as low as necessary and the pulse length as long as possible to reduce the risk of an inner ear injury.

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The Use of CO₂ Laser in Revision Stapes Surgery

Experimental Studies on Heat Transmission to the Vestibule

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Abstract

The aim of the study was to assess the effect of CO₂ laser on stapes prostheses and measure the heat transmission to the vestibule in experiment model. CO₂ laser was applied on two types of prostheses with power settings (2 and 6 W; 0.05 s). Transmission of heat to the ‘vestibule’ was measured using type K thermocouple and DC-80 data logger during application of the laser on prostheses using a training model of temporal bone. Application of the laser on stainless steel prosthesis did not have any effect on the structure of the prosthesis. The use of the laser on fluoroplastic-wire piston caused melting and produced holes in the piston. Greater temperature rises occurred with stainless steel than with the fluoroplastic-wire piston. Application of CO₂ laser on stainless steel pistons with 6 W can produce inner ear trauma. The use of the laser on fluoroplastic-wire piston is not likely to irritate the inner ear.

The use of the CO₂ laser is advocated in primary and revision stapes surgery. The main advantage of using the laser in primary surgery is the capability of performing a calibrated opening in the footplate without the risk of mobilizing it. Many experimental studies [1, 2] and clinical trials demonstrated the safety and effectiveness of the CO₂ laser in stapes surgery. In some revision cases, it is necessary to clean the oval window niche from granulation tissue or fat used in primary surgery to visualize the margins of the footplate and to check if the piston is in the stapedotomy opening. Any manipulations with instruments may cause sensorineural hearing loss. Lesinski and Stein [3] widely used the CO₂ laser to clean the oval window. This may cause an inadvertent
application of the laser to the prosthesis. It is crucial to be aware of the impact of the laser on a prosthesis that may still be in the stapedotomy opening.

The aim of the study was to assess the effect of the CO\textsubscript{2} laser on stapes prostheses and measure the heat transmission to the vestibule after applying the laser on the piston in an experiment model.

The experiments were carried out using Pettigrew Temporal Bones\textsuperscript{®}, which are plastic temporal bones prepared for training. The ‘vestibule’ had to be drilled out. The plastic stapes arch was removed and the footplate was fenestrated with a microdrill.

A fluoroplastic-wire Schuknecht piston (0.6 mm in diameter) and a stainless steel McGee piston (0.8 mm in diameter) were used. The pistons passed through the ‘stapedotomy opening’ so that their lower ends protruded to the ‘vestibule’. A type K (chromium and aluminium) thermocouple (1.2 mm in diameter) was attached to the module so that its end encircled the tip of the prosthesis. The ‘vestibule’ was filled with normal saline so that the tip of the piston and the thermocouple were surrounded by fluid. Temperature data were sampled to a computer at the rate of 100 recordings per second using a data logger (model TC-08, Pico Ltd.).

A CO\textsubscript{2} laser (Sharplan 30C) was used to deliver energy to a stapes piston directed with a micromanipulator. Power settings suggested by the manufacturer were used (power: 2 and 6 W; pulse duration: 0.05 s; continuous-wave mode). Impulses were delivered at approximately one pulse per second. The procedure was repeated three times for both types of prostheses. A further series of impulses was applied to the prostheses after placing the vein graft on the footplate. The effect of the laser on the prostheses was assessed with a microscope.

Application of the laser to the stainless steel prosthesis did not have any effect on the structure of the prosthesis. The use of the laser on the fluoroplastic piston caused local melting and produced superficial burns in the piston. These changes were more evident with the 6-watt than with the 2-watt power setting (fig. 1).

Delivering 6 bursts of laser caused a mean rise of the temperature in the ‘vestibule’ of 12.3°C for the stainless steel prosthesis and of 5.4°C for the fluoroplastic-wire prosthesis. The maximum temperatures recorded during the experiments were 13.0°C for the stainless steel and 7.6°C for the fluoroplastic-wire prosthesis. Addition of a vein graft reduced the heat transmission to 2.4 and 0.6°C, respectively. A specimen temperature graph from the experiment with the fluoroplastic-wire piston is shown in figure 2.

Wanamaker and Silverstein [4] and more recently Gerlinger et al. [5] examined the effect of the KTP laser on middle ear implants. Both studies showed that the KTP laser might damage fluoroplastic pistons, especially when
**Fig. 1.** Fluoroplastic-wire piston exposed to the CO\textsubscript{2} laser (6 W; 0.05 s, continuous wave).

**Fig. 2.** Temperature at the inferior end of a fluoroplastic-wire piston during laser application (6 W).
blood was added to the pistons. Data from our previous work on KTP laser [6] did not support those results. We showed that applying the KTP laser to fluoroplastic or stainless steel pistons with the manufacturer’s power settings is not likely to cause inner ear irritation or piston damage.

Most studies with temperature experiments examined the temperature in the vestibule during perforating the footplate with a laser in primary or revision stapes surgery. Lesinski and Stein [3] performed in vitro experiments in stapedectomy revision with the CO\textsubscript{2} laser. They showed that a single use of the CO\textsubscript{2} laser on the open vestibule caused a rise in the temperature of only 0.3°C. They advocate a gradual vaporization of the granulation tissue in the oval window, concentrically until the margins and the depth of the oval niche are visible.

The possible effect on the piston was not analyzed. In the present study, the CO\textsubscript{2} laser caused melting of the fluoroplastic pistons. Those changes are not important when it is decided to remove the old piston and replace it with a new one. In situations were the piston cannot be removed because of suspected adhesions to the inner ear structures, exposing the fluoroplastic pistons to the laser should be avoided.

The inner ear thermal damage depends not only on the temperature level reached but also on the time of exposure. Drettner et al. [7] demonstrated that in patients with Ménière’s disease subjected to ultrasonic irradiation of the labyrinth, a temperature rise in the vestibule of up to 4°C for about 7–8 min did not cause any deterioration of hearing. Barnett [8] carried out an in vivo study to analyze the effect of the heat on the inner ear in cats and guinea pigs. He recorded changes in cochlear microphonic potentials (CM) during ultrasound irradiation of the cochlea through the round window. A temperature rise in the vestibule of 5°C had no effect on the CM. A series of experiments showed that the CM impairment threshold was around 7°C above the normal body temperature. However, even applying temperatures just above this threshold for up to 30 s caused a completely reversible slight reduction of the CM. The maximum temperature rise in the vestibule of 7.6°C after exposing the fluoroplastic-wire piston to the laser seems unlikely to cause any inner ear damage. The stainless steel piston transmitted heat better than the fluoroplastic-wire piston. Application of the laser to the stainless steel piston increased the temperature by 13.0°C, which is above the threshold of 7°C set by Barnett [8]; thus, even when the time of exposure is much less than 30 s, thermal trauma of the inner ear cannot be excluded.

The addition of a vein graft in our experiments significantly reduced the heat transmission to the vestibule. In vivo, even in cases where the vein graft was not used, the healing process produces a neomembrane which may also decrease the heat transmission.
Inner ear irritation at temperatures recorded by us cannot be excluded. Therefore, it is advised to avoid exposing the pistons to laser energy and make pauses between the subsequent impulses to allow cooling of the piston.

References

Technical and Clinical Aspects of ‘One-Shot’ CO₂ Laser Stapedotomoy

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Abstract

Objective: In order to further optimize the surgical technique with the CO₂ laser in stapes surgery, a scanner system was used to obtain a footplate perforation of 0.5–0.6 mm with only one laser application (‘one-shot’ stapedotomy). Study Design: 240 patients with otosclerosis were submitted to a primary CO₂ laser stapedotomy with the SurgiTouch™ scanner. This study surveys the surgical technique and clinical results. Results: An adequately large perforation diameter could be achieved with a single shot in 68% of the patients treated with the SurgiTouch scanner. In 14% of the patients, a second laser application at the same site was necessary. In 18%, the perforation had to be enlarged by several slightly overlapping laser applications without scanner. The clinical data of this study clearly document that there is no evidence of laser-depending inner ear affections. The closure of the air-bone gap in our study is comparable to conventional stapes surgery. Conclusion: The CO₂ laser combined with modern scanner systems is well suited for application in stapes surgery.

The advantages of laser stapedotomy compared to the conventional technique without a laser have already been confirmed by numerous authors. Clinical studies have demonstrated that laser stapedotomy causes fewer inner ear damages and less vertigo than conventional operations [1–7].

Since the introduction of the CO₂ laser in stapes surgery [3, 4] and the publication of the authors’ experimental and clinical studies confirming that CO₂ laser is suitable for stapedotomy [8–15], this wavelength in the far-infrared range has become a widely accepted parameter for ear surgery [6, 9, 15, 16].

The aim of CO₂ laser stapedotomy is to achieve an adequately large (0.5–0.7 mm in diameter), sharply defined, nearly round perforation with clean-cut edges and without appreciable thermal or acoustic damage to the middle or inner ear structures.
The total energy minimization required to prevent inner ear damage is best achieved by the single application of a focussed laser beam [12–14].

The laser industry (Lumenis Co., Tel Aviv, Israel) cooperated in the development of microprocessor-controlled scanner systems that move the focussed laser beam over a defined and selectable area in short time intervals with the aid of rotating mirrors. These systems are the first to achieve a perforation large enough for a piston by applying the laser a few times or only once.

This study surveys the surgical technique and clinical results of single-shot stapedotomy with the new scanner system SurgiTouch™.

Materials and Methods

Laser and Application System

The CO\(_2\) laser system (type: 40c, Lumenis Co.) combined with a micromanipulator (type Acuspot™ 712, Lumenis Co.) was clinically applied. The laser beam could be focussed to a diameter of about 180 \(\mu\)m at a working distance of 250 mm. The scanner system with the rotating mirrors is situated between the micromanipulator and the hinged mirror arm. With the SurgiTouch scanner (Lumenis Co.), irradiation fields of 0.5, 0.6 and 0.7 mm in diameter can be selected for stapedotomy. The times for a complete scan range between 0.03 and 0.05 s, depending on the selected diameter.

Effective and Safe Laser Parameters

Based on previously published data obtained in petrous bone preparations, a cochlea model and animal experiments [10, 12–14], effective and safe parameters were determined for stapedotomy with the CO\(_2\) laser. The mode was continuous wave. For the laser system, a power setting of 1–20 W and a pulse duration of 0.03–0.05 s were found to be most effective for soft tissue and bone vaporization with minimum thermal conduction (table 1). The power density at these settings ranged from 4,000 to 80,000 W/cm\(^2\). Strict adherence to the laser energy parameters minimizes any risk of damage to middle and inner ear structures by thermal or acoustic stress.

Since the transmission of CO\(_2\) laser irradiation via the hinged mirror arm and micromanipulator involves power losses varying from 20 to 30% depending on the system used, the power indicated on the laser does not correspond to that actually applied in tissue. The specified powers correspond to real powers ultimately applied by the system.

Patients

Between the years 1999 and 2004, 240 patients with otosclerosis were submitted to a primary CO\(_2\) laser stapedotomy with the SurgiTouch scanner and the ‘one-shot’ technique. The patients had a mean age of 44.8 years (range 20–70); as to the sex distribution, there was a female-to-male ratio of 1.9:1 (158 women and 82 men). The mean age was 44.4 years for women and 45.6 years for men. One hundred and thirty-four right and 106 left ears were operated. Altogether, left- and right-sided operations were performed in 20 cases.
Table 1. Effective laser energy parameters for stapedotomy (SHARPLAN 40c CO\textsubscript{2} lasers)

<table>
<thead>
<tr>
<th>Anatom. structure</th>
<th>Real power W</th>
<th>Power density W/cm\textsuperscript{2}</th>
<th>Pulse duration, s</th>
<th>Mode</th>
<th>Diameter of irradiation mm</th>
<th>Number of pulses</th>
<th>Diameter of perforation mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stapedius tendon</td>
<td>2</td>
<td>8,000</td>
<td>0.05</td>
<td>cw</td>
<td>0.18</td>
<td>2–3</td>
<td></td>
</tr>
<tr>
<td>Incudostapedial joint</td>
<td>6</td>
<td>24,000</td>
<td>0.05</td>
<td>cw</td>
<td>0.18</td>
<td>8–14</td>
<td></td>
</tr>
<tr>
<td>Crura</td>
<td>6</td>
<td>24,000</td>
<td>0.05</td>
<td>cw</td>
<td>0.18</td>
<td>4–8</td>
<td></td>
</tr>
<tr>
<td>Stapes footplate</td>
<td>20–22\textsuperscript{1}</td>
<td>80,000–88,000</td>
<td>0.03 or 0.05</td>
<td>cw</td>
<td>approx. 0.5, 0.6 or 0.7</td>
<td>1</td>
<td>0.5–0.7</td>
</tr>
</tbody>
</table>

Focal length: $f = 250$ mm; focal size: 0.18 mm (Acuspot 712). cw = Continuous wave. Specified powers correspond to real powers at the end of the application system. The use of rotating application systems at the stapes footplate may require perforation enlargement by additional individual applications without a rotating laser beam (power: 6 W, power density: 24,000 W/cm\textsuperscript{2}, pulse duration: 0.05 s).

\textsuperscript{1}Application of laser irradiation with rotating mirrors (SurgiTouch).
Surgical Technique

CO₂ laser stapedotomy can be performed under local or general anesthesia. The author preferred general anesthesia in most cases (99%), since it provides surgical control and does not require patient cooperation.

Application of the CO₂ laser is preceded by some test shots on a wooden spatula to ensure aiming beam alignment with the CO₂ laser beam.

The stapedius tendon is first vaporized with 2–3 single pulses at a low power of 1 W (power density 4,000 W/cm²) and a pulse duration of 0.05 s.

With a completely fixed footplate, the incudostapedial joint is conventionally severed as a rule. Laser-assisted joint severance is performed in cases with only a partially fixed stapes. Vaporizing the head of the stapes with 8–14 single pulses of the laser beam at 6 W (power density 24,000 W/cm²) and a pulse duration of 0.05 s separates the incudostapedial joint. Since the CO₂ laser beam does not strike perpendicular to the joint, the separation may not be complete. Any remaining tissue is severed with a 90° hook.

Vaporization of the posterior crus requires 4–8 laser shots with a power of 6 W set at a pulse duration of 0.05 s. While severing the joint and posterior crus with this relatively high laser power, care must be taken that middle ear structures in the path of the beam and beyond the target (e.g., footplate, facial nerve canal) are not accidentally irradiated and damaged. Adequate protection is provided by filling the tympanic cavity with saline or covering the nontarget structures with a saline-soaked gelatin sponge (Gelita™, Spongostan™).

The anterior crus of the stapes is usually not directly accessible to the laser beam. It is therefore fractured with a hook. However, in some cases, the anterior crus may be partially visible. Protecting the nontarget areas, the crus is vaporized with the CO₂ laser beam, using the same parameters as for the posterior crus. Should vaporization be incomplete, the residual bone can be severed with a minimum of force, using a cold instrument. Footplate mobilization or even partial or total footplate extraction is thus almost entirely avoided. The stapes suprastructure is removed with the microforceps.

The energy setting for footplate perforation with the one-shot application technique using the SurgiTouch scanner depends on the thickness of the footplate and the irradiation diameter of the scanning figure applied. In the author’s experience, a power setting of 20–22 W (power density 80,000–88,000 W/cm²) with an exposure time of 0.03–0.05 s per pulse creates a round perforation 0.4–0.7 mm in diameter (fig. 1).

In those cases in which the desired perforation diameter cannot be achieved with one shot, the perforation is enlarged by additional laser applications either with or without the scanner system, depending on the perforation diameter already achieved. While a second scanner was applied at the same site for perforations up to 0.3 mm in diameter, enlargement to 0.4 mm or more was achieved with a few juxtapositioned, slightly overlapping multiple-shot applications of laser energy without the SurgiTouch scanner. With a beam diameter of 180 μm, the power is set at 6 W (power density 24,000 W/cm²) and the pulse duration at 0.05 s.

Care must be taken to ensure that the vestibulum is filled with perilymph to achieve adequate protection of inner ear structures and prevent damage by direct laser irradiation. If the perilymph is inadvertently aspirated from the vestibulum, no further laser irradiation should be applied to the footplate.

A 0.4-mm platinum Teflon piston is then inserted in the perforation and attached to the incus neck. The prosthesis diameter is 0.1–0.2 mm smaller than the perforation diameter. Finally, the oval niche is sealed with connective tissue or a blood clot.
Technical and Clinical Aspects of 'One-Shot' CO\textsubscript{2} Laser Stapedotomy

Audiometric Examination

Patients’ hearing was tested by determining the pure-tone thresholds in the frequency range of 0.125–4 kHz by air and bone conduction. To determine possible surgical damages to hearing, the bone conduction measurements were made 1 day preoperatively and 1.5–6 months postoperatively. An audiological examination could be performed in 174 of the 240 patients treated by CO\textsubscript{2} laser stapedotomy. The mean value with the standard deviation and the intraindividual differences between post- and preoperative values were calculated for statistical evaluation of hearing losses. Statistical evaluation and comparison of the pre- and postoperative audiological data within the patient group were performed by Wilcoxon’s test for paired differences. A significant difference was assumed for \( p < 0.05 \).

The air-bone gap was calculated by the four-tone pure-tone average at the frequencies of 0.5, 1, 2 and 3 kHz for air conduction minus the average for bone conduction. Hundred and ten of the 240 patients submitted to CO\textsubscript{2} laser stapedotomy could be audiologically examined over a postoperative period of \( \geq 1 \) year (1–4 years).

Results

Application Technique for the Footplate Perforation

An analysis of the number of laser applications required in patients treated with the SurgiTouch scanner showed that an adequately large perforation diameter could be achieved with a single shot in 164 interventions (68%) (fig. 2), while 33 patients (14%) required a second laser application at the same site. In 43 cases (18%), too small a perforation had to be enlarged by several slightly overlapping applications of the laser beam without a scanner (fig. 2).

Hearing Results

Preoperatively, the mean sensorineural hearing loss was 12 dB HL at 0.5 kHz, 26 dB HL at 2 kHz (Carhart phenomenon) and 22 dB at 4 kHz. One and

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Fig. 1. \( a \) HeNe laser beam of the CO\textsubscript{2} laser with the SurgiTouch scanner, with a scanning diameter of 0.6 mm aiming at the stapes footplate after removal of the suprastructure. \( b \) One-shot perforation of the stapes footplate of approx. 0.6 mm in diameter (power: 20 W, pulse duration: 0.04 s).
a half to 6 months postoperatively, the mean bone conduction threshold showed an improvement of 4 dB at 0.5 kHz, 7 dB at 2 kHz and 2 dB at 4 kHz (fig. 3). This is a statistically significant improvement of the bone conduction threshold at all frequencies (Wilcoxon test, \( p < 0.01 \)).

The air-bone gap improved continuously within the first year. After 1 year, 99% of the patients showed a successfully closed air-bone gap of \( \leq 20 \) dB. The air-bone gap was 0–10 dB in 76% of the operated patients and 11–20 dB in 23%. One patient (1%) developed poor hearing with an air-bone gap of \( > 30 \) dB and was submitted to revision surgery. Afterwards the air-bone gap was within the range of 0–10 dB (fig. 4).
Complications

Five of the 240 patients (2%) required revision surgery, 7 days postoperatively at the earliest and after 9 months at the latest.

Intraoperative Complications. No intraoperative complications [accidental mobilization of the footplate (floating footplate), accidental fracturing of a thin footplate] occurred. Neither of the 2 patients who underwent surgery under local anesthesia complained of vertigo during and/or directly following vaporization of the stapes footplate with the CO$_2$ laser.

Postoperative Complications. Two (1%) of the 240 patients postoperatively developed a progressive significant sensorineural hearing loss. In 1 case, a threshold shift of up to 20 dB in all frequencies occurred together with a persistent tinnitus. One patient (0.5%) developed a severe sensorineural hearing loss of up to 40 dB in all frequencies 1 week postoperatively. These 2 patients who underwent revision surgery after 1 week were found to have a too short a prosthesis with a perilymph fistula. Revision surgery improved the sensorineural hearing loss and the tinnitus. Early and/or late cases of deafness were not observed in our group of patients. No patient suffered from permanent tinnitus, which did not exist preoperatively, and only 2 patients reported a slight increase in preexistent tinnitus. One patient had to undergo revision within the first postoperative week because of persistent vestibular symptoms caused by too long a prosthesis. The complaints disappeared after insertion of a shorter one. In the first postoperative week, 7 patients reported mild vertigo with queasiness when standing up or during rapid head movements. Four weeks postoperatively, none of the patients had any residual symptoms of vestibular irritation. Four patients (2%) had transient taste disturbance. There were no tympanic membrane perforations.

![Distribution of the patients with a postoperative air-bone gap (average of 0.5, 1, 2 and 3 kHz for air conduction minus the average for bone conduction) of 0–10 dB, 11–20 dB, 21–30 dB or 30 dB with a follow-up of at least 1 year postoperatively.](image-url)
Delayed Complications. Two additional patients underwent revision surgery for conductive hearing loss 5–9 months postoperatively. One patient had a displaced prosthesis, combined with total incus erosion due to a too short a prosthesis. The new prosthesis could be fixed at the residual incus. One patient developed a loose wire with prosthesis and incus fixation resulting from adhesions. Lasering these adhesions and refixing the prosthesis at the incus improved the conductive hearing loss.

Discussion

The aim of laser stapedotomy is to enable management of the stapes in such a way as to ensure the greatest possible protection of the inner ear and to avoid damage to residual middle ear structures. Advocates of the laser technique agree that noncontact laser vaporization of the bone covering the vestibule is less traumatic for the inner ear than manual instrumental extraction or perforation of the stapes footplate. It is also true, however, that the laser-related absorption of irradiation energy and generation of heat potentially endanger membranous inner ear structures during perforation of the stapes footplate.

The energy setting should be such that a 0.5- to 0.7-mm perforation diameter is achieved with a one-shot application. The laser perforation should be circular with a clean-cut edge. This study demonstrated that an adequate footplate perforation diameter of 0.5–0.7 mm could be achieved with a single laser application by using a suitable scanner system.

Integrating the control of the scanner in the laser system (SurgiTouch scanner) enabled synchronization of the spiral laser beam course with the triggering of a laser impulse, so that the laser beam starts the spiral figure at the same point and runs through the same figure each time. This results in higher reproducibility of the laser-induced tissue effect. In addition, the laser beam is moved at an increased speed, so that the spiral completes its course in only 0.04 or 0.05 s. With a maximal single-pulse energy of ≤1 J, the laser power of a single scanner application can thus be increased to 20–22 W (power density of 80,000–88,000 W/cm²). In this way, the success rate of the one-shot technique, i.e. creating an adequately large perforation with a single laser application, could be increased to 68% of the cases. In 14%, the requisite perforation size was achieved by a second application with the scanner at the same site, and in 18% the perforation was enlarged at the edge by slightly overlapping applications without using a scanner.

The results of previous studies support the use of both visible (argon and KTP) and invisible, far-infrared (CO₂ and Er:YAG) laser systems for primary otosclerosis surgery [1–7, 16–28].
All studies use the multiple-application technique for footplate perforation. Since the beam of the argon or KTP laser has a diameter of about 0.15 mm, most authors use the so-called rosette technique with a multiple circular application pattern.

Argon and KTP lasers appear to be valuable tools in primary and revision cases [1, 2, 5, 17, 29]. Here, the insertion of a fiber-optic microhandpiece (Endo-Otoprobe) [2] is superior to laser application with micromanipulators attached to the microscope, since the strong laser beam divergence at the exit of the optical fiber rapidly decreases the power density in relation to the increase in distance [21, 20]. This reduces the risk of inner ear damage associated with the penetration depth and temperature problem in the perilymph. Moreover, the use of the fiber-optic microhandpiece facilitates the vaporization, especially also of the anterior crus, while reducing the amount of technical equipment required [25].

The CO$_2$ laser is also widely applied in the clinical routine [6, 7, 16, 22, 30, 31, 34]. With a beam diameter of 0.18–0.2 mm, all authors use the multiple-application technique for footplate perforation.

In the group of pulsed laser systems, the Er:YAG laser at first seemed to possess the most suitable wavelength for middle ear surgery. The Er:YAG and CO$_2$ lasers do not coincide in their tissue impact and effectiveness, since they differ in their wavelength and irradiation time ratio. The continuous-wave CO$_2$ laser is suitable for use on soft tissue and, if well focussed, for vaporization of thin bone structures [12], while the Er:YAG laser offers advantages mainly in the treatment of bone structures [17, 23, 32]. However, as soon as bleeding occurs, the oligothermic Er:YAG laser radiation is completely absorbed by blood and no longer reaches the target area. It is then ineffective.

The introduction of new techniques in stapes surgery is always associated with the question of possible risks to inner ear structures. The clinical application must be preceded by experimental in vitro studies for risk assessment [10–14]. In the final analysis, however, only the postoperative audiometric results can provide information about the effects on inner ear structures. A comparison between post- and preoperative bone conduction auditory thresholds showed that, on average, patients in the authors’ population had no postoperative deterioration of inner ear function in the examined frequency range of 0.5–4 kHz. Thus, applying higher powers using the one-shot technique with the scanner does not have a higher potential for damage than the multiple-application technique [15].

Comparing published audiometric results after laser stapedotomy in relation to mean differences in the bone conduction auditory thresholds in the main speech region shows that postoperative improvements of 0.53–5.6 dB in those thresholds are achieved regardless of the laser system applied [6, 7, 22, 24, 28, 30, 31].
The mean value for the frequency range of 0.5–4 kHz is 4.3 dB in our patient population.

The higher sound level measured in Er:YAG laser therapy is associated with the risk of inner ear trauma and tinnitus [13, 24, 32]. Moreover, it is suspected that the pressure waves resulting from Er:YAG laser therapy may cause transitory or even permanent inner ear damage such as high-frequency hearing loss or tinnitus [24; our own experience]. Thus, the Er:YAG laser has a lower application safety than the CO\textsubscript{2} laser and cannot be recommended for stapes surgery at the present time.

The literature comparing hearing results after conventional and laser stapedotomy is not suitable for all series, since most authors dealt with more or less selected groups. Older studies often averaged the air-bone gap for 0.5, 1 and 2 kHz, whereas the more recent ones include the frequencies of 3 or 4 kHz as well.

In this study, 99% of the patients showed successful closure of the post-operative air-bone gap to \(\leq 20\) dB (average of 0.5, 1, 2 and 3 kHz). In the literature, closure of the air-bone gap to \(\leq 10\) dB was achieved by 67–99% and closure to \(\leq 20\) dB by 85–99% of the patients who underwent laser stapedotomy [1, 2, 4–7]. Assessing the results of conventional stapes surgery in the literature showed that a mean residual air-bone gap of \(\leq 10\) dB was achieved by 40–96% of the patients and a gap of \(\leq 20\) dB by 68–99% [25, 33–37]. These data are comparable to those of laser stapes surgery.

**Conclusion**

Our findings as well as data in the literature suggest that CO\textsubscript{2} laser stapedotomy is a safe procedure with a lower incidence and severity of intra- and post-operative complications (e.g. floating footplate, accidental fracturing of a thin footplate, vertigo) than conventional interventions [6, 7, 16]. Our results support these published data. No laser-induced sensorineural hearing loss could be observed in our patients. The closure of the air-bone gap in our study is comparable to conventional stapes surgery.

One-shot stapedotomy achieves an adequately large (0.5–0.7 mm in diameter) circular footplate perforation without appreciable thermal damage to the surrounding area. It represents a considerable advance in CO\textsubscript{2} laser stapedotomy.

The CO\textsubscript{2} laser combined with modern scanner systems is well suited for application in stapes surgery, and, with strict adherence to the parameters, will help to optimize this high-precision intervention and should reduce the incidence of inner ear damage.
References


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Performing stapes surgery for otosclerosis is known to be potentially irreversibly harmful to the inner ear function in about 1% of the cases. An early postoperative transient depression of the bone conduction (BC) thresholds is frequently detected after stapes surgery. The purpose of this study was to compare the evolution of BC thresholds after primary stapedotomy with two different techniques: skeeter versus CO\textsubscript{2} laser stapedotomy. Audiological data of 336 otosclerosis operations performed by 2 surgeons between 1997 and 2003 were subjected to analysis. The calibrated hole in the footplate was performed randomly either with the skeeter drill or with the CO\textsubscript{2} laser. Preoperative BC thresholds were compared with the postoperative levels (day 2–3, week 2, week 6 and month 6) in all patients. Evolution of the BC was compared for the two studied subgroups (laser versus skeeter).
Three hundred and thirty-six patients were evaluated between 1997 and 2003. A CO\textsubscript{2} laser stapedotomy was performed in 205 patients (61%) and the skeeter technique was used in 131 cases (39%).

Figure 1 shows the mean preoperative and postoperative air (0.125–8 kHz) and BC thresholds (0.25–4 kHz). The average preoperative air conduction thresholds revealed a Fletcher index (average threshold for 0.5, 1, and 2 kHz) of 55 dB and an air-bone gap of 29 dB in the Fletcher frequencies. The BC over-closure for the Fletcher index was 4.2 dB. The average air conduction gain for the Fletcher frequencies was 27.2 dB.

The evolution of the BC thresholds for the different frequencies is summarized and magnified to a larger scale in figure 2 and shows a minimal but significant downward shift (first arrow on the left) on days 2–3 in all frequencies (p < 0.001). On days 2–3, an overall average loss of 1.8 dB was measured in the Fletcher frequencies. The temporary drop was minimal for frequencies 0.5, 1 and 2 kHz, but BC measured at 4 kHz dropped by 7 dB.

The upward-directed arrows in figure 2 show the gradual BC recovery. After 2 weeks, there was a partial BC recovery, but this was too slight to be statistically significant (p > 0.05). The most important recovery, with statistical significance (p < 0.05), is visible between week 2 and week 6. Some further slight improvement is noticed after 6 months.

Figure 3 summarizes the evolution of the BC threshold shifts (postoperative BC threshold minus preoperative BC) for the different frequencies. The largest negative BC shifts were observed for the frequencies 250 and 4,000 Hz. The residual BC loss at 6 months for 250 Hz averaged 1.6 dB, and for 4,000 Hz...
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2.7 dB. On the other hand, the largest positive shift or overclosure is seen at frequency 2,000 Hz (the Carhart notch frequency).

Figure 4 shows how often and to which degree a negative BC shift was observed on days 2–3 for the different frequencies. At 250 Hz, a BC drop, even of the slightest degree, was seen in 63% of all cases. At 500 Hz, this was the case in 50%, at 1,000 Hz in 41%, at 2,000 Hz in 48% and at 4,000 Hz in 64%. If we only take the BC losses of ≥20 dB into consideration, the incidences are: 16% (250 Hz), 9% (500 Hz), 5% (1,000 Hz), 3.5% (2,000 Hz), and 13.5% (4,000 Hz).

The evolution of the BC thresholds for the laser stapedotomy is seen in figure 5 and for the skeeter stapedotomy in figure 6.
**Fig. 3.** This graph shows the evolution of the BC shift expressed as the difference between the postoperative minus the preoperative BC thresholds and this for different frequencies. A negative value is a BC loss (most obvious at 250 and 4,000 Hz) and a positive value is a sign of BC overclosure (the most obvious being for 2,000 Hz).

**Fig. 4.** Incidence of occurrence of BC for the different frequencies with different grades of BC shift (<10 dB, between 10 and 20 dB, between 20 and 30 dB, >30 dB).
No statistically significant difference was detected between the skeeter and laser technique groups in the downward shifting as well as in the recovery (independent-sample t test: p > 0.05).

**Conclusion**

In conclusion, our study confirmed the frequent presence of a transient but usually recoverable cochlear dysfunction after stapedotomy. Testing in a large
group showed significant bone conduction changes at all frequencies but mainly at 0.25 and 4 kHz. These usually recover after a few weeks and are without clinical consequence. Early BC measurement can be used to monitor inner ear function so as to detect those cases which may have been subjected to more than usual inner ear trauma.

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Revision Stapes Surgery – Retrospective Analysis of Surgical Findings in a Series of 21 Otosclerosis Patients

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\textbf{Abstract}

\textbf{Aim:} Retrospective analysis of surgical findings in revision stapes surgery in a group of 21 otosclerosis patients qualified for the secondary procedure at the Otosurgery Department of the Medical University of Lodz, Poland, from 1980 to 2002. \textbf{Materials and Methods:} 21 cases of revision stapes surgery out of a total of 350 surgically treated otosclerosis cases are discussed. Group A consisted of 17 cases of revision surgery out of 274 patients who had undergone total stapedectomy (1980–1995) and group B consisted of 4 cases out of 76 patients after stapedotomy (1996–2002). \textbf{Results:} In group A, 17 patients underwent revision surgery, corresponding to 6.2\% out of 274 total stapedectomy cases. Among the indications for the secondary surgical procedure in this group of patients were: (a) platinum wire prosthesis displacement with ossicular chain discontinuity (n = 12); (b) perichondrium or adipose tissue atrophy (n = 3), and (c) incudostapedial joint luxation (n = 2). Group B was composed of 4 cases, i.e. 5.3\% out of 76 stapedotomy patients (Teflon piston operation, 0.6 mm). For both groups, the mean percentage of revision cases was 6\% of all patients operated for otosclerosis. Time from the initial surgical procedure to reoperation varied from 1 to 8 years. \textbf{Conclusions:} (1) The most common indication for revision stapes surgery in patients after total stapedectomy was prosthesis displacement and necrosis of the long crus of the incus. (2) Obliteration of the stapes footplate after small fenestra operation was observed to be the most frequent indication for the secondary stapes procedure in our patient groups.

The growing number of stapes surgeries performed in an increasing number of otologic centers brings the inevitable risk of complications leading to the decision to carry out a revision otosurgical procedure. Lack of hearing improvement after the surgery or hearing deterioration, vertigo and tinnitus are the most frequent signs and symptoms occurring in both the early and late postoperative course in stapes surgery cases.
According to the literature, there is a significantly higher risk of perceptive hearing loss, inner ear damage and vertigo of labyrinthine origin as a result of revision stapes surgery compared to the primary operations [1–3]. Therefore, it is extremely important to consider all pros and cons before making the decision of performing a revision surgery [4].

The most common indications for performing revision stapes surgery (despite the hearing gain) given by various authors are: fluctuation of hearing, progressive hearing decrease, periodical or permanent vertigo, and increase in air-bone gap [2, 4, 5].

However, it is very important to differentiate between the cochlear localization of otosclerosis and cochlear hydrops coexisting with otosclerosis. The diagnosis of the above-mentioned pathologies may be a contraindication to performing a secondary surgical procedure because of the very high risk of membranaceous labyrinth injury leading to the deafness of the operated ear [6–8]. Therefore, radiologic studies are of growing importance in the management of otosclerosis.

The aim of the present study was a retrospective analysis of the surgical findings in revision stapes surgery in a group of 21 otosclerosis patients qualified for the secondary procedure at the Otosurgery Department of the Medical University of Lodz from 1980 to 2002.

**Materials and Methods**

A series of 21 cases of revision stapes surgery out of a total of 350 patients surgically treated for otosclerosis underwent a retrospective analysis (table 1). All studied patients were divided into two groups according to the type of the primary stapes procedure. Group A consisted of 17 cases of revision surgery out of 274 patients who had undergone total stapedectomy (1980–1995) and group B consisted of 4 cases out of 76 patients after stapedotomy (1996–2002). All the patients were operated by one surgeon. All subjects underwent a routine audiologic examination performed by the same staff as before the primary surgery. The most common indications for the revision surgery were conductive hearing loss with an air-bone gap ≥20 dB for the frequencies 0.5, 1, 2, 4 kHz and vertigo spells with progressive hearing loss. Time from the initial surgical procedure to reoperation varied from 1 to 8 years.

**Results**

In group A, 17 patients underwent revision surgery corresponding to 6.2% out of 274 total stapedectomy cases. Among the indications for the secondary surgical procedure in this group of patients were: (a) platinum wire prosthesis displacement with ossicular chain discontinuity (n = 12); (b) perichondrium or adipose tissue atrophy (n = 3), and (c) incudostapedial joint luxation (n = 2).
Group B was composed of 4 cases, i.e. 5.3% out of 76 stapedotomy patients (Teflon piston operation, 0.6 mm). Obliteration of the stapes footplate was observed to be an indication for all the revision surgery cases in this group. For both groups, the mean percentage of revision surgeries was 6% of all treated patients.

**Discussion**

The percentage of revision cases found in the literature varies from 2 to 6% [1, 2, 9, 10]. The main reasons to perform secondary surgeries are technical problems with the stapes replacement prosthesis. In most cases, the connection between the prosthesis and the long crus of the incus is too loose. Another very common problem is the adequate length of the prosthesis.

In this case, the difficulty lies in the measurement of the distance between the incudostapedial joint and the footplate of the stapes because this is not a constant value due to the various materials used to seal the oval window.

In the presented series of patients, the perichondrium was used for oval window sealing. Based on our own measurements, we can conclude that in the studied material, the most frequently used length of the prosthesis varied from 3.75 to 4.00 mm due to the variable depth of the oval window niche [2]. We did not encounter problems with the right length of the prosthesis, but only with its displacement and fixation in the oval window niche.

Necrosis of the long process of the incus or vertigo and fluctuating hearing loss (perilymphatic fistula) are other key issues considering indications for

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**Table 1.** Summary of the retrospective analysis of intraoperative surgical findings in revision stapes surgery in the series of 350 otosclerosis patients

<table>
<thead>
<tr>
<th>Type of primary procedure</th>
<th>Total number of operated patients</th>
<th>Total number of revision cases</th>
<th>Intraoperative surgical findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total stapedectomy</td>
<td>274</td>
<td>17 (6.2%)</td>
<td>(a) prosthesis displacement (n = 12; 70.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(b) perichondrium flap replacement (n = 3; 17.7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(c) incudostapedial joint luxation (n = 2; 11.8%)</td>
</tr>
<tr>
<td>Stapedotomy (Teflon piston)</td>
<td>76</td>
<td>4 (5.3%)</td>
<td>obliteration of the stapes footplate (n = 4; 100%)</td>
</tr>
<tr>
<td>Total number</td>
<td>350</td>
<td>21</td>
<td>21</td>
</tr>
</tbody>
</table>

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revision surgery. During analysis of our series of patients, we observed 3 cases of necrosis of the long process of the incus and 6 cases of perilymphatic fistula. In the latter cases, the perilymph was not seen in the area of the oval window niche. That is the reason we prefer not to remove the material sealing the oval window niche but first to perform scarification of the mucosa and then to use a fibrin glue as a sealing material. In our opinion, this significantly lowers the risk of membranaceuous labyrinth injury.

In 2 cases qualified for the secondary procedure due to unsatisfactory hearing improvement, we decided to replace the prosthesis despite its adequate length and position after the primary surgery. In both cases, the postoperative audiometric test showed nonsignificant hearing improvement without any rational explanation concerning the surgical technique or audiometric preoperative evaluation.

Analyzing revision surgeries in patients after stapedotomy (Teflon piston operation in all 4 secondary cases), we observed obliteration of the small fenestra in the footplate of the stapes. The most probable explanation for this was prosthesis displacement in the upward direction. In such a case, the procedure of choice is prosthesis replacement as well as restoration of the small fenestra hole, resulting in significant postoperative hearing improvement [8].

Based on our clinical experience, we think that it is advisable that revision surgery must be performed by the same surgeon as the primary procedures. Removing the tissue sealing the vestibule window niche requires extreme precision and accuracy from the surgeon in order to prevent profound hearing impairment as a complication. Performing the stapedotomy procedures with Teflon piston prostheses considerably reduces the possibility of such a postoperative complication [9].

**Conclusions**

(1) The most common indication for revision stapes surgery in patients after total stapedectomy was prosthesis displacement and necrosis of the long crus of the incus.

(2) Obliteration of the stapes footplate after small fenestra operation was observed to be the most frequent indication for the secondary stapes procedure in our patient groups.

**Acknowledgement**

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How to Prevent a Stapes Gusher

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Abstract

A stapes gusher is the result of a congenital inner ear anomaly showing at tone audiometry a conductive or mixed hearing loss. The conductive part of the hearing loss could lead to the thought to explore the middle ear. The congenital origin should lead to a high resolution. CT-scanning to evaluate a widening of the internal acoustic canal. Repeated audiometry could show especially a large conductive impairment in the lowest frequencies with a closure of the airbone gap at 2 khz and a high sensorineural high frequency loss at 4 and 8 khz. Contralateral stapedial reflexes may be present. Since the x-recessive mixed deafness syndrome (DFN3) frequently involves males with an early childhood hearing impairment, clinical suspicion should be high. When stapes surgery is considered a precise medical history is essential regarding on the start of the hearing impairment. A continuous suspicion will guide to the audiological, radiological and molecular genetic clues to trace the correct diagnosis before embarking on stapes surgery.

A stapes gusher is a gusher of perilymph, i.e. cerebrospinal fluid filling the external ear canal after opening the stapedial footplate [1–3]. It has been shown to be the result of a too wide communication between the intracranial space and the vestibule along the internal acoustic canal [1]. A bony widening of the lateral part of the internal acoustic canal has been shown especially in the X-recessive stapes gusher syndrome (fig. 1) [3–7].

Prevention of a stapes gusher may be possible in the preoperative diagnostic evaluation focussing on features in the medical history, audiometry results and CT scanning. Genetic testing of the X chromosome may confirm the clinical diagnosis of the X-linked stapes gusher syndrome.
Medical History

A mainly conductive or mixed progressive hearing impairment already present in childhood without any indication for an acquired etiology in a male subject should evoke a first suspicion to diagnose a stapes gusher syndrome. In the X-recessive stapes gusher syndrome, the hearing impairment is more severe in the males compared to the affected females as a result of the mode of inheritance [1–3, 8–11]. Over decades, the hearing impairment is progressive leading to profound deafness. Head trauma may evoke a deterioration of the hearing level (fig. 2). In the medical history, affected males may be found in the family of the mother who is an obligate carrier as a result of the mode of inheritance. Her father is affected in case he has transmitted an affected X chromosome to her.

A history of a stapes gusher during stapes surgery may be present in that family.
Audiometric Evaluation

Preoperative audiograms of adolescents exhibiting a perilymphatic gusher immediately after opening the stapes footplate have shown remarkably large air-bone gaps for the low frequencies (0.5, 1.0 kHz) and an almost nonpresent air-bone gap at 2 kHz (fig. 2). At the higher frequencies, there is again a larger hearing impairment. Another remarkable finding may be the presence of contralaterally evoked stapedial reflexes [12].

The stapedial footplate may be fixed, which contributes to a large air-bone gap (figs. 2–4). In case the air-bone gap is smaller, i.e. about 20 dB, this may be the result of the congenital widened bony vestibule that leads to the presence of a third window (fig. 2–4). As a result, acoustic energy is lost on its way to the tectorial membrane. In the pure-tone audiogram, this is reflected in a conductive component, while brainstem audiometry indicates an inner ear hearing loss.

High-Resolution CT Scanning

A widening of the vestibule, and especially a widening of the internal acoustic canal, is seen on high-resolution CT scans (figs. 5–7). This has been
shown to be the case in males affected by the X-recessive stapes gusher syndrome. The typical CT image of this anomaly has been used by several authors, even as a diagnostic case of the month in ORL journals, to help raise suspicion of this anomaly (figs. 3–7). Before embarking on an exploratory tympanotomy
in patients with a congenital ossicular chain anomaly, it is wise to have performed high-resolution CT scanning of the temporal bone, in case there is a remarkable inner ear component in the hearing loss. There is a severe argument to suspect an inner ear anomaly.

**Molecular Diagnosis**

The DFN3 gene was mapped to the Xq21 region by genetic linkage analyses and the identification of deletions in syndromic and nonsyndromic DFN3 patients [13–16]. The underlying gene POU3F4 was identified. POU3F4 mutations or deletions are the cause of 60% of all stapes gusher cases investigated. Deletions located far upstream of the POU3F4 gene likely disrupt a transcriptional regulator element. The Nijmegen otogenetic lab has the facilities to perform a search for POU3F4 mutations and deletions.

**Surgical Aspects**

A long-standing perilymphatic gusher may cause a deterioration of the sensorineural component in the hearing loss. As a result of the stapedectomy, the conductive part may increase. A stapes gusher may continue for about a week during hospitalization. A lumbar CSF tap could shorten that period. So, it is desirable to stop that stapes gusher immediately after its presentation. Nowadays, openings of the stapes footplate are limited in size by use of a small microdiamond drill or laser. By an endaural incision, fibrous tissue can be gained and placed directly in the oval window niche helped to stay in place by the long process of the incus.

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Additional placement of Oxycel® proved to be of help according to our experience to completely stop the gusher surgically. In case the stapes is not fixed as may occur in the stapes gusher syndrome, perilymphatic fluid may be seen during testing of the mobility of the stapes footplate. This sign could help the surgeon to stop the scheduled surgical intervention of a stapedotomy.

**Discussion**

A good preoperative evaluation may be of help to diagnose the X-linked stapes gusher syndrome and so to prevent an unneeded stapedotomy procedure. In case a stapes gusher occurs, it will be helpful for the surgeon to understand the origin of this complication of stapes surgery. Packing of the oval window with fibrous tissue has shown to be successful to stop this stapes gusher. Doing so, it will be helpful to prevent additional inner ear damage.

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Postoperative Granuloma after Stapedectomy: Is It Destiny or Avoidable?

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Abstract

Objective: The aims of this study were (1) to investigate the pathophysiological characteristics of the middle ear mucoperiosteum against the caustic nature of the gastric content (GC), which consists largely of acid and pepsin components, and (2) to investigate the possible role of gastroesophageal reflux and postoperative vomiting (POV) in the etiology of poststapedectomy granuloma. Methods: 40 Spraque-Dawley rats of either sex and with a body weight of 200–300 g were used, and divided into different study groups: group 1: GC administration to the middle ear (n = 8); group 2: phosphate-buffered saline administration to the middle ear (n = 8); group 3: GC (pH: 2) administration in the presence of a Teflon piston (TP) (n = 6); group 4: phosphate-buffered saline administration in the presence of a TP (n = 6); group 5: GC administration in the presence of a wired piston (WP) (n = 6); group 6: phosphate-buffered saline administration in the presence of a WP (n = 6). GC was administrated to the middle ear cavities by way of the eustachian tube (ET). In order to overcome the pressure of the ET, a pump mechanism was used. The increased nasopharyngeal pressure caused a passive opening of the ET, and transferred a bolus to the middle ear. The animals were decapitated after 1 week, and the bullae were isolated. The tympanic bullae were serially cut and examined with light microscopy. Results: In the saline controls, there was only a mild amount of polymorphonuclear cell (PMN) infiltration in the mildly thickened subepithelial space, indicating a less pronounced inflammation as compared to the gastric acid group. In the GC group, in addition to focal hemorrhage and severe subepithelial infiltration of PMNs, the middle ear mucosa was dramatically thickened with subepithelial edema and dilated capillaries. In the subepithelial tissue, retention cysts and granulation tissue were present. In the piston groups (TP and WP), there was extensive subepithelial inflammation and edema after GC and saline administrations. Granulation tissue filling the entire bulla around the piston segments was detected. Conclusion: The relationship between the administration of GC and middle ear inflammation, and the possible role of POV in the etiology of poststapedectomy granuloma are emphasized with our experimental study. The length of the TP may be considerably important to prevent POV which may lead to gastric reflux to the middle ear.

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Gastroesophageal reflux (GER) has been defined as the recurrence of lesions or signs and symptoms secondary to the reflux of the gastric content (GC) into the oral cavity or airways.

The GC is injurious to the upper respiratory airways leading to inflammation as observed in recent studies [1, 2]. The histological structure of the upper respiratory airways facilitates the damage caused by the GC. The otorhinolaryngologic symptoms of the GER are associated with the histopathological changes on the mucosa from direct and continuous micropenetration of the GC.

The formation of reparative granuloma is known as one of the causes for sensorineural hearing loss being a complication of stapedectomy. The pathophysiology of so-called ‘reparative granuloma’ occurring after stapedectomy has not been determined and a universally accepted management of this rare complication has not yet been established [3].

The normal incidence of postoperative nausea and vomiting (PONV) is 35% after surgery. However, the reported incidence of PONV in patients undergoing middle ear surgery is 62–80% when no prophylactic antiemetic is provided [4].

Following surgery, the positive pressure in the nasopharynx, air loss in the middle ear, changes in the eustachian tube (ET) physiology and decreased protecting reflex may facilitate the reflow of the GC to the middle ear [1, 2, 4–6]. The GC may cause an excessive inflammation and granulation tissue formation on the damaged mucosa after the middle ear surgery, which may complicate the procedure [7, 8]. In this controlled study, the effect of the GC on the normal and exhausted middle ear mucosa is investigated by GC administration via the ET.

**Materials and Methods**

Rodents were chosen because of the similarities in ventilation and drainage of the human and rat middle ears despite minor differences [8–11].

Forty Spraque-Dawley rats of either sex and with a body weight of 200–300 g were randomly divided into six groups: group 1: GC administration to the middle ear (n = 8); group 2: phosphate-buffered saline administration to the middle ear (n = 8); group 3: GC (pH: 2) administration in the presence of a Teflon piston (TP) (n = 6); group 4: phosphate-buffered saline administration in the presence of a TP (n = 6); group 5: GC administration in the presence of a wired piston (WP) (n = 6); group 6: phosphate-buffered saline administration in the presence of a WP (n = 6). GC was administrated to the middle ear cavities by way of the ET (table 1).

The rats were observed during a 7-day prestudy quarantine period. Ten additional animals were chosen and used for providing the GC. The pylori of these animals were ligated in order to provide the GC, low in pH and high in pepsin; the animals were left without pellets, but with water ad libitum. After 24 h of duodenal obstruction, 50 ml of GC was provided after sacrifice.
After induction of anesthesia with ketamine and xylazine, each rat was examined by microscopic otoscopy at a magnification of ×16 and a 2-mm speculum before the beginning of the experiment and found to be without evidence of middle ear disease before inclusion in this study.

The animals were anesthetized with an intraperitoneal ketamine (100 mg/kg) and xylazine hydrochloride (10 mg/kg) injection. A postauricular approach was used with careful dissection. The tympanic cavity was entered making either a mucosal lesion or placing the piston in the middle ear.

After surgery, the rats were placed on paper towels in a recumbent supine position and allowed to recover from anesthesia under a warm lamp. To overcome the pressure of the ET, 100 cm of gastric acid or physiologic saline was administered by a pump mechanism after 2 h of the operation. For inflation, the pump was inserted into the nasopharynx from the nose and secured in place. The velum was elevated with a tongue blade, and the pump was deflated quickly. To evaluate the resistance to the tubal opening and the forces to close an open tube, pressure was continuously increased by an air pump at a constant flow rate of 8 ml/min until the tube was forced open, as indicated by a sudden pressure decrease (fig. 1). The resulting increased nasopharyngeal pressure caused a passive opening of the ET and transferred a bolus to the middle ear. At this stage, the animals could protect themselves against aspiration of the GC.

**Table 1.** Groups in this experimental study

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n = 8)</td>
<td>GC administration to the middle ear</td>
</tr>
<tr>
<td>2 (n = 8)</td>
<td>phosphate-buffered saline administration to the middle ear</td>
</tr>
<tr>
<td>3 (n = 6)</td>
<td>GC (pH: 2) administration in the presence of TP</td>
</tr>
<tr>
<td>4 (n = 6)</td>
<td>phosphate-buffered saline administration in the presence of TP</td>
</tr>
<tr>
<td>5 (n = 6)</td>
<td>GC administration in the presence of WP</td>
</tr>
<tr>
<td>6 (n = 6)</td>
<td>phosphate-buffered saline administration in the presence of WP</td>
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**Fig. 1.** The mechanism to provide a standard pressure to overcome the passive opening pressure of the ET.
In order to assure the reflux through the ET, this mechanism is controlled by a radiologic contrast material in another Sprague-Dawley rat. The increased nasopharyngeal pressure provided by the mechanism caused the passive opening of the ET, and thus transferred a bolus of material to the tympanic bullae (fig. 2).

The animals were sacrificed with an overdose of ketamine injections after a 1-week interval. The heads were dissected to remove the skin, isolating the temporal bone. After fixing in formalin for 24–48 h, the specimens were placed in a ‘rapid decalcifier’ solution for 2–3 days, until ready to be cut. After decalcification, the specimens were dehydrated with ethyl alcohol and embedded in paraffin. The tympanic bullae were serially cut by the standard histologic technique into three segments of approximately 7 mm each, in the coronal plane from the mastoid cells to the ET orifice and stained with hematoxylin and eosin and periodic acid-Schiff/Alcian blue (PAS/AB).

By microscopic examination of the middle ears, middle ear epithelium, subepithelial layers, vascularity, and ossicles, any distortion of these structures was noted. The histologic observations were performed in a blinded fashion by a pathologist, who viewed each slide twice. On the PAS/AB-stained sections, the mean number of PAS-positive cells (i.e. goblet cells) was counted per millimeter of the epithelial surface of the tympanic cavity. Both the subjective mucosal grading scale and the objective amount of goblet cells per millimeter were compared between the study groups.

Results

In this study, there was only a mild amount of polymorphonuclear cell (PMN) infiltration in the mildly thickened subepithelial space of saline
controls, indicating a less pronounced inflammation as compared to the GC group (fig. 3). In the GC group, in addition to focal hemorrhage and severe subepithelial infiltration of PMNs, the middle ear mucosa was dramatically thickened with subepithelial edema and dilated capillaries. In the subepithelial tissue, retention cysts and granulation tissue were present (figs. 4–6). In the piston groups (TP and WP), there was extensive subepithelial inflammation and edema after GC administrations. Granulation tissue filling the entire bulla around the piston segments was detected (fig. 7). In the piston groups with
saline administration, relatively thickened mucosal lining without granuloma formation was observed (fig. 8).

**Discussion**

GER has been implicated in the pathogenesis of several otolaryngologic disorders, such as recurrent rhinopharyngitis, otitis media, subglottic stenosis,
chronic pharyngitis, posterior laryngitis, laryngeal contact ulcer or granuloma, esophageal webs, pachydermia, paroxysmal laryngospasm, vocal cord nodule, Reinke’s edema, Sandifer’s syndrome, laryngotracheal stenosis, globus pharyngeus, laryngeal and hypopharyngeal carcinoma, chronic sinusitis and sudden infant death syndrome.

The major causes of the GER disease include (1) increased frequency of reflux episodes, (2) decreased esophageal clearance of refluxate, (3) increased...
duration of refluxate exposure, (4) increased noxiousness of refluxate, (5) defective mucosal resistance to refluxate, (6) upper esophageal dysfunction, and (7) the effects of sleep.

The reflux of gastric secretions into the tissues of the upper aerodigestive tract has been demonstrated in pH probe studies. The caustic nature of these gastric secretions, due to their acid and pepsin components, is thought to produce a chronic irritation of tissues. Repeated tissue damage and inflammation are thought to be a possible mutagenic factor, and hyperregenerative state promoter [12].

The epithelial lining of the middle ear consisted of a single layer of squamous cells that were contiguous with the promontorial epithelial cells. The latter adhered to each other by finger-like projections with tight junctions close to the epithelial surface. A basement membrane separated the outer layer from the middle connective tissue layer. The epithelium of the normal rat middle ear did not contain ciliated cells. The epithelial cell surface exhibited microvilli, most frequently close to the cell borders. The subepithelial layer consisted of a connective tissue layer, containing fibroblasts, fibrocytes, blood vessels, and nerves. The blood vessels were located close to the bony attachments. Elastic fibers were sparse and/or absent. Collagen fibers occupied most of the middle layer. The distribution of the fibers was mostly vertically (longitudinally) arranged in the core, although transversely sectioned fibers were also common. The fibrocytes were the predominant cells in the connective tissue layer forming thin cytoplasmic extensions, which were frequently present near the outer bony attachment area [13].

The normal rat middle ear mucosa was lined by 1 or 2 layers of flat or cuboidal epithelium. The mucosa of the ET orifice was lined by pseudostratified ciliated epithelium containing goblet and basal cells. These cells extended from the tubal orifice along the medial wall, inferior to the promontory, and to the round window niche. The subepithelial stroma consisted of fibrocytes, plasma cells, lymphocytes and thin capillaries. The subepithelial layer under the flat and cuboidal epithelium was thin; in some areas, the epithelial cells were layered over the periosteal cells [14].

Postoperative reparative granuloma formation has long been recognized as a cause of sensorineural hearing loss following stapedectomy. The incidence of sensorineural hearing loss has been reported in several studies. Kaufman and Schuknecht [15], for example, found 10 granulomas in a total of 780 recent stapedectomy cases with an incidence of 1.3% and concluded that granuloma formation is a major cause of sensorineural hearing loss following stapedectomy. Harris and Weiss [16] found 6 granulomas in 119 patients with an incidence of 5%.
There are various typical clinical presentations of this entity. Sudden hearing loss, gradual hearing loss, vertigo, distortion of sounds and lack of hearing improvement can be presenting symptoms of reparative granuloma [15].

The term granuloma implies a tumor-like mass of granulation tissue. Actively growing fibroblasts, fibrous tissue, capillary buds, occasional foreign body giant cells, clusters of round cells and varying numbers of PMNs indicate granuloma formation [15]. If there is an inflammation at the middle ear mucosa, the outcomes of the surgery are poor. The pathophysiology of so-called ‘reparative granuloma’ occurring after stapes surgery has not been determined and a universally accepted management of this rare complication has not yet been established [3, 17–19].

The overall incidence of PONV is found to be 35% after surgery. The reported incidence of PONV in patients undergoing middle ear surgery is 62–80% when no prophylactic antiemetic is provided [4].

PONV after middle ear surgery is multifactorial. The technique of the anesthesia, complications of anesthetic drugs, the stress on the middle and inner ear (i.e. caloric effect, negative pressure of aspiration, drilling of the temporal bone, duration of the surgery) and postoperative pain can be the cause of PONV [4, 20, 21].

A diminished reflex protecting the airway may result in PONV, increasing the risk of complications [4].

In this study, investigating the mucosal changes with acid-pepsin reflux through the ET revealed a strong evidence of granuloma formation. In the saline controls, a mild amount of PMN infiltration with slight thickening of subepithelial spaces was observed. On the other hand, the appearance of an aggressive granulomatous reaction in the TP and WP groups could be one of the most dangerous complications encountered during stapes surgery. The lack of evidence of reparative granulomas arising from the powder of surgical gloves, fat tissue necrosis and WP alone has been reported elsewhere [17]. In the saline groups with TP and WP, a lack of excessive granulation formation was observed. PONV following stapes surgery as a result of vestibular irritation is probably one of the most common reasons expected to produce reflux of acid-pepsin through the ET. Especially longer pistons which can produce more irritation in the vestibule are apt to produce extensive vomiting, thus possibly resulting in granuloma formation.

**Conclusion**

In this study, a model of reflux to the middle ear through the ET is designed. The pathological specimens confirmed the possibility of granuloma...
formation in the middle ear with acid-pepsin reflux, whereas the controls revealed slight inflammatory changes in the middle ear mucosa. The relationship between the administration of GC and middle ear inflammation, and the possible role of PONV in the etiology of poststapedectomy granuloma are emphasized with our experimental study.

Poststapedectomy granuloma might arise from the reflux of the GC through the ET in a vomiting patient. Reflux through the ET should be avoided in the postoperative period. The excessive length of the TP initiating vertigo, which results in PONV, may also be considerably important to prevent gastric reflux causing reparative granuloma in the middle ear.

References


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Reparative Granuloma Related to Perilymphatic Fistula

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Abstract

Reparative granuloma is defined as an ‘exaggeration of the normal reparative process’ (Schuknecht) after stapes surgery, often resulting in a destruction of the labyrinth. It is ascribed to a foreign body reaction, yet there are insufficient histological data to prove this and although rare, the problem is still with us. We encountered two patients in whom the history contains elements evoking a perilymphatic fistula. Cerebrospinal fluid causes irritation of the middle ear mucosa. This is demonstrated in an exemplary way in case of a spontaneously developed cerebrospinal fluid leak from a defect in the tegmen tympani. The leak itself may be very small, but is almost always surrounded by a large mass of granulation tissue. Since the chemical composition of perilymph and cerebrospinal fluid is known to be identical, a persistent perilymphatic leak might likewise be responsible for the formation of a granuloma in the middle ear, eventually invading and destroying the labyrinth. Laboratory experiments to investigate this hypothesis are recommended.

Reparative granuloma is a rare complication of stapes surgery, occurring in 0.07% of stapedotomy to 0.1% of stapedectomy cases [1]. First reported in 1962 [2, 3], the term ‘reparative granuloma’ was coined by Schuknecht to describe an apparent ‘exaggeration of the normal reparative process’ [4]. The histopathologic findings in Schuknecht’s series of 10 cases revealed occasional multinucleated giant cells both in fat-wire and Gelfoam-wire implants, and Schuknecht did not consider a foreign body reaction as being a causative agent. In some institutions, no new cases were observed since all textiles and surgical glove powder were eliminated [5]. Gelfoam was suspected to cause inflammatory reactions, but this problem is resolved since the company has abandoned the use of formaldehyde in the sterilization procedure [6]. Although Teflon generates a foreign body reaction when embedded in soft tissues [7], and has been...
implicated in one report [8], the ear is known as being remarkably immunotolerant, and a combined Teflon-carbon implant material was well tolerated in the cat’s vestibule [9]. In one series using gold pistons, the incidence of reparative granuloma was substantially higher [10], but this could be attributed to the particular tendency of gold to elicit a predominantly lymphocytic infiltrate in the collagenous capsule that surrounds the prosthesis [11]. In a previous publication, the same author reported on the histopathology of a single case after a gold piston implantation, revealing multinucleated giant cells to be concentrated around vacuoles that presumably contained fat [12]. Breakdown of lipids and formation of cholesterol crystals induce foreign body granulation tissue, known as cholesterol granuloma. Nevertheless, reparative granulomas still arise and perhaps even more frequently than previously thought [13]. For instance, in a recent French imaging study on immediate postoperative labyrinthine problems with stapes surgery, 7 out of 11 cases were associated with either ‘reparative granuloma’ or ‘periprosthetic granuloma’ [14]. Thus, the etiology of reparative granuloma remains obscure. In our personal series of over 350 stapedotomies, 3 patients lost their hearing. In 2 of them, a reparative granuloma was diagnosed and in both of them the history contains elements evoking a perilymphatic fistula as a possible cause.

The first patient, after small-hole stapedotomy with a platinum-Teflon piston encircled by fibrous tissue and an excellent subjective hearing result, was bumped by a horse on the tenth postoperative day with the operated ear against the stable door. Immediately thereafter, he noted throbbing in and deviation towards that side. He waited another 5 days before presenting with a 60-dB flat sensorineural hearing loss. There was no improvement after 48 h of intravenous steroid treatment. Reexploration confirmed the otoscopic suspicion of a reparative granuloma. Although it was removed, the hearing could not be saved.

The second patient was referred for a revision stapedectomy. There was no apparent cause for the persisting air-bone gap of 50 dB. The prosthesis was replaced by a slightly longer platinum-Teflon piston. Twenty-eight hours postoperatively, he began to experience vertigo, showing a grade one nystagmus towards the operated ear. Another 4 h later, the nystagmus had reversed to the other side, gradually increasing to a grade three. Accordingly, the tuning fork initially lateralized to the operated ear, but on day 4 the ear was deafened. Six months later, he was referred again with intractable otorrhea from a pinpoint perforation in the anterosuperior quadrant, under which CT showed the presence of the tip of the prosthesis, lying upon a large mass, which at surgery proved to be a giant reparative granuloma with denudation of the facial nerve and invasion of the labyrinth. Treatment consisted in removal of the granuloma, labyrinthectomy and cartilage tympanoplasty. In both cases, histological examination failed to reveal foreign body histiocytes.
At the beginning, both of our cases showed signs of endolymphatic hydrops. These consisted in dysequilibrium and a flat audiogram in the first patient, and a nystagmus initially beating towards the affected ear in the second. The latter is a typical finding at the outset of a Ménière’s attack, and has been observed in other reparative granuloma cases [13]. Moreover, in the first case, the symptoms started immediately after a trauma to the operated ear and its possible complication of a perilymphatic fistula. Endolymphatic hydrops is induced by a perilymphatic fistula, as a result of intralabyrinthine fluid displacements.

Cerebrospinal fluid (CSF) causes irritation of the middle ear mucosa. This is demonstrated in an exemplary way in case of a spontaneously developed CSF leak from a defect in the tegmen tympani [15]. The leak itself might be very discrete, but it is almost always surrounded by a large mass of granulation tissue. The latter obviously is the result and not the cause of the leak [15].

Consequently, if CSF irritates the middle ear mucosa, perilymph may act in a similar way, given the identical chemical nature of CSF and perilymph. So, there are grounds to suspect a persistent perilymphatic leak to be the origin of a reparative granuloma. To our knowledge, the fate of the middle ear mucosa in contact with perilymph has been studied once, and no inflammatory response was found [16]. However, consideration must be given to the role of the grafting material to seal the oval window niche [10]. The incidence of reparative granuloma was reported to be the highest with Gelfoam, followed by fat [1]. The sealing material may provide a tissue substrate for the formation of a granuloma. This would call for the smallest possible gap between piston and footplate fenestra.

References

Reparative Granuloma Related to Perilymphatic Fistula


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Protecting the Cochlea during Stapes Surgery: Is There a Role for Corticosteroids?

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Abstract

The aim of the present study was to evaluate possible protective effects of corticosteroids on the inner ear after surgical trauma and to exclude any ototoxicity. A corticosteroid (triamcinolone, Volon A\textsuperscript{b}) was topically applied to the inner ear of guinea pigs, either by extracochlear application with permeation and diffusion through the round window membrane or by intracochlear application with direct infusion into the inner ear via a cochleostomy. Threshold and input/output functions of compound action potentials (CAPs) were determined before and after application of the corticosteroid. We found that extracochlear application of the corticosteroid induced insignificant mild shifts of mean CAP thresholds, but significantly increased mean maximal amplitudes of input/output function after the 14th day following application of the steroid. No detrimental effects on cochlear function were noted in the extracochlear group, indicating absence of ototoxicity with the concentrations used. In the intracochlear group, CAP thresholds and amplitudes of input/output function recovered from partial hearing loss due to cochleostomy between 7 and 14 days after application of the steroid, whereas in controls without steroid application, no such recovery of hearing was detected. These results suggest that topical application of triamcinolone has no ototoxic effect and that it leads to increased recovery of cochlear functions after trauma in the guinea pig inner ear.

Stapes surgery in experienced hands is a safe procedure and inner ear damage with hearing loss or severe vertigo only seldom occurs. However, in these rare instances, it represents a severe complication and should be avoided in any
case. The most important issue in prevention of hearing loss after stapes surgery is a meticulous surgical technique; nevertheless, hearing loss may occur even in technically correct and uneventful surgical procedures. Mechanisms other than direct mechanical trauma, e.g. inflammation or infection, acoustic and metabolic stress and disturbance of fluid balance, may be at the origin of postoperative hearing loss. Additional pharmacological treatment for the protection of the inner ear, e.g. with corticosteroids, has found interest and is applied in clinical practice in an attempt to prevent or alleviate auditory dysfunction.

Corticosteroids have been shown to reduce noise-induced cochlear damage and hearing loss [1–3], increase recovery after noise trauma [4, 5] and are the mainstay in the treatment of sudden sensorineural hearing loss [6, 7]. However, efficacy in stapedoplasty is still under debate. Riechelmann et al. [8] found no positive effect but increased patient discomfort after intravenous administration of corticosteroids in stapedoplasty; Hendershot [9] stated that short-acting corticosteroids were able to alleviate postoperative serous labyrinthitis, whereas long-acting corticosteroids increased the incidence of postoperative vertigo and reduced the success rate. Spandow et al. [10] reported possible ototoxicity after local administration of hydrocortisone.

Possible ways of application are systemic and local application, either via diffusion through the round window or by direct instillation after opening of inner ear spaces.

Niedermeyer et al. [11] have measured concentrations of prednisolone in the human perilymph after systemic application and found that high doses of 250 mg were necessary to obtain a significant increase of concentration. They also noted a great interindividual variability of results.

Tobita et al. [12] were able to measure uptake of prednisolone, with a peak 1 h after application and a prolonged stay in cochlear tissue only at high doses of 100 mg/kg (corresponding to a human dosage of 7,000 mg for a 70-kg patient); at 30 mg/kg, corresponding to 1,000 mg human dosage, they could not detect an increase in steroid concentration in the tissue with their measurement system. Relatively high doses of corticosteroid seem to be necessary to exert measurable effects in the inner ear, but they carry the risk of systemic side effects. Therefore, direct instillation of drugs into the cochlea offers several advantages, allowing delivery of high drug concentrations to the target organ while minimizing side effects. Some attempts at steroid delivery directly into the cochlea, such as intratympanic therapy [13] and osmotic micropump infusion [14, 15], have been reported.

To further evaluate the efficacy and exclude any ototoxic effects, we decided to design an experimental study on the safety of topically applied steroid and protective effects on acoustic hearing in guinea pigs after specific trauma.
Methods

Study Design
The design of the study included two arms. In the first study arm, steroids were applied extracochlearly at the round window, avoiding any direct mechanical impingement on the cochlea, to test whether steroids have any ototoxic effect. In the second arm of the study, steroids were applied intracochlearly to evaluate possible protective effects of a locally applied steroid on the inner ear after a specific surgical trauma to the cochlea, namely cochleostomy.

Animal Preparation and Application of Corticosteroids
This study complied with the guidelines of the Institutional Review Board. All efforts were made to minimize both the number of animals used and their suffering.

Eleven pigmented guinea pigs (21 ears), weighing from 400 to 630 g, were used in the study. Guinea pigs were anesthetized by intraperitoneal injection of Ketavet (ketamine, Pharmacia & Upjohn GmbH, Erlangen, Germany; dose: 85 mg/kg), xylazine (Rompun, Bayer, Leverkusen, Germany; dose: 8.5 mg/kg), and atropine (Braun, Melsungen, Germany; dose: 0.3 mg/kg). Body temperature was maintained at 37°C during the experiments. The otic bulla was exposed via a postauricular incision and opened with a hole of 2 × 2 mm to allow visualization of the round window.

In the extracochlear study arm, a size of 1 × 1 mm Gelfoam with 5 μl Volon A® (crystalline triamcinolone acetonide solution, 5 ears, verum group) or saline (Ringer’s solution, 5 ears, control group) was implanted in contact with the round window membrane. In the intracochlear study arm, a cochleostomy of about 1 × 1 mm in the basal turn of the cochlea was drilled and 3 μl Volon A (7 ears, verum group), or Ringer’s solution (4 ears, control group) were infused into the scala tympani, using a microsyringe.

Measurements of Compound Action Potentials
A gold hook electrode was anchored to the bony edge of the round window and connected to a percutaneous plug at the vertex to serve as recording electrodes for the acoustically evoked compound action potentials (CAPs) of the auditory nerve.

Acoustic thresholds were determined in a soundproof chamber using frequency-specific gauss pips. The acoustic stimuli were delivered to the ear via a tightly sealed tubed earphone. The intensity of the gauss pip was changed in 5-dB steps between 20 and 119 dB SPL. Thresholds of CAPs were determined at 25 frequencies, distributed logarithmically between 250 Hz and 64 kHz. In addition, input/output (I/O) functions of CAPs in response to click stimuli of increasing intensity were recorded to assess the cochlear function at threshold and suprathreshold levels. CAP amplitudes were measured from the first negative peak to the subsequent positive peak of the waveform through a programmed algorithm.

Frequency-specific thresholds and I/O functions were determined after opening of the bulla, prior to the placement of Gelfoam at the round window or before cochleostomy, and repeated soon after the placement of Gelfoam or cochleostomy and regularly on days 1, 3, 7, 14, 21 and 28 after the operation.

Statistical Analyses
Paired t tests were used to analyze pre- and postoperative results within animals. Unpaired t tests were used for comparison of group results. Differences were considered statistically significant when p < 0.05. Mean values are given ± SD.
Results

Extracochlear Study Arm

No significant shifts of mean CAP thresholds at different frequencies have been observed after the application of the corticosteroid or in the control group. Whereas thresholds remained unchanged, mean maximal amplitudes of I/O function in response to click stimuli at suprathreshold levels increased significantly (p < 0.05) at days 14, 21, and 28 after application of the steroid in comparison with amplitudes prior to the application. There were no significant changes of amplitudes from pre- to postapplication of saline in the control group (fig. 1). These results indicate that there are no ototoxic effects, but on the contrary, steroids increased amplitudes of CAPs.

Intracochlear Study Arm

Soon after cochleostomy, thresholds increased up to about 10–20 dB in both the corticosteroid group as well as in the control group. Cochleostomy itself induced a significant hearing loss (p < 0.05) in comparison with the
values prior to cochleostomy. The shift of thresholds was most prominent in the high-frequency range from 8 to 64 kHz.

In the control group without corticosteroids, thresholds continued to increase up to day 7 and only little recovery has been seen afterwards.

In the steroid group, thresholds also increased up to day 3, but then, recovery of CAP thresholds was found on day 7, and gradually continued until day 28, when it returned close to the presurgical level. In the control group, no notable recovery occurred until the end of the experiment. Statistic comparison of mean CAP thresholds in the steroid group showed significant differences between pre- and postcochleostomy at the time of surgery and on days 1, 3, 7 and 14, but no longer on days 21, and 28, whereas in the control group, statistically significant differences of mean CAP thresholds persisted at all intervals (fig. 2).

Mean maximal amplitudes of I/O function, both from the steroid and the control group, decreased immediately after cochleostomy, and were down to the lowest level at the 3rd day. In the steroid group, recovery could be found on day 14, which continued until day 28. Amplitudes from the control group stayed at a low level until day 14 and recovered only after the 21st day following operation, about 1 week later than in the steroid group.

Fig. 2. Mean changes of thresholds after cochleostomy in the steroid and the control group at different time intervals after operation. Significant changes (p < 0.05) are marked with an asterisk.
Discussion

The safety and efficacy of topic application of steroids to the inner ear is still controversial and few reports on possible ototoxicity are available. Doubts about the effects of steroids on inner ear function still exist [16–18].

In this study, we investigated the safety of topically applied steroid and possible protective effects on acoustic hearing in guinea pigs after surgical trauma to the inner ear. Our findings from this study were consistent with those studies which did not find ototoxic effects.

In the extracochlear group, hearing of animals in both the steroid as well as the control group did not change significantly from the time of application of the drug up to 28 days after surgery; on the contrary, even enhanced amplitudes of CAPs were found in the steroid group. The latter phenomena could be partially interpreted by the study of Shirwany et al. [19], in which they observed that blood flow in the cochlea increased after application of the steroid. Another possible interpretation could be that the surgical procedure of preparation and opening of the bulla and placing the recording electrode already introduced a minor trauma to the inner ear. Application of the steroid might, as in the intracochlear group, have some rescuing effect on inner ear structures. Results from this first set of experiments clearly demonstrated absence of ototoxicity of the steroid for the substance, concentration and route of application that were used. Applying drugs onto the round window membrane has previously been shown to be a reliable route for the delivery of drugs to the inner ear. Nomura [20], Bachmann et al. [21] and Parnes et al. [13] using triamcinolone, dexamethasone, prednisolone-21-hydrogen succinate and hydrocortisone, respectively, demonstrated that corticosteroids permeate through the round window membrane into the perilymph and they reported success in the treatment of patients with sudden hearing loss [22, 23].

In the case of intracochlear application of steroid to the inner ear after a surgical trauma, hearing of animals decreased soon after cochleostomy in both groups. While hearing loss was initially similar in both groups, thresholds in the steroid group started to recover from the 7th day and returned close to the preapplication level on day 28, whereas recovery of thresholds in the control group did not reach the preapplication level on day 28. Possible reasons of hearing loss after cochleostomy may be loss of perilymph, acoustic trauma due to drilling noise, and inflammation due to surgical disturbance. In principle, perilymph loss should be stopped by sealing the opening of the cochleostomy and should be compensated spontaneously by cerebrospinal fluid, which reaches the cochlea via the open cochlear aqueduct. Influence of drilling noise on hearing can either be a temporal threshold shift, disappearing within a few hours to a week, or a permanent damage. Corticosteroids may contribute to related intracochlear
recovery processes associated with restoration of the auditory function by influence on carbohydrate metabolism, transcription of specific genes, as indicated by an increase in specific mRNAs, and influence on potassium turnover in the stria vascularis. Inflammation can severely impair the inner ear structure, if without effective control. It is well known that corticosteroids have a strong anti-inflammatory action, inhibiting the reactive processes of inflammation and scar tissue formation. In this study, recovery of hearing in the intracochlear steroid group may be partly attributable to the inflammation-inhibiting effect of steroid.

In recent years, more studies on apoptosis in the auditory system have been reported. It is agreed that any trauma associated with cochlear implant electrode insertion has the potential to form reactive oxygen species and to result in loss of auditory sensory cells through oxidative stress-induced apoptosis [24]. It is hypothesized that steroids may have the ability to block the initiating pathways of sensory cell apoptosis and inhibit the subsequent degeneration of the peripheral processes of the auditory neurons, thereby enhancing neural preservation for patients receiving cochlear implants.

In conclusion, results from this study indicated that topical application of steroid had no ototoxic effect and was able to rescue some cochlear functions in the guinea pig after trauma to the inner ear. Moreover, it was shown that corticosteroids can have a protective effect against damage of inner ear structures and hearing loss in stapes surgery. They were not able to prevent hearing loss but to increase recovery. There are indications that local application by direct instillation is more effective than diffusion via the round window and can avoid the side effect of systemic application. However, possible local effects, e.g. delayed healing, will have to be investigated.

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Imaging of Postoperative Sensorineural Complications of Stapes Surgery

A Pictorial Essay

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Abstract

Sensorineural hearing loss and/or vertigo are rare but severe complications of stapes surgery for otosclerosis, ranging from 0.2 to 3%. Management of such complications depends on the underlying cause: intravestibular protrusion of the prosthesis, perilymph fistula, labyrinthitis, and reparative granuloma extending into the vestibule. Surgery is mandatory in cases of intravestibular prosthesis or of persistent perilymph fistula. In cases of suppurative labyrinthitis or reparative granuloma extending into the vestibule, prognosis is usually poor, despite aggressive medical therapy or revision surgery. CT scan or magnetic resonance imaging can frequently help to determine the cause of the inner ear complication of stapedectomy. Demonstrative cases are presented to illustrate the prominent place of imaging in managing sensorineural complications of stapes surgery.

Sensorineural hearing loss (SNHL) is a rare but severe complication of stapes surgery, frequently associated with vertigo, ranging from 0.2 to 3% in primary stapedectomy for otosclerosis [1, 2]. Management and prognosis of postoperative SNHL are closely related to its etiology. According to previous reports [1, 3, 4], surgical revision is mandatory in cases of intravestibular prosthesis or perilymph fistula (PLF). On the other hand, suppurative labyrinthitis and granuloma extending into the vestibule are of poor prognosis despite surgical revision [1, 3, 4]. To improve diagnosis of post-stapedectomy SNHL, imaging plays a more and more important role [5–8].
In case of postoperative SNHL or disabling vertigo, CT is performed in emergency because it can show causes which need to be surgically managed promptly. The imaging technique consists in helical CT with multiplanar reconstructions (MPR), with particular attention to reconstructing images along the main axis of the prosthesis.

**Too Long Prosthesis**

As there is no standard definition, we consider the diagnosis of too long piston syndrome when postoperative vertigo or SNHL are associated with a penetration of the prosthesis of more than 1 mm into the vestibule. This can easily be depicted with CT (fig. 1), leading to revision surgery.

**Pneumolabyrinth**

A pneumolabyrinth is defined as the presence of an air bubble in the labyrinth, and has been considered to be the only pathognomonic imaging sign of PLF [7, 8]. Nevertheless, a pneumolabyrinth can be observed on CT within the first postoperative days following stapes surgery, without any pejorative meaning (fig. 2).

A pneumolabyrinth can readily suggest PLF if it is not observed in the immediate postoperative period (fig. 3), leading the otologist to prompt revision surgery.

*Fig. 1.* Intravestibular protrusion of the tip of the prosthesis on axial CT with MPR.
surgery. On the other hand, if a pneumolabyrinth is observed in the immediate postoperative period, the decision on whether or not to perform revision surgery must take into account the evolution of the clinical presentation and audiologic evaluations with aggressive medical therapy.

**Noncontributive CT Findings**

In case of postoperative sensorineural complications of stapes surgery, CT is considered as negative when it shows a well-located prosthesis without a
pneumolabyrinth or opacity of the middle ear, or when it reveals a nonspecific opacity of the middle ear in the immediate postoperative period.

**MRI Findings**

When CT findings are not relevant, MRI can be helpful to assess the underlying causes of the postoperative inner ear complications.

*Intralabyrinthine Hemorrhage*

MR examination may show an intralabyrinthine hemorrhage presenting as a high signal intensity of labyrinthine cavities on both T$_1$- and T$_2$-weighted images (fig. 4). If vestibular bleeding is the only cause to assess postoperative complication, the prognosis is usually good with rest and medical therapy [9].

*Intralabyrinthine Reparative Granuloma*

Intravestibular extension of a reparative granuloma is a rare but severe complication of stapes surgery. CT examination usually shows a nonspecific soft tissue mass filling in the oval window fossa. Conversely, intralabyrinthine focal hypointensity on T$_2$-weighted images with associated enhancement on postcontrast T$_1$-weighted images is highly suggestive of reparative granuloma (fig. 5). Reparative granuloma has a poor prognosis despite aggressive medical therapy, and even revision surgery [4].
Fig. 5. In this case of postoperative SNHL, the axial T₂-weighted image shows the obliteration of the labyrinthine fluids corresponding to an extension of the reparative granuloma into the labyrinth.

Fig. 6. a In case of postoperative labyrinthitis, the axial T₂-weighted image shows partial obliteration of the labyrinthine cavities. b The axial T₁-weighted image after contrast administration shows an enhancement of the cochlea, vestibule and fundus of the internal auditory canal.
Suppurative labyrinthitis is a rare complication usually associated with a poor prognosis. CT findings are nonspecific. MRI demonstrates an obliteration of the intralabyrinthine fluids on T2-weighted images associated with an extensive enhancement of the labyrinth on postcontrast T1-weighted images (fig. 6). In case of suppurative labyrinthitis or reparative granuloma, MRI findings are very similar, suggestive of an inflammatory process obliterating the labyrinthine cavities.

**Conclusion**

Imaging has a predominant role in managing post-stapedectomy SNHL. CT is the first imaging technique to perform. It can depict an excessive penetration of the prosthesis into the vestibule or a pneumolabyrinth caused by PLF. In case of negative or noncontributive findings, MRI might be helpful, as it can show reparative granuloma extending into the vestibule, labyrinthitis or important bleeding into the vestibule.

**References**

Revision Stapes Surgery

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Abstract

We present the results of our revision stapes operations from 1989 to 2004 (n = 217). Long-term follow-up was performed in the first 135 cases. Eighteen of these patients were revised because of inner ear symptoms, predominantly within the first year. One hundred and sixteen cases underwent revision surgery due to conductive hearing loss, on average after 10.6 years. One patient was operated because of dysgeusia. In 1999, we first described inner ear damage after implantation of gold prostheses. Therefore, we developed a titanium implant that was initially investigated in cell culture and subsequently tested in a clinical trial. We report on the most frequent causes that led to revision surgery such as adhesions, prosthetic problems, erosions of the long process of the incus, or refixation of the footplate, and on the different surgical techniques. In a first series of patients with a conductive hearing loss, a significant hearing improvement of 69.4% of these cases was obtained. However, this result very much depends on the selection of cases. There was no case of additional sensorineural hearing loss. Since 1999, we had mainly used titanium implants for replacement in stapes revision surgery. In a second series, a significant hearing improvement of 76.2% was found. One patient with a platinum Teflon implant had to be revised because of vertigo and conductive hearing loss which was observed during MRI.

Stapes surgery is one of the most standardized and successful procedures in otology. This does not apply to revision surgery, which is performed after shorter or longer periods of time due to very different causes of failure. The results of the revision surgery are considerably influenced by the selection of cases and the specific surgical techniques used.

The aim of this study was to describe pre- and intraoperative findings in 217 cases, our general surgical rules and special techniques as well as the postoperative results of the first 135 cases.
Patients and Methods

From April 1989 to December 2004, one author (K.J.) performed 217 revision stapes surgeries. The mean age of the patients was 48.7 years (range 11–78 years). Long-term follow-up was performed in the first 135 cases, done until December 2000.

Eighteen of these patients were revised because of inner ear symptoms, predominantly within the first year (n = 11), after an interval of 1–10 years (n = 6) and after more than 10 years (n = 1). Six cases mainly complained of progressive sensorineural hearing loss; in 10 cases, sensorineural hearing loss together with vertigo was observed, and 2 patients exclusively had vertigo.

One hundred and sixteen cases underwent revision surgery due to significant conductive hearing loss; the interval between the two operations was less than 1 year in 12 cases, 1–10 years in 60 cases and more than 10 years in 44 cases. One patient was operated because of dysgeusia. In total, 76% of the patients had previously been operated on elsewhere. All patients had otosclerosis except 5 with minor ear malformations and 1 with a stapes fracture after skull base trauma.

Additionally, the short-term results of the last 82 cases will be reported.

Results

Surgical Procedures

In stapes revision surgery, there are some important rules according to Dietrich Plester. First, all operations should be performed under local anesthesia whenever possible so that there is control of vertigo when carefully touching the implant inserted during the first procedure. During the last few years, two medialized implants had to be left in place because of vertigo while trying to lateralize them. In addition, it is an advantage to examine hearing improvement at the end of surgery. Everything has to be explained to the patient prior to surgery. Furthermore, there must be an informed consent that the surgeon has the option to postpone surgery at any stage.

During the last few years, the erbium:YAG laser proved to be advantageous when scars and bony fragments were noted near the vestibulum.

Intraoperative Findings

The causes of inner ear symptoms were inner ear otosclerosis, middle ear inflammation, excessively long prostheses, gold incompatibility, adherent swab/particles and a fistula. In the 2 patients sent to our department with middle ear inflammation within 2 weeks postoperatively, the residual hearing capacity could be saved and slightly improved by rinsing the middle ear with antibiotics and corticoid solution.

In 1999, we first described inner ear damage after implantation of gold stapes prostheses [1]. Usually, sensorineural hearing loss developed within the
first postoperative weeks starting in the high frequencies (n = 4). Early revision showed significant granulation tissue formation around the implant verified by histology (fig. 1a). Topical and systemic corticoid therapy resulted in partial recovery of the high-tone loss in 3 cases (fig. 1b). Dermal tests with such implants demonstrated a metal allergy only in 1 of 4 cases. Therefore, it is more likely that the high current conductibility of this metal – in contrast to titanium – plays a significant role in such cases [Helm, J., pers. comment].

After our report, we got the information that in some other departments single cases of complete deafness were observed. Therefore, we developed stapes prostheses made of titanium in co-operation with an industrial partner. In a first step, the biocompatibility of titanium was confirmed in in vitro studies with human stapes osteoblasts (fig. 2a) [2]. It is well known that the potential of titanium to form a tight connection with bone depends on the surface structure. Consequently, the piston was polished and the loop grasping around the incus was roughened (fig. 2b). The loop was altered so that it could not hinder itself when pinched around the long process. During that time, we noticed that Fisch et al. [3] had also used titanium implants for stapes replacement in a few selected cases.

Within a prospective clinical study, the initial 47 implants were analyzed. It was seen that the titanium stapes prosthesis was at least as good in practical use
as the conventional implants used until now. We have observed no hints of any side effects or incompatibility since autumn 1999, when this new implant was introduced [4].

The clinical trial demonstrated an excellent inner ear compatibility. Up to now, we have not observed any sensorineural hearing loss in more than 300 cases. Therefore, we think that a possible advantage of titanium implants is an excellent compatibility when the implant is in contact with the perilymph of the vestibulum as well as with the long process of the incus. On the other hand, it cannot be judged if there is an increased risk of an osseous fixation by recurrent otosclerosis of the oval window niche.

In many revision cases on the basis of conductive hearing loss (n = 116), different causes were seen (table 1).

According to the findings, the operation techniques were very different: in 102 cases, the adhesions were cut, e.g. between the long process of the incus and the tympanic membrane, or in other cases, scar tissue was carefully removed from the oval window niche, sometimes with the erbium:YAG laser. In 28 cases, only a new adjustment of the prosthesis was necessary; however, in the majority of cases, a new implant was inserted (n = 86), mostly a piston. When the end of the long process of the incus was completely cut, which was particularly observed with the platinum band Teflon piston, the angled implant

*Fig 2* Titanium stapes prostheses. *a* Excellent biocompatibility was confirmed in in vitro studies with human stapes prostheses. *b* Essen titanium stapes prosthesis.
was used. In cases in which the Schuknecht wire prosthesis had been used in the first intervention according to Plester, it proved to be very advantageous to cut the wire with scissors and leave the end in place (n = 9) (fig. 3). In a next step, the vestibulum had to be opened carefully at the posterior circumference, where a new piston was inserted.

Ninety-eight of the patients could be followed up in the long term. There was no single case of a significant additional sensorineural hearing loss. The hearing improvement in patients with conductive hearing loss was more than

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**Table 1.** Most frequent causes leading to revision surgery

<table>
<thead>
<tr>
<th>Cause</th>
<th>n</th>
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<tr>
<td>Adhesions</td>
<td>102</td>
</tr>
<tr>
<td>Prosthetic problems</td>
<td>60</td>
</tr>
<tr>
<td>Lateralization</td>
<td>26</td>
</tr>
<tr>
<td>Loose implant</td>
<td>19</td>
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<tr>
<td>Malpositioned implant</td>
<td>12</td>
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<tr>
<td>Too short implant</td>
<td>6</td>
</tr>
<tr>
<td>Erosion of the long process of the incus</td>
<td>42</td>
</tr>
<tr>
<td>Refixation of the footplate</td>
<td>28</td>
</tr>
<tr>
<td>Dysfunction of the eustachian tube</td>
<td>5</td>
</tr>
<tr>
<td>Malleus head fixation</td>
<td>3</td>
</tr>
</tbody>
</table>

**Fig 3** Plester’s technique: Divide the shaft of the Schuknecht wire prosthesis, leave the end in place, open the vestibulum posteriorly (arrow).
20 dB in 32 cases and 5–20 dB in 36 cases, i.e. a significant hearing improvement of 69.4% in this series.

From 2001 to 2004, stapes revision surgery was performed in a further 82 patients. Six of these revisions were performed on the basis of inner ear problems. All had vertigo, 2 had additional sensorineural hearing loss, 1 of these 2 additional conductive hearing loss.

For replacement in stapes revision, we mainly used titanium implants (n = 50). The short-term results in this second series showed a significant hearing improvement of 76.2%.

In the case of an 81-year-old lady, transient vertigo and a significant combined hearing loss occurred during NMR spectroscopy with 1.5 T. Revision stapes surgery was performed 9 months after this event and 10 years after the first procedure. Intraoperatively, the platinum Teflon implant was found to be lateralized and the long process of the incus was completely divided, so apparently the implant was first medialized and then lateralized during NMR spectroscopy, resulting in the above-mentioned symptoms. With the implant removed it was shown that it could not have been dislocated by the magnetic field. Therefore, it is more likely that this event was due to changes in the gradient fields. After that, a titanium implant was inserted and hearing significantly improved.

References

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**Abstract**

With our growing experience with the Vibrant Soundbridge (VSB) middle ear implant, the question emerged of its indication in mixed hearing loss due to advanced otosclerosis. We describe the VSB implantation technique in primary otosclerosis performed together with a stapedotomy piston procedure. Hearing results under headphone and free-field conditions show that the stapedotomy piston procedure closes the air-bone gap as expected and that the VSB provides comparable gain to that usually recorded for pure sensorineural hearing loss. The gains of the two procedures add up. These results open the field of mixed hearing loss to the VSB middle ear implant.

With our growing experience with the Vibrant Soundbridge (VSB) middle ear implant, the question emerged of its indication in advanced otosclerosis. The feasibility and indication of the VSB implantation together with a successful stapedotomy piston procedure have to be considered in primary nonoperated and in previously operated otosclerosis.

Acute trials during classical VSB implantation demonstrate that there is enough space to fit the loop of a Teflon piston and the clip of the floating mass transducer (FMT) of the VSB on the long process of the incus. In primary otosclerosis, the loop of the Teflon piston has to be fitted over the clip of the FMT, whereas in previously operated otosclerosis, the clip of the FMT has to be fitted over the loop of the piston.
Primary Otosclerosis: Stapedotomy Piston and VSB Single-Stage Procedure

For the first case, we decided to associate a retroauricular facial recess approach for the VSB with an ear canal approach for the stapedotomy piston procedure, as the reference technique for the two [1, 2].

The surgical technique requires a combined ear canal and retroauricular approach. The retroauricular approach was performed with a facial recess approach. The internal part of the VSB was fitted in the retroauricular field, and the FMT was placed in the posterior tympanotomy opening, ready to be clipped on the incus. Then the ear canal approach was performed. The stapes superstructures were removed, the calibrated stapedotomy was performed and covered with the vein interposition. Coming back to the facial recess approach, the FMT was fitted on the long process of the incus and its clip tightened. Coming back to the ear canal approach, the Teflon piston was placed in the stapedotomy opening, on the vein, and its loop fitted on the long process of the incus, over the clip of the FMT, and tightened (fig. 1). Classical closure and ear canal packing were observed.

The results of the first case show that the stapedotomy piston procedure closes the air-bone gap as usual. The VSB gives a gain comparable to that in classical indications. The gains of the two procedures add up (fig. 2).

We demonstrated the feasibility and described the surgical technique to implant a VSB middle ear implant in mixed hearing loss due to otosclerosis.

Fig. 1. VSB in primary otosclerosis: loop of the piston over the clip of the FMT.
The indication of the VSB has to be decided according to the sensorineural part of the mixed hearing loss, with the same criteria as for pure sensorineural hearing loss. The implantation of the FMT by the ear canal approach, without the facial recess approach, may be discussed.

**Fig. 2.** Primary otosclerosis in a 42-year-old man (first case). ABG = Air-bone gap; AC = air conduction.

The indication of the VSB has to be decided according to the sensorineural part of the mixed hearing loss, with the same criteria as for pure sensorineural hearing loss. The implantation of the FMT by the ear canal approach, without the facial recess approach, may be discussed.

**References**


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Cochlear Implantation and Far-Advanced Otosclerosis

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Abstract

Objective: To evaluate results of cochlear implantation in patients with far-advanced otosclerosis. Methods: Sixteen patients with far-advanced otosclerosis had undergone unilateral (n = 13) or bilateral (n = 3) cochlear implantation. Surgical difficulties, incidence of complications and postoperative benefit were analyzed. Results: A full electrode insertion was achieved in all patients without surgical difficulties. All patients demonstrated excellent benefit of cochlear implantation. Binaural implantation still improves speech performances, compared to unilateral implantation. In case of residual cochlear function of one nonoperated side, a stapes surgery, performed during the same surgical time as cochlear implantation, can improve speech scores and restore bilateral hearing. Facial nerve stimulation occurred only in 1 patient. Conclusion: Cochlear implantation is the method of choice for rehabilitation of patients with otosclerosis, presenting profound or total hearing loss. Patients obtain excellent benefit with a low rate of complications.

Cochlear implantation in far-advanced otosclerosis may represent a surgical challenge because of a possible partial ossification of the cochlea. Moreover, a high incidence of facial stimulation is reported in this population [1, 2]. In addition, some authors report a satisfactory benefit obtained by a stapes surgery and hearing aid amplification in this population, even in patients with no cochlear reserve [3].

This study presents our management of patients with otosclerosis and severe or profound hearing loss, showing the excellent performances of cochlear implantation in this population and the low incidence of complications.
**Materials and Methods**

Between 1991 and 2003, 134 adult patients had undergone cochlear implantation at our institution. The cause of the hearing loss was otosclerosis in 16 cases (12%), selected for this study. Thirteen patients had been implanted with a Nucleus device (5 Nucleus 22 and 8 Nucleus 24; Cochlear AG, Basel, Switzerland) and 3 patients had been bilaterally implanted with a Med-El® Combi-40 device (Innsbruck, Austria). The data were reviewed regarding preoperative patient history, radiological findings (CT scan and MRI available for all patients), surgical difficulties, complications, and preoperative and postoperative audiological assessments. For comparison of speech perception performances between otosclerosis patients and patients with other causes of hearing loss, a one-way ANOVA was applied.

**Results**

The characteristics of the population are detailed in table 1. In 8 cases, an important rarefaction of the otic capsule bone was observed on CT scan. MRI did not show objective cochlear duct obliteration in any patient. Six patients required a partial drill-out of the basal turn of the cochlea because of a partial ossification. A full electrode insertion into the scala tympani was achieved in all patients.

The incidence of side effects was very low. A reimplantation was required in 1 patient because of a traumatic device failure. Facial nerve stimulation occurred only in this patient, after reimplantation, controlled after deactivation of the 6 offending electrodes. Speech recognition scores in quiet were not modified, but the patient reported alteration of the sound quality and speech intelligibility in noisy environments.

<table>
<thead>
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<th>Table 1. Characteristics of the study population</th>
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<tr>
<td>Male: female ratio</td>
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<tr>
<td>Mean age, years</td>
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<tr>
<td>Mean duration of profound deafness, years</td>
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<tr>
<td>Stapes surgery before implantation</td>
</tr>
<tr>
<td>Unilateral</td>
</tr>
<tr>
<td>Bilateral</td>
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<tr>
<td>Hearing aid at the time of implantation</td>
</tr>
<tr>
<td>Device implanted</td>
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<tr>
<td>Nucleus (unilateral)</td>
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<tr>
<td>Med-El Combi-40 (bilateral)</td>
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<tr>
<td>Stapes surgery during implantation</td>
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<tr>
<td>Blindness</td>
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Postoperative speech perception scores were available for 12 out of 13 patients with unilateral implants. The mean follow-up was 31 months in this group (6–96 months). All patients gained excellent benefit from their cochlear implants. Nine patients were able to use the telephone. Twelve months after surgery, the mean speech perception scores in patients with otosclerosis (disyllable words = 70 ± 21%, sentences = 89 ± 11%, n = 9) were similar to those of patients with other causes (disyllable words = 74 ± 28%, sentences = 86 ± 22%, n = 55). However, the recent challenge was to restore binaural hearing. In patients with nonmeasurable bone conduction levels on both ears and no benefit from hearing aids, we proposed a bilateral implantation. The follow-up was 6 months for 1 patient and 1 year for 2 patients. All 3 patients reported better speech perception with bilateral implants compared to a unilateral implant (fig. 1), especially in noisy environments. In case of measurable bone conduction on one side, a stapedotomy on one side and a cochlear implantation on the other side were performed during the same surgical time in 2 patients. Stapedotomy improved the hearing level in both patients, who obtained serviceable hearing with a hearing aid. Six months after surgery, binaural hearing improved disyllable word and sentence scores, compared to performances with a cochlear implant alone (fig. 2).

**Discussion**

In patients with otosclerosis, osteoneogenesis is usually localized on the proximal part of the scala tympani and detected by CT scan. In most patients, a
complete insertion of the electrode is achieved after a drill-out of the cochlear basal turn. A modification of the surgical management, such as an insertion of the electrode in the scala vestibuli, is rarely required [4].

In our cohort, the incidence of facial nerve stimulation is very low (6%), compared to other studies which report an incidence of 25–78% in patients with otosclerosis [1, 2, 4–6]. It is suggested that otospongiotic changes in the otic capsule reduce the bone impedance, or that massive bone resorption reduces the distance between the facial nerve and the cochlea.

This study confirms the excellent performances of cochlear implantation in patients with otosclerosis, as previously reported by Ruckenstein et al. [4]. Considering these results and the low incidence of surgical difficulties or complications, we propose cochlear implantation as soon as one hearing aid becomes ineffective. When there is no benefit of both hearing aids and no cochlear reserve, bilateral implantation optimizes the performances. In case of residual cochlear function of one nonoperated side, a stapes surgery, performed during the same surgical time as cochlear implantation, improves speech scores and restores binaural hearing.

References


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Cochlear Implantation in Otosclerotic Deafness

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Abstract

The otosclerotic process commonly involves the otic capsule and may cause quite widespread demineralisation which leads to a progressive and often profound bilateral sensorineural hearing loss. In this situation cochlear implantation may be the only effective treatment. This chapter considers the pathology of this hearing loss, the effects of cochlear obliteration on implantation, and the effects of demineralisation of the otic capsule on placement of the electrode and nonauditory stimulation. A study is reported from 4 cochlear implant centres in the UK and the Netherlands of 53 patients with cochlear otosclerosis who received cochlear implantation. The CT features of their petrous bones are presented and a classification of the radiological features suggested. 38\% of patients experienced facial nerve stimulation presumably due to spread of current through an otic capsule with lower than usual electrical impedance. The most common rogue electrodes were in the proximity of the geniculate ganglion. These could usually be successfully programmed out of the MAP.

Otosclerosis is associated with a progressive usually bilateral hearing loss which may have both conductive and sensorineural components. Fixation of the stapes in the oval window causes a conductive loss, which may reach about 60 dB, but is amenable to correction either with a hearing aid or by means of stapes surgery. Demineralization of the otic capsule may involve the inner ear and cause a sensorineural hearing loss that may be severe. This process is referred to as cochlear otosclerosis. Cochlear otosclerosis and stapedial fixation can of course coexist in the same ear. Cochlear implantation offers a means of rehabilitation for many of those individuals with a severe to profound hearing loss.
Cochlear Implantation in Otosclerotic Deafness

Table 1. Aspects of otosclerosis of particular interest

| Pathology of profound deafness in otosclerosis |
| Effects of demineralization of the otic capsule on |
| Placement of the electrode |
| Nonauditory stimulation |
| Role of stapedectomy in the era of cochlear implantation |

loss from otosclerosis. In this paper, we shall consider the aspects of otosclerosis that are of particular interest to the cochlear implant surgeon (table 1), and give some details of a multicenter study that investigated the problems and outcomes in a series of 53 implanted otosclerotic patients.

Loss of cochlear function begins when the otospongiotic process involves the endosteum of the cochlea and the severity of the effects on hearing seems to be related to the extent of endosteal involvement [1]. Typically, there is atrophy and hyalinization of the stria vascularis and of the spiral ligament. Changes in the metabolism of the cochlear fluids occur and some loss of hair cells is observed, although this is relatively modest, certainly in the early stages of cochlear otosclerosis. There is only limited loss of the spiral ganglion cells, which is a good prognosticator for outcome following cochlear implantation. In severe otospongiosis, there may be marked demineralization around the cochlea with cavitation of the petrous bone. The cochlea may at times seem almost to be floating in a cavity within the petrous bone. Pathological bone formation may also at times involve the internal auditory meatus causing compression of the nerves within that canal.

Total bilateral hearing loss rarely occurs in ears that have undergone stapes surgery. The authors have experience of one such patient who had had bilateral stapedectomy some years previously and who suffered a total loss of hearing in both ears when making a rapid descent in an unpressurized aircraft in New Zealand. She was successfully treated with a cochlear implant and became a star performer.

Pathological bone may invade and cause obliteration of the lumen of the cochlea, causing potential problems with implant insertion. Osteoid material is deposited in a mesh of fibrous tissue, and the new bone is clearly seen to be otospongiotic. The process has usually been said to be confined to the basal turn of the cochlea and to the scala tympani. Green et al. [2] stated that the extent of the obliteration of the scala tympani is rarely more than 6 mm from the round window. The experience of implant surgeons suggests that the degree and location of the obstruction of the cochlear lumen are less predictable than these
observations state. New bone is relatively soft and if located in the basal turn alone may be easily removed using the microdrill. However, an apparently good insertion may come to a halt when the surgeon encounters obstruction higher in the cochlea in an area not easily reachable with the microdrill.

The other issue that is of considerable interest to the cochlear implant surgeon and the implant team relates to the effects of demineralization of the otic capsule, to implant insertion and to the occurrence of nonauditory effects after switching on the implant. The authors have personal experience of inserting an implant into a clear scala tympani only to encounter resistance at around 8 mm from the cochleostomy. Minor readjustments and manipulation overcame this resistance and it was assumed that the electrode had passed into the middle turn of the cochlea. Postoperative imaging revealed the true state of affairs. The electrode had passed through the endosteum of the anterior end of the basal turn into a large cavity in the otic capsule. Loss of part of the wall of the cochlea may establish a connection between the cochlear lumen and the internal auditory meatus and allow inadvertent insertion of the implant into the meatus.

Nonauditory stimulation (NAS) has been described by several authors as being more common in implanted otosclerotics than other groups of patients. Unwanted twitching of the facial nerve is the commonest nonauditory phenomenon, but there may be pain in the ear from stimulation of the tympanic plexus or dizziness from stimulation of vestibular structures. As the hearing thresholds (T values) are similar in otosclerotics and nonotosclerotics, it is almost certain that NAS results from current flow through paths of low electrical resistance resulting from the otospongiotic changes in the otic capsule [3]. Interestingly, the other group of implantees who are more likely to suffer from NAS are those with skull base fractures which again provide a line of low electric impedance for current to escape from the cochlea [4]. Most studies have noted an overall incidence of facial nerve stimulation of between 12 and 14.5% [4–7]. On the other hand, Cohen [8] quoted an incidence of 0.9% and Kelsall et al. [9] 3.0%. In otosclerosis, the incidence is quoted as 75% by Muckle et al. [10], 50% by Broomfield et al. [4], 75% by Rayner et al. [11] and 25% by Ruckenstein et al. [12]. These reports, however, deal with very small samples (4, 12, 9, and 8 patients, respectively). Muckle et al. [10] comment on the need to remove electrodes from the MAP in order to reduce NAS and state that in some cases this may reduce the efficacy of the device.

It was suggested that modiolus-hugging electrodes should be less likely to cause NAS because their position close to the spiral ganglion requires a lower current than a peripherally positioned electrode. In addition, an electrode situated at a distance from the outer wall of the cochlea is slightly removed from the facial nerve. Rayner et al. [11] found that NAS was less likely with the Clarion High Focus electrode, which was positioned close to the modiolus, than with
the Nucleus CI 22 device, which had fully banded electrodes and was situated more peripherally in the cochlea. The plastic positioner used with the Clarion device may also have acted as an electrical insulator to some extent.

The final point which must be considered concerns the roles of stapes surgery for advanced otosclerosis now that good results are obtainable with cochlear implantation. Before the implant era, stapes surgery was considered even in cases with scarcely recordable hearing and very poor speech discrimination scores, in the hope that the patient would become able to wear a hearing aid in that ear. There is a school of thought that would support implantation in these patients rather than stapedotomy. Ruckenstein et al. [12] carried out cochlear implantation as the primary procedure in 6 out of 8 patients in whom there was only a vibrotactile response on bone conduction, and achieved excellent results. Others would carry out primary stapes surgery and retain the option of implantation for those whose outcome from stapes surgery was poor [13]. There is inadequate information available at the present time on the outcomes in these groups to allow a valid comparison to be made, but this clearly is an area for future collaborative research.

**Multicenter Study**

The cochlear implant teams in Manchester, Nijmegen, Birmingham and Utrecht combined to conduct a multicenter retrospective study of the radiological changes in the temporal bone and the incidence of NAS [14].

Fifty-three otosclerotic patients received a cochlear implant. Imaging details were therefore available for 106 ears. Three patterns of otosclerotic involvement of the temporal bone were recognized (table 2). The result of the CT scans of the 53 patients (106 ears) are shown in table 3.

The fact that 16% of patients had no radiological evidence of demineralization should come as no surprise. Small degrees of changes in bone density confined to the fenestral area are likely to be too small for detection on CT scanning. In these cases, the diagnosis of otosclerosis was certain on the basis of history including previous stapes surgery. Fenestral otosclerosis may be combined with other more extensive changes in the otic capsule. In very extensive otosclerosis (type 3), assessment of fenestral involvement is very difficult. Figure 1 demonstrates examples of type 2a and type 3 changes.

Fifty-seven cochlear implant operations were carried out on the 53 patients. Four had revision surgery. In all but 1 case, multichannel devices were inserted of which the majority (n = 46) were Nucleus devices and the other 6 Clarion. A narrow or obstructed basal turn was suggested on CT in 27 cases (51%), but at surgery narrowing of the basal turn was found in 17 (37%). A full scala
tympani insertion was possible in 42 cases and a scala vestibuli insertion was performed in 1 case because of obliteration of the scala tympani. In 10 cases (19%), insertion was difficult with a partial insertion in 7 ears (4–19 electrodes) and misplacement of the electrodes in 3 cases. CT evidence of cochlear pathology was more prevalent in the group with partial or difficult insertions, but the association did not reach statistical significance.

NAS (facial nerve) occurred in 20 of the 53 ears (38%). It was most likely to be caused by electrodes close to the geniculate ganglion (fig. 1) and in nearly every case it was possible to program out the rogue electrodes, either by completely removing them from the MAP or by reducing the current to the responsible electrodes. NAS was less common in ears with a type 1 CT scan, and more common in those with a type 3 CT scan, but the relationships did not reach statistical significance. The majority of electrode arrays used in this study were not modiolus huggers.

The audiological outcomes were assessed by assigning the patients into one of three groups depending on their performance with BKB sentences at 9 months after implantation. The results are shown in table 4. Poor performers tended to have a type 3 CT scan, but this trend did not reach significance.

---

**Table 2.** Patterns of otosclerotic involvement of the temporal bone

<table>
<thead>
<tr>
<th>Type 1</th>
<th>Anterofenestral with involvement confined to the region of the fissula ante fenestram and with fixation of the stapes footplate</th>
</tr>
</thead>
</table>
| Type 2 | (a) Double ring with no encroachment on cochlear lumen  
(b) Narrowing of cochlear lumen  
(c) Double ring with narrowing of cochlear lumen |
| Type 3 | Severe retrofenestral demineralization with loss of architecture |

**Table 3.** Results of the CT scans

<table>
<thead>
<tr>
<th>Type</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CT evidence of otosclerosis</td>
<td>17 (16)</td>
</tr>
<tr>
<td>Type 1 Solely fenestral</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Type 2 Double ring</td>
<td>55 (52)</td>
</tr>
<tr>
<td>Type 2 Narrow basal turn</td>
<td>26 (25)</td>
</tr>
<tr>
<td>Type 2 Combined</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Type 3 Severe retrofenestral</td>
<td>25 (23)</td>
</tr>
</tbody>
</table>

Figures in parentheses indicate percentages.
Moreover, poor performers tended to be associated with partial insertion, but this trend did not reach statistical significance either. However, group 1 performers did have a lower percentage of NAS and fewer programmed out electrodes.

**Conclusions**

Different degrees of severity of demineralization of the petrous bone may be seen on CT in otosclerosis ranging from localized demineralization in the region of the oval window to widespread affliction of the petrous bone. Cochlear obliteration and demineralization may present problems for the surgeon. Difficulties in electrode insertion tend to be associated with the degree of CT

---

**Table 4.** Audiological outcomes

<table>
<thead>
<tr>
<th>Use of BKB sentences</th>
<th>Proportion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>&gt;75% BKB sentences</td>
</tr>
<tr>
<td>Group 2</td>
<td>25–50% BKB sentences</td>
</tr>
<tr>
<td>Group 3</td>
<td>&lt;25% BKB sentences</td>
</tr>
</tbody>
</table>

Moreover, poor performers tended to be associated with partial insertion, but this trend did not reach statistical significance either. However, group 1 performers did have a lower percentage of NAS and fewer programmed out electrodes.
change, but this tendency does not reach significance. NAS also tends to be associated with the degree of demineralization seen on CT. Performance with the implant also tends to be associated with the extent of CT change, without reaching significance. NAS is most commonly caused by electrodes in the vicinity of the geniculate ganglion, and can usually be managed by changing the MAP.

References


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A Prospective Multicentre Otology Database

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Abstract

Why Is an International Otology Database Important? There are many reports on the outcome of otological interventions in the literature. However, it is difficult to make direct comparisons between these reports because of the lack of uniformity in reporting outcomes and patient selection. The aim is to create an interactive otology database for surgeons in the UK and Europe. Methodology: The proposed project is the creation of a common database on a website. Two levels of data entry are available: (1) level I: minimum database (only main outcomes are included; for any otolaryngologist in Europe who wishes to join), and (2) level II: comprehensive database (detailed information on pathologies, risk factors and surgical procedure are also recorded; for invited otologists). As both databases share the same core data, clinicians using database I can still compare their outcome with those using database II. There has already been an international consensus on the content of the common otology database. A previous pilot study by 3 different hospitals also confirmed the user-friendliness of data input and retrieval using the web-based system. The system is now ready for international implementation. Who Might Benefit from the Database and How? The size of the database allows statistical analysis to be made on various otological interventions with sufficient power. The web-based system can be a useful learning tool for surgeons because it gives instant feedback to the individual surgeon. It also provides the opportunity for hospitals to collaborate in clinical trials using this common data entry system.

Background behind the Proposal of an International Otology Database

To date, most postoperative evaluations of middle ear surgery have been limited to a personal view of the problem and a personal experience. The lack of standardisation in the reporting of surgical outcome makes it difficult to draw any conclusion from the existing literature. A Medline search of the existing
literature failed to identify a single systematic review or meta-analysis on tympanoplasty. Jean Marquet [1], one of the eminent otologists in the 20th century, called on the international otology community to set up an international, standardised method of data recording, processing and reporting. Sadly, this never materialized. Until it happens, it is difficult to translate basic scientific research into evidence-based clinical benefits. Surgeons will continue to make clinical decisions based on expert opinions rather than based on evidence.

The proposed international audit system and database is the first real attempt by the international otological community to standardise the reporting of ear surgery and to create an international database. The aims of the project are:

1. to identify common audit data amongst clinicians;
2. to provide an IT system to store otology data for clinicians;
3. to create a large database which allows statistical analysis to be made on various otological interventions with sufficient power;
4. to produce standards or a benchmark for the audit or outcome of ear surgery (the web-based system can be a useful learning tool for surgeons because it gives instant feedback to the individual surgeon, which enables clinicians to monitor their own surgical practice against these standards; governing bodies for surgical trainees can even use it as a tool to implement competency-based training for surgical trainees);
5. to provide a mechanism for hospitals to collaborate in clinical trials using the common data entry methodology.

The ultimate goal of the proposed project is to provide primary potential research data that are lacking at the moment.

Methodology

The proposed project is to produce a web-based international common otology database. The methodology aims to provide the following features:

1. there should be international consensus on the content of the proposed database;
2. the identity of surgeon and patient must remain anonymous;
3. the system must be user-friendly, both in data input and retrieval;
4. data used as a benchmark or ‘standards’ are validated;
5. the use of the database should not be exclusive to a few selected otologists;
6. it allows individual surgeons to compare surgical outcome with others and to interrogate the database for information;
7. the system can also be used as a research tool to collate specific data used for collaborative clinical research amongst hospitals.

International Consensus

A working party of international otologists from 11 countries has already agreed on the content of a common ear database. The panel lists included:
UK – M. Yung, I. Swan;
Belgium – P. van den Heyning, E. Offecier, M. Gersdorff;
Switzerland – R. Haussler, T. Linder;
France – P. Tran-ba-Huy, C. Martin, J. Magnan, B. Fraysee;
Germany – H. Hildman;
Croatia – M. Gjuric;
Holland – R. Tange;
Sweden – D. Bagger-Sjoback, L. Eldfelt;
Poland – J. Skladzien;
Slovak Republic – M. Profant;
Denmark – S.-E. Stangerup.

The Website
The website www.ear-audit.net is already up and running, with the ear surgery database stored in SQL server. Users are asked to input data prospectively onto the website.

Data Entry
Two levels of data entry are available.

(1) Level I (a minimum database): this is designed for any otolaryngologists in Europe. Only main surgical outcomes are recorded.

(2) Level II (a comprehensive database): this is designed for selected otologists. Detailed information on pathologies, risk factors and surgical procedure are recorded.

As both databases share the same core data, clinicians using database I can still compare their main surgical outcome with those using database II.

The methodology requires surgeons to put in pre-operative data on all patients scheduled for ear surgery, thus eliminating bias from selective reporting of operations. Separate data entry forms will be available on the website for pre-operative, operative and postoperative data entry. Every field on the data form needs to be completed before the form is accepted, thus ensuring completeness of data entry. Separate postoperative forms are available for each postoperative entry.

The content of database II includes:

(1) all known risk factors in ear surgery;
(2) aims of surgery and whether they have been achieved;
(3) bone and air conduction levels of the operated ear and non-operated ear;
(4) surgical findings, including status of the eardrum, ossicles, facial nerve, middle ear mucosa;
(5) types of otological intervention, including surgical techniques, prostheses, grafting materials, anaesthetic techniques, and types of instrumentations (fig. 1);
(6) complications from the ear operation;
(7) main outcome parameters, such as activity of the disease and status of the reconstructed eardrum or ossicles;
(8) follow-up intervals.

Security
Each surgeon is allocated an access code and a password. They can change their own password once they log in. The identity of the patients and the surgeons is anonymous. Each hospital would be given a hospital code number and each surgeon a surgeon code number.
Each patient is identified on the database with an encrypted patient code number created by the individual surgeon.

**Membership**

The level I system (the minimal ear database) is available to any surgeons who perform middle ear operation in the UK and Europe. However, only surgeons who are willing to participate in data validation are allowed to join the level II system (the comprehensive ear database).

**Feedback to Individual Surgeon**

The cumulative data from the level II database will be used as the benchmark in the audit system because the results are validated.

Each surgeon can download his surgical results from the website into an Excel file in almost real time. He will not know the results of other surgeons. However, a table comparing his own surgical results against the cumulative results in the level II database will be made available to each individual surgeon on the website in almost real time.

The web-based system is interactive because it allows each surgeon to make an enquiry to the webmaster. The identity of each individual hospital or surgeon will remain confidential unless the surgeon wishes to participate in joint audits or collaborate in research projects.

**Data Quality Assurance and Validation**

Bias reporting or incorrect data entry will contaminate the quality of the cumulative database. Therefore, validation of data in database II is important. This can be done by site visit of each hospital by an external inspector/auditor (another user of the web-based system) to perform random inspection of patient records. The benefit of using peers to validate data from each centre gives a further opportunity for clinicians to learn from each other. Only surgeons who wish to contribute to the level II database would be required to have the ear data validated.

**User-Friendliness of the System**

Three surgeons from the working group had previously participated in a pilot study using the web-based system. Data entry and retrieval were found to be efficient and user-friendly.

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**Fig. 1.** An example of the data fields for stapes surgery in the level II database.

| OPERATION: Central fenestra/Partial stapedectomy/Stapedectomy |
| CHORDA TYMPANI: Displaced/Not Displaced/Lacerated/Cut/N/A |
| FENESTRATION METHOD: Pick/Drill/Laser (Argon/KTP/CO₂/Er Yag/Diode)/N/A |
| FENESTRATION SIZE: 0.3/0.4/0.5/0.6/0.7/0.8/not checked/1000 (=Unknown) |
| PROSTHESIS TYPE: Teflon/Teflon Wire/Titanium/Clip/N/A |
| PROSTHESIS SIZE: 0.3/0.4/0.5/0.6/0.8/1000 (=Unknown) |
| ATTACHMENT: Incus/Malleus/N/A |
| INTERPOSITION TISSUE: Nil/Vein/Fascia/Perichondrium |
| OVAL WINDOW SEAL: Nil/fat/other connective tissue/blood clot |

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Ownership of the Data

Only validated data in the level II database will be used for research studies. The collective data will remain the ownership of all the members who contributed to the level II database.

Possible Clinical or Commercial Exploitation

The network of otologists within Europe could provide a powerful vehicle for academic departments or commercial companies to run clinical trials. Because of the potential number of centres that can collaborate in a clinical trial, the result could be available within a shorter time frame. It is estimated that 2,000 new cases will be entered into the database each year from the UK and Europe.

Reference


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Stapes Surgery – Outcome Evaluation

Preliminary Results

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ENT Department, University Hospital of Tromsø, Tromsø, Norway

Abstract

23 patients were studied preoperatively, 17 at 2 months and 11 at 6 months. Using cutoff at 30 dB HL (air-conduction), 2-month success rate was 5 of 17 patients (PTA: 0.5-1-2-4 kHz), 7 of 17 (PTA: 0.5-1-2-3 kHz), 9 of 17 (PTA: 0.5-1-2 kHz) and 15 of 17 (SRT: Speech recognition threshold). At 6 months, success rate was 6 of 11 patients (PTA: 0.5-1-2 kHz), 7 of 11 (PTA: 0.5-1-2-3 kHz), 8 of 11 (PTA: 0.5-1-2 kHz) and 10 of 11 (SRT). When evaluating 6-month outcome by air-conduction measures, the highest success rates (91%) after stapes surgery were seen using SRT, and lowest (55%) using the 4-frequency average PTA: 0.5-1-2-4 kHz.

There are different ways of assessing outcome after stapes surgery. The outcome in a given clinical population can vary according to the method that is chosen for outcome assessment. Traditionally, postoperative closure of the air-bone gap (ABG) at the frequencies 0.5, 1 and 2 kHz has been used for reporting postoperative results [pure-tone average (PTA) at 0.5, 1, 2 kHz].

We evaluated all but 2 patients who had undergone stapedotomy in our Department from October 2002 until December 2003. The patients were tested preoperatively, and 2 and 6 months postoperatively. We did the following tests: pure-tone audiometry for air and bone conduction, two-syllabic speech audiometry for air and bone conduction and transient evoked otoacoustic emissions.

Audiometric tests were done using a Madsen audiometer (Orbiter 92 vs. 2 with Sennheiser HDA 200 circumaural earphones), with a frontally located Radioear B-71 bone conductor. The audiometer was calibrated according to current ISO standards.

So far, we have examined 24 patients preoperatively, 23 at 2 months and 16 at 6 months postoperatively. The results in table 1 apply to air conduction audiometry.
After 2 months, we had the following results: PTA (0.5, 1, 2 kHz) of 30 dB HL or better in 12 of 23 patients; PTA (0.5, 1, 2, 3 kHz) of 30 dB HL or better in 10 of 23 patients; PTA (0.5, 1, 2, 4 kHz) of 30 dB HL or better in 8 of 23 patients; speech recognition threshold (SRT) of 30 dB HL or better in 19 of 23 patients; ABG (0.5, 1, 2, 3 kHz) of 10 dB HL or better in 14 of 23 patients, and ABG (0.5, 1, 2, 3 kHz) of 20 dB HL or better in 22 of 23 patients.

After 6 months, the results were as follows: PTA (0.5, 1, 2 kHz) of 30 dB HL or better in 12 of 16 patients; PTA (0.5, 1, 2, 3 kHz) of 30 dB HL or better in 9 of 16 patients; PTA (0.5, 1, 2, 4 kHz) of 30 dB HL or better in 9 of 16 patients; SRT of 30 dB HL or better in 19 of 23 patients; ABG (0.5, 1, 2, 3 kHz) of 10 dB HL or better in 14 of 23 patients, and ABG (0.5, 1, 2, 3 kHz) of 20 dB HL or better in 22 of 23 patients.

At 6 months, we asked the patients if they were satisfied with the outcome of the operation: 14 out of 16 were satisfied and 2 did not respond.

We compared our results with a study of stapes surgery outcome conducted by Mair [1] in Tromso in 1989. The results are presented in table 2. We believe the results are comparable, although the preoperative/postoperative differences

### Table 1. Mean air conduction thresholds preoperatively and postoperatively after 2 and 6 months (dB HL)

<table>
<thead>
<tr>
<th></th>
<th>Preoperatively</th>
<th>After 2 months</th>
<th>After 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRT</td>
<td>24</td>
<td>23</td>
<td>16</td>
</tr>
<tr>
<td>PTA (0.5, 1, 2 kHz)</td>
<td>38.5</td>
<td>20.6</td>
<td>17.3</td>
</tr>
<tr>
<td>PTA (0.5, 1, 2, 3 kHz)</td>
<td>50.6</td>
<td>29.7</td>
<td>28.3</td>
</tr>
<tr>
<td>PTA (0.5, 1, 2, 4 kHz)</td>
<td>50.4</td>
<td>31.4</td>
<td>30.2</td>
</tr>
<tr>
<td>PTA (0.5, 1, 2 kHz)</td>
<td>50.0</td>
<td>32.7</td>
<td>30.9</td>
</tr>
</tbody>
</table>

### Table 2. Mean differences between pre- and postoperative air conduction thresholds (dB HL)

<table>
<thead>
<tr>
<th></th>
<th>Mair [1]</th>
<th>Our study</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 kHz</td>
<td>30.8 (18.7)</td>
<td>29.3 (13.6)</td>
</tr>
<tr>
<td>0.5 kHz</td>
<td>32.1 (16.3)</td>
<td>29.0 (14.4)</td>
</tr>
<tr>
<td>1 kHz</td>
<td>28.7 (17.4)</td>
<td>26.7 (17.2)</td>
</tr>
<tr>
<td>2 kHz</td>
<td>22.7 (18.0)</td>
<td>19.0 (12.3)</td>
</tr>
<tr>
<td>4 kHz</td>
<td>14.7 (20.7)</td>
<td>12.7 (19.4)</td>
</tr>
<tr>
<td>8 kHz</td>
<td>0.3 (23.7)</td>
<td>0.0 (16.6)</td>
</tr>
</tbody>
</table>

Standard deviations are in parentheses.
were larger in Mair’s study. The standard deviations were also larger in his study, reflecting greater heterogeneity of the results. Furthermore, his number of patients was higher than ours, the follow-up time longer and the technique was different (i.e. stapedectomy was performed) in a sizeable proportion of subjects.

When outcome is evaluated using air conduction audiometric thresholds, the highest success rates after stapes surgery were seen using SRT. (An even higher success rate was found for an ABG of 20 dB HL or less, although we do not consider this outcome to be a valid criterion for successful stapes surgery.) An ABG at the frequencies 0.5, 1, 2, 4 kHz of ≥10 dB HL yields the poorest results. The most appropriate parameter for reporting outcome after stapes surgery remains a subject of discussion [2]. Although the choice of outcome criteria should reflect the patients’ functional hearing, simply asking the patients about their postoperative hearing may be of limited value.

References


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How Does Stapes Surgery Influence Severe Disabling Tinnitus in Otosclerosis Patients?

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Abstract
Tinnitus is a common symptom in otosclerosis patients. Many papers have been written about tinnitus outcome after stapes surgery. However, none has attempted to quantify the intensity of the symptom pre- and postoperatively in order to evaluate the influence of surgery on the degree of annoyance caused by tinnitus. Severe disabling tinnitus (SDT) is defined by Shulman as a symptom severe enough to disrupt the patient’s routine and to prevent him from performing his daily tasks. We have studied 48 consecutive otosclerosis patients by means of a visual analogue scale measuring tinnitus intensity before and after stapes surgery. We have accepted tinnitus as severe and disabling when the symptom score was 7 or above in a visual analogue scale from 1 to 10. Of 19 patients with preoperative SDT, 10 reported complete remission and 7 reported significant improvement. Two patients had no change and none reported worsening of tinnitus after stapes surgery. We conclude that stapes surgery can improve SDT significantly in 90% of otosclerosis patients and is very unlikely to make the symptom worse.

Many papers have been written about tinnitus outcome after stapes surgery in otosclerosis patients [1–8]. These articles have measured tinnitus pitch pre- and postoperatively, but none have measured tinnitus intensity before and after stapes surgery.

In 1953, Heller and Bergman [9] showed that over 90% of normal-hearing people reported tinnitus when placed in a soundproof cabin. However, the symptom did not cause any discomfort to those patients in daily life. Being so, it becomes necessary to separate common garden variety tinnitus from serious, disrupting ones.
Shulman [10] coined the term severe disabling tinnitus (SDT) for a symptom that is severe enough to disrupt the patient’s routine and to keep him from performing his daily tasks. Usually, this kind of patient seeks medical attention because of his tinnitus, while in less severe cases the symptom is mentioned during medical consultation for other problems.

Tinnitus is certainly very common among otosclerosis patients; some of them report very intense annoyance from the symptom and ask what will happen to the symptom after stapes surgery.

We tried to quantify the intensity of tinnitus in otosclerosis patients pre- and postoperatively by means of a visual analogue scale (VAS) going from 1 (very low intensity) to 10 (unbearable intensity). We considered SDT as having an intensity of 7–10 on the VAS. By comparing the tinnitus score before and after stapes surgery for otosclerosis, we tried to determine the influence of the surgical procedure on SDT. The results of this study are reported below.

**Materials and Methods**

This is a prospective study. We applied a VAS, in which 1 meant a very low intensity and 10 an unbearable intensity for the symptom of tinnitus, to 48 consecutive otosclerosis patients before and after stapes surgery. We considered SDT as yielding a score of 7 or above on the VAS.

In all patients, pure-tone audiometry and a word discrimination test were performed pre- and postoperatively.

Forty-four patients underwent stapedotomy and 4 stapedectomy. Hearing results were evaluated by comparing the pre- and postoperative four-tone average air-bone gaps. The influence of surgery on SDT was measured by comparing pre- and postoperative scores for the symptom on the VAS. The operative notes were carefully reviewed for any problem occurring during surgery.

The VAS was applied 4–10 months after surgery. We considered significant a score improvement of ≥ 2 points on the VAS. Twenty-five patients were contacted 14–48 months after surgery and were asked about the tinnitus status at this late follow-up time.

The protocol was approved by the ethics committee on research involving human subjects of our institution.

**Results**

There were 29 female and 19 male patients. Forty-four of the 48 patients reported tinnitus preoperatively (91.6%). Mean age was 44.5 years (range 16–62).

SDT was present in 19 patients preoperatively (39.6%) and female patients tended to report more SDT than male counterparts (55.5% of female and 15.8% of male patients).
Overall 40 (90.9%) tinnitus patients reported postoperative improvement and 4 (9.09%) noted no change in tinnitus. None said the symptom was worse.

Table 1 shows postoperative tinnitus outcome of the 19 SDT patients. Ten of the 19 tinnitus patients reported total remission of tinnitus after surgery and 6 had a significant improvement (at least 2 points on the VAS). One reported a slight improvement and 2 noted no change in the symptom.

The intensity of preoperative tinnitus was not related to the preoperative air-bone gap (mean air-bone gap of 34.3 dB for SDT and 31.4 dB for less intense tinnitus). However, larger preoperative air-bone gaps seemed to predict better postoperative improvement in SDT (table 2) when a good hearing result was achieved. Smaller postoperative air-bone gaps correlated with more remission and improvement of SDT postoperatively (table 3).
There was a trend for lower preoperative bone conduction levels to correlate with preoperative SDT (44.1% of patients with a four-tone average bone conduction level below 40 dB had preoperative SDT while 28.5% of patients with a preoperative four-tone average bone conduction level above 40 dB had SDT).

Twenty-five patients (7 SDT) contacted 14–48 months after surgery said their tinnitus status had not changed since surgery.

There were no untoward events during surgery and no postoperative complications other than 6 patients with an air-bone gap above 20 dB were seen.

**Comments**

In 1999, Oliveira et al. [11] applied a tinnitus questionnaire that included a VAS to all new patients seen at the Otology Clinic of the Brasília University Hospital for a 6-month period of time. Five hundred tinnitus patients were identified. These patients had presbycusis, chronic otitis media, otosclerosis, acoustic trauma, Ménière’s disease, ototoxicity and vestibular schwannoma in this order of frequency. However, 81% of the tinnitus patients had a very mild symptom and only mentioned tinnitus because they were asked about it. Eighteen percent had a mild symptom they could tolerate well or were easily relieved with routine medical treatment. Only 1% had tinnitus that was very intense (above 7 on the VAS), disrupting the patients’ routine, and they were refractory to medical treatment (central vasodilators, vestibular suppressants, calcium channel blockers, anticholinergics, anticonvulsants). To sum up, tinnitus is a very common symptom among patients of an otology clinic but only 1% of these patients have SDT.

Otosclerosis was the 3rd most frequent diagnosis listed above and we have found an incidence of tinnitus (91.6%) in our 48 otosclerosis patients similar to the one in the general population [9]. However, 39.6% of our otosclerosis patients had SDT as compared to 1% in the patients of our otology clinic. Therefore, otosclerosis seems to be strongly associated with SDT.

Otosclerosis patients who have SDT are the ones who always ask the doctor what will happen to their tinnitus after stapes surgery and often mention tinnitus relief as their priority. Because all papers published up to now [1–8] had not targeted SDT, we undertook the present study.

Our results allow the following statements:

(1) Otosclerosis is a major cause for SDT. How the otosclerosis process leads to severe tinnitus remains to be clarified.

(2) Stapes surgery (namely stapedotomy, because 44 of our 48 patients had this operation performed) can totally relieve SDT in roughly 50% of cases.
and significantly improve another 31%. About 10.4% of SDT patients will not have any relief after stapes surgery. These patients probably have already developed a paradoxical memory in the medial temporal lobe system as proposed by Shulman et al. [10] and will not respond to any treatment of the peripheral organ.

3. Because larger air-bone gaps preoperatively predict better tinnitus improvement when the stapes surgery results in smaller postoperative air-bone gaps (tables 2 and 3), we suggest that the masking effect produced by better postoperative hearing is probably responsible for the tinnitus improvement.

4. Since 25 tinnitus patients (7 SDT) contacted up to 48 months after surgery said their tinnitus status had not changed compared to the early follow-up situation, it is safe to say that the influence of stapes surgery on SDT in otosclerosis patients is long-lasting.

5. Worsening of SDT after stapes surgery is unlikely provided an atraumatic procedure was performed.

References


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Patients’ Lives following Stapedectomy Complications

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Abstract
Nowadays, it is widely accepted that patients must be informed about the risks associated with any type of surgical procedure. Usually, the information provided consists of quoting a list of risks and their probability of occurrence based on data from the literature, and, more appropriately, the figures reflecting the surgeon’s personal experience. As a rule, such data are sufficient to hold up in court in the event of a lawsuit, but may be insufficient to help patients make the most appropriate choice. We report two cases that presented complications following stapedotomy. Both cases had a sensorineural hearing loss and a vestibular deficit. This paper aims at describing the important psychological and social consequences of these complications. The potential impact of such complications on the quality of life and the projects for the future of these young patients was predictable. In order to better assist patients in choosing amongst options, we have taken action and modified our approach in advising our patients eligible for stapedotomy procedures.

The efficiency of the surgical techniques used for the correction of the conductive hearing loss caused by otosclerosis, the so-called stapedectomy [1] or stapedotomy [2], has been extensively reported in the literature: the benefits of the procedure can be quantified in terms of hearing gain [3, 4] as well as improvement in quality of life [5]. Complications are rare, consisting of a sensorineural hearing loss, vertigo or imbalance, dysgeusia, facial nerve paralysis, or meningitis. Sensorineural hearing loss may be immediate or delayed. The rate varies among series between 0 and 7% (mean: 0.9%) [3]. Whilst transitory postoperative vertigo is often reported as a complication, persistent imbalance
resulting from a total vestibular loss is not even mentioned in some papers and occurs in up to 7% in others [6]. The cause of these deficits is unknown and therefore such complications may occur in any center! The other complications are much rarer, and generally result from surgical technique defaults.

In general, the preoperative counseling of the patient consists of quoting a list of benefits as well as risks and their probability of occurrence. The information is based on data from the literature or more appropriately, on figures reflecting the surgeon’s own experience. As a rule, such data are sufficient to hold up in court in the event of a lawsuit, but may be insufficient to help patients make the most appropriate choice.

The purpose of this paper was to describe the psychological and social consequences of a total loss of auditory and vestibular function following stapes surgery in 2 patients, and to critically review the way to better assist patients eligible for stapedotomy procedures in choosing amongst options.

**Case Report**

**Case 1**

A 48-year-old male was referred to our department with a progressive left hearing loss. He was a native of Portugal and had been living in Geneva for 10 years, working in a large company as a bricklayer. Otoscopy was normal. The Weber test was lateralized to the left, the Rinne negative on the left. The pure-tone audiogram showed a 40-dB left conductive hearing loss, and the stapedial reflex was absent except to the right in response to an ipsilateral stimulation. On March 6, 1998, the patient underwent a stapedotomy. The procedure was standard, as described by Schuknecht [7]. It was performed as an outpatient procedure, under local anesthesia and using a transcanal approach through the ear speculum. A posterior tympanomeatal flap was elevated, the stapedius tendon cut, and the crural arch fractured and removed. A 0.8-mm perforation of the footplate was carried out with a motor-driven sharp-cutting bur, and a 0.6-mm Teflon wire piston inserted. The oval window was sealed with a piece of perilobar fat tissue. The tympanomeatal flap was replaced and the external ear packed with silk strips and cotton soaked in neomycin, polymyxin and hydrocortisone (Corticosporin®). The procedure was uneventful.

Three days after surgery, the patient experienced a violent vertigo of sudden onset. Clinical examination revealed a spontaneous right-beating nystagmus. The packing was removed. There was complete hearing loss. The surgical exploration showed no displacement of the prosthesis, and no abnormal middle ear tissue. Four weeks after revision surgery, the patient mentioned he was having nightmares and could not sleep well. He was obviously suffering from an acute depressive episode. He was referred to a psychiatrist who diagnosed the resurgence of a past psychological disorder in reaction to the horrors the patient had witnessed as a soldier during the war in Angola, back in the seventies. Vertigo gradually subsided over months. Unfortunately, there was no hearing recovery. A 2-year psychological treatment was necessary to improve the mood of the patient.
Case 2

A 37-year-old male was seen 6 months after a stapedotomy complicated by a cochleovestibular deficit. He was suffering from a progressive bilateral hearing loss. He was an electronic engineer, working as technical vice director of a small company. He was planning to create his own company in the near future, and wanted the operation in order to facilitate communication with his future employees. On October 1, 2001, he underwent a left stapedotomy, by a renowned otologist. Surgery was performed as an outpatient procedure, under local anesthesia and through the external auditory canal. According to the patient and the documents we had access to, the procedure was uneventful.

Four days after surgery, the patient experienced an intense rotatory vertigo with nausea and vomiting. He refused surgical exploration of the ear and was given oral corticosteroids for 5 days. The vertigo gradually subsided in 4–5 days but the patient noticed a total loss of hearing and a persisting imbalance. He was able to return to work only 6 months after surgery.

At the last visit, 3 years after surgery, there is no hearing recovery, and a slight imbalance persists. The patient wears a hearing aid on the contralateral ear. He complains of intense fatigue and considers himself inefficient at work. He was downgraded from vice director to employee, with obvious financial consequences. His project to start his own company is definitely cancelled. In his own words, his life has been radically changed by the surgery. He states the obvious negative impacts, but also positive aspects such as a reduction of his ambient stress that resulted from the decrease in his ambitions.

Discussion

These cases illustrate that patients’ lives may require radical modifications due to stapedectomy complications. The first case demonstrates how vertigo is a frightening experience. Vertigo weakens patients physically and mentally, allowing the reactivation of sometimes already successfully treated past psychological disorders. This has been shown in many other instances, in particular in large series of patients suffering from Ménière’s disease [8, 9]. The second case illustrates that the complications of stapedectomy have sometimes major professional and financial consequences. Although in the long run patients cope with the new physical condition, it is at the price of a tremendous effort in professional, family, mental, and emotional adaptation, the result of surgery being the opposite of the expectation, a hearing loss rather than gain and persisting imbalance!

In 1998, a debate on the ethics of stapedectomy was published [10–16]. As wearing a hearing aid would give functional results comparable to those achieved by surgery, when should surgery be performed? Due to the risks of serious complications, all the authors considered stapedectomy ethical after the patient has given a fully informed consent, one adding that patients should undergo surgery only after a trial of hearing aid use [10]. However, the risk of persisting imbalance was not even mentioned in this debate, which raises the
question on the definition of an informed consent! Knowing every possible outcome, would our patients have chosen surgery over a hearing aid?

Eriksson-Mangold et al. [17] have shown that patients confronted with the significant impact of stapes surgery on their life report conflicting feelings of both added responsibility and anxiety, resulting in emotional turmoil. Their choice between a hearing aid versus surgery is thus based on rational, but also many irrational considerations. Indeed, patients may choose an operation to make others aware that the situation is serious and to gain sympathy, which ‘may promote adaptation to the handicap’, or to the contrary, ‘impede adaptation to the necessary hearing aids’ [17]. The opinions of the people in contact with the patient are important, as hearing deficit is the single greatest handicap in communicating with others [Degive, C., pers. commun.]. In the population, deafness is associated with mental deficiency, and hearing aids with aging and/or poor communication. Obviously, wearing a hearing aid makes the handicap visible. In spite of this, we think that it is also the responsibility of surgeons to promote nonsurgical solutions to a problem. In addition, from an ethical point of view, to dispel preconceptions about hearing aids is also the role of doctors. As a consequence, today, our patients are clearly informed of all the benefits and risks of the operation, and informed that a hearing aid would provide satisfactory results. Finally, a period is given for them to fully assimilate the information, which appears essential before a proper decision can be made.

Many doctors consider that information regarding the benefits and risks of an operation is given to the patients in order to hold up in court in the event of a lawsuit [11]. Such a conception weakens the patient-doctor relationship as the physician’s role is reduced to merely implementing a treatment with a looming threat of punishment in case of problems, whereas the lawyer’s role is elevated, as he establishes the rules and controls their application. Conversely, if the information is dispensed with the intention of helping the patient choose the best course of action, the patient-doctor relationship is strengthened as the responsibility is evenly shared between both actors. The trust thus forged would certainly diminish the number of lawsuits [18], which have a negative impact on not only the surgeon, but also the patient who, due to the length of the proceedings, takes a longer time to accept the functional loss, and often goes as far as presenting a major depressive event.

As a renowned myopic surgeon, would you accept an operation to cure your myopia which presents as little as a one-percent chance of total visual loss, or wear glasses? And what information would you need to make your choice? These are the kinds of questions we have in mind when giving information to a patient suffering from otosclerosis with a conductive hearing loss, being a candidate for a stapedotomy.
Acknowledgments

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References

Abstract

This paper is a review of concepts and methods presented as a tribute to a great pioneer and teacher, Harold Frederic Schuknecht. His book entitled *Stapedectomy*, published in 1971, is based on past experience of ‘6,200 stapedectomy operations over a period of 13 years’ and on experience gained from teaching the procedure to numerous residents and fellows. His concepts are still valid and represent a solid base for teachers and students of this elegant but precarious procedure.

I am grateful to Harold Frederic Schuknecht who personally taught me stapes surgery in 1967.

His textbook entitled *Stapedectomy*, published in 1971 [1], encompasses all aspects of how to teach this procedure. This book is based on past experience of ‘6,200 stapedectomy operations over a period of 13 years’, and on ‘experience gained from teaching the procedure to 60 residents and fellows’.

For Schuknecht, responsible teaching begins with long-term assessment of the teacher’s own experiences and presentation of concepts.

‘Time has shown that stapedectomy, when performed on carefully selected patients, by a skilled surgeon, can be expected to provide prolonged improvement of hearing; however, with this procedure, as with all surgical procedures, there are undesirable results. It is quite clear to me, that the incidence of complications is closely related to the surgeon’s technical adaptness and experience as well as to his understanding of the pathology and clinical manifestations of otosclerosis.’ I would be very disappointed if this book were to be used as a cookbook by the uninitiated surgeon pursuing his vested right to operate, because he is licensed to do so.

The book is illustrated with numerous drawings that are as helpful for the student as for the teacher. A selection of some of these drawings are shown to
exemplify the methods and aesthetics praised by Harold F. Schuknecht (figs. 1–9). After training with Harold Schuknecht, I have also personally performed and taught stapes surgery over a period of 30 years. It gave me the opportunity
Fig. 3. Manipulation of microsurgical instruments for transcanal access to the middle ear.

to witness the short- and very long-term results of this procedure performed not only by myself, but also by my students and others.

I came to the conclusion that stapes surgery is one of the most precarious operations you can do in the ear.

Of all ear surgeries, some look extremely impressive, such as removal of deep-seated cholesteatomas or tumors in the temporal bone, but of all of them, stapedectomy is the most worrisome. It is elective, as otosclerosis is not a life-threatening disease. The aim of the operation is to improve hearing. There is a reasonable alternative: hearing aids. Although immediate and long-term results are generally very satisfactory, complications do exist and can make the life of the patients less enjoyable than before. Most of these complications can be corrected but may require additional surgery. The most common are vertigo, recurring conductive hearing loss, severe sensorineural hearing loss, tinnitus, loss of taste, dry mouth and facial palsy.

Surgical techniques are well standardized and the operations can look easy and elegant, particularly when shown on videotapes in meetings.

In reality, the anatomy of the ear is inconsistent and varies to such an extent that stapes operations cannot really be standardized. It requires a perfect
knowledge of all possible variations and a plastic three-dimensional mind image on the part of the surgeon, at all times. The dehiscent facial nerve can mask part of the stapes or run across the footplate. The oval window may be very narrow. The shape of the ossicle can vary and the chorda tympani is almost always in the way, although it should not be moved or stretched!

The current operations all rupture the perilymph compartment of the inner ear and most leave in place a metallic or plastic foreign body. Recent research has shown the extreme importance of inner ear homeostasis and the role of the circulating fluids as defense mechanisms of the very fragile sensory cells of the cochlea and the vestibular system.

Surgical rupture of this delicate system might well upset an essential electrolyte balance!

Teaching stapedectomy or stapedotomy, or stapedoplasty or whatever you want to call it, requires a great sense of responsibility to potential patients who will be submitted to the procedure and to the surgical students who will attend these patients and bear the burden of potential mishaps.

Fig. 4. Adequate exposure is a prerequisite to successful stapes surgery.
Fig. 5. Crimping of the prosthesis and positioning of the piston are very important steps.

Fig. 6. Length of the prosthesis and sealing of the stapedotomy are essential features.
Fig. 7. How to overcome additional pathologies, such as malleus bony ankylosis.

Fig. 8. How to extract a ‘floating’ footplate.

How should one teach stapes surgery? I suggest the following course of action.
(1) The first prerequisite is to have a precise knowledge of the temporal bone anatomy, including all possible variations, and a clear understanding of middle ear and inner ear physiology, histopathology and physiopathology.
(2) Numerous procedures performed by an experienced surgeon should be observed.
(3) An acute understanding of postoperative evolutions is imperative. Therefore, many office consultations of postoperative controls need to be attended.
(4) Theoretical knowledge of how to remedy all possible surgical difficulties and complications should be thoroughly understood.

(5) The surgeon should have an essential surgical ability coupled with modesty and common sense not to overestimate his ability.

(6) Surgical technique should be mastered by practicing on model or cadaver temporal bones.

(7) Previous experience of other surgical procedures in the temporal bone such as myringoplasty, ossiculoplasty, mastoidectomy and canalplasty is recommended.

(8) The particularities of each instrument (e.g. microscope, drills, laser) should be known. The young surgeon should also know what to do if one is missing or breaks down, where replacement parts are available or where another complete replacement set of instruments is!

(9) The student will learn step by step during live operations performed by the supervision of his teacher, first by doing local anesthesia, then opening the middle ear, and so on, and only last placing the prosthesis himself. The teacher must attend every single step.

(10) For his first procedures alone, the student should be assisted by the best team of nurses and anesthesiologists, with the best set of instruments, and the best microscope, until he can really master the procedure. The
teacher should be available in a few minutes’ delay during the first ten procedures.

A common problem in students from the university medical center is the ease and comfort of having anything they need at ‘one’s beck and call’. In reality, when they will be practicing in the smaller area center or back in their third world country, conditions might be more precarious and only with real mastery will they know how to handle the situation.

The teacher should remember that teaching in Medicine is teaching in a field that constantly benefits from new discoveries provided by basic research and the availability of new updated technical tools.

Therefore, the teacher’s aim is not only to transmit his own experience, but to prepare the students to access new developments and improvements with a critical mind and eventually, achieve better results than the teacher himself.

Reference

The Learning Curve in Stapes Surgery and Its Implication for Training

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Abstract

Objective: To identify the ‘stapedotomy’ learning curve of 2 UK otolaryngologists. Study Design: A retrospective review of the outcome of the first 100 stapedotomy operations by each surgeon. Included in the study was a postal survey of the incidence of stapes surgery by UK otolaryngologists. Setting: Two tertiary referral centres. Patients: All ears in which primary stapedotomy was performed for otosclerosis. Non-otosclerotic cases and malleus stapedotomy cases were excluded. Intervention: One surgeon used the technique of small fenestra stapedotomy with either a Teflon\textsuperscript{TM} wire or titanium piston, but without vein graft interposition, whilst the second employed the technique of stapedotomy with vein graft interposition, and a Teflon\textsuperscript{TM} piston. Main Outcome Measures: The first 100 stapes operations performed by each surgeon were subdivided into consecutive groups of 10. Using a postoperative air-bone gap of 20 dB or better as a definition of ‘success’, the ‘success rates’ of each group were plotted on graphs – the learning curves. The end point of the learning curve was defined as the point ‘where the curve reaches its plateau’. Results: The learning curves of both surgeons included 70–80 operations. Both surgeons had one ‘dead ear’ in their first 15 cases. The postal survey showed that some trainers only perform a small number of stapes surgeries, whereas some otolaryngologists who regularly perform stapedotomies were not trainers. Conclusions: This is a mismatch of trainers and trainees in stapes surgery. If the current trend of decline in stapes surgery continues, it will take many years for some otolaryngologists to complete their learning curves.

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Over the last 20 years, the number of stapes operations performed has decreased steadily. Most of the backlog of patients with otosclerosis had their surgery performed in the 1960s and 1970s. Other possible reasons for the reduction could be the fluoridation of water supplies [1] and improvement of the...
quality of hearing aids [2]. As the number of practising otolaryngologists steadily increases, it is inevitable that fewer cases of otosclerosis present to each surgeon.

This inadequate exposure to stapes surgery poses problems for both trainees and trainers. Many institutions reported concerns in the 1980s and 1990s that hearing results for resident-performed stapedectomies were significantly worse than those for experienced otologic surgeons [3–6]. The trainers of this period were probably trained at the time when stapes surgery was still a common operation, i.e. during the 1960s and 1970s. With the declining number of stapes operations in the last 30 years, the lack of experience gained by trainees has led to the inevitable consequence that as they progress to become trainers the majority of trainers are relatively inexperienced when compared to ‘past masters’.

Some otolaryngologists only perform their first ‘complete’ stapes operation when they become consultants. It is natural that they go through a learning curve before they can achieve good results, let alone become a trainer in stapes surgery. A previous report by Hughes [7] indicates that it took 50 stapes operations for him to complete his learning curve. He defined the end point of his learning curve to be a ‘10-dB or better postoperative air-bone gap in 90% of patients’. Another report by Sargent [8] confirmed that his results of stapedotomy improve with experience, although he did not specify how steep the learning curve was. Both authors went through the residency or fellowship training in the USA.

The aim of this study was to compare the learning curves of 2 UK surgeons, each using a different technique for stapes surgery. Both authors had completed 8 years of otolaryngology surgical training. In addition to that training, the first author (M.W.Y.) had a further 6 months of fellowship training in otology.

**Materials and Methods**

**National Survey on Stapes Surgery**

A postal survey was sent to the members of the British Association of Otorhinolaryngologists, Head and Neck Surgeons in 2001 to enquire about the number of stapes operations they had performed during the previous 12 months. They were also asked whether they had been involved in stapes surgery training for the higher surgical trainees.

**Study of the Learning Curves**

**Ears**

The audiometric results of the first 100 consecutive primary stapes operations from each author (M.W.Y. and J.O.) were reviewed retrospectively. Revision cases, non-otosclerotic cases and malleus stapedotomy cases were excluded.
Surgical Techniques

There had been many minor modifications of the surgical techniques by both authors throughout the years. However, the basic surgical procedure used by each author remained unchanged. The first author (M.W. Y.) used the technique of small fenestra stapedotomy without vein graft interposition. The operations were routinely performed under local anaesthesia. The first 30 stapes operations were non-laser assisted but all the subsequent ones were laser assisted using the argon or KTP laser. A Teflon™ wire or titanium piston was inserted into a 0.6-mm hole on the footplate. The oval window was then sealed using connective tissue plugs. For the first 44 cases, a stapes piston was used with a diameter of 0.6 mm. The diameter was changed to 0.4 mm in subsequent cases.

The second author (J.O.) used the technique of stapedotomy with vein graft interposition. The operation was performed under general anaesthesia and laser assisted using the KTP laser in all cases. A piece of vein graft, harvested from the wrist or hand, was placed over a 0.8-mm hole created in the stapes footplate and a 0.4-mm Causse Teflon Piston™ or a Robinson Teflon™ 'bucket handle' prosthesis was used for reconstruction.

Audiometric Assessment

The pre- and postoperative air-bone gaps (at 6 months or longer) for each ear were examined. The postoperative air-bone gap was calculated using postoperative bone conduction and postoperative air conduction thresholds. The 4-frequency average of 500, 1,000, 2,000 and 3,000 Hz was used to calculate the mean hearing level on the ears as recommended by the American Academy of Otolaryngology – Head and Neck Surgery’s Committee on Hearing and Equilibrium [9].

Analysis

The hearing results of the first 100 ears operated by each author were analysed separately. They were divided into small consecutive groups of 10 cases. The ‘success rates’ of each small group were plotted on graphs – i.e. the learning curves of the individual authors. These graphs showed the postoperative air-bone gaps and the percentage of ears with closure of the postoperative air-bone gaps to within 10 and 15 dB. It was recognised that the postoperative hearing results based on postoperative air-bone gaps may not identify those ears with cochlear damage from the operation. Hence, ears with deterioration of the bone conduction threshold of more than 20 dB were highlighted in each graph. The present authors defined the end point of the learning curve as ‘when the curve reaches its plateau’.

Results

National Survey on Stapes Surgery

Five hundred and eighteen questionnaires were sent to the members of the British Association of Otorhinolaryngologists, Head and Neck Surgeons. Of these, 225 responded, giving a response rate of 43%. Ninety-six surgeons had performed at least one stapes operation during the previous 12 months. The respondents were divided into groups according to the number of stapes operations...
they performed (table 1). The number of trainers of stapes surgery in each group is also shown in table 1. Four trainer surgeons performed less than 5 stapes operations in 1 year. On the other hand, 4 out of 8 surgeons who performed more than 25 stapes operations per year were not involved in the training of stapes surgery.

### Study of the Learning Curve

The learning curves for each level of results are illustrated in figures 1–3. Both authors had a ‘dead’ ear at an early stage of their learning curve – case 13 for M.W.Y. and case 5 for J.O. This gives a dead ear rate of 1% for both authors in their first 100 stapes operations. On top of that, 3 other ears had a deterioration of the bone conduction threshold of more than 20 dB following surgery (cases 4 and 5 for M.W.Y. and case 62 for J.O.) indicating cochlear damage. For M.W.Y., all 3 cases (case 13 with a dead ear; cases 4 and 5 with partial inner ear damage) happened early on in his learning curve, before the introduction of laser in his practice. The complication of case 13 was due to a perilymph leak, as the oval window was not plugged with connective tissue. It was wrongly presumed at that time that the 0.6-mm piston in a 0.6-mm hole might be sufficient to prevent leakage.

For J.O., the cases of cochlear damage with a loss of 20 dB or greater were separated by several years (case 5 with a dead ear and case 62 with partial inner ear damage). He re-explored both cases but the cause of the complication in both cases was not clear.

For M.W.Y., the plateau of the learning curve was reached after 70 cases of stapedotomy operations. This number of stapes surgeries was accumulated over a 9-year period. For J.O., the plateau was reached after 80 cases. This number was accumulated over a 7-year period.

### Table 1. Result of the postal survey on stapes surgery experience amongst UK otolaryngologists and the number of stapes surgery trainers

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**Discussion**

The survey amongst UK otolaryngologists confirms that there is some mismatch between trainee and trainers. Some surgeons perform relatively few stapes operations, yet they have to provide training for this delicate operation. On the other hand, several regular ‘stapedectomists’ were not involved in training. We did not identify the occasional ‘stapedectomists’ who might have had vast experience in stapes surgery previously. Still, these surgeons did not continue to practise stapes surgery in adequate numbers to provide effective training. However, the authors accept that there is no agreement as to what constitutes an ‘adequate number’.

For a relatively uncommon operation like stapes surgery, it may take years to complete the learning curve. It took 9 years and 70 operations for M.W.Y. to complete his learning curve and 7 years and 80 operations for J.O. to complete.
his. All but one ear with inner ear damage were from the first 20 cases for both authors.

The authors recognised that learning differs from surgeon to surgeon. Some surgeons master new surgical techniques quicker than others. Both authors are career otologists who perform large numbers of middle ear operations every year and also run courses on ear surgery. It can therefore be argued that less dedicated otolaryngologists may take even longer to complete their learning curves.

It is interesting that Hughes [7], an American surgeon who went through the US Residency and an Otology fellowship training programme, took 50 cases to complete his learning curve. The present authors defined the end point of the learning curve as ‘when the curve reaches its plateau’. This was different from the definition by Hughes who defined the end point of his learning curve as a ‘10-dB closure in the postoperative air-bone gap in 90% of ears’. Hughes only achieved this result at one point on his learning curve, but did not provide evidence that this was sustainable.

**Fig. 2.** Authors’ learning curves in stapes surgery: points along the curves represent the percentage of ears in each consecutive group of 10 operations for M.W.Y. (**a**) and J.O. (**b**) that had a postoperative air-bone gap of ≤10 dB. The case number of ears that had an increase of the bone conduction threshold of 20 dB or more is identified.
The difference in the learning curves between the 2 UK authors is not large, despite the fact that they use different surgical techniques. The extra otology fellowship training by M.W. Y. may have given him a head start in his learning curve. He performed 10 stapes surgeries during this period but the results were not available. J.O. performed a large number of tympanomastoid operations during his training, but only 1 stapes operation that was supervised by an experienced ‘stapedectomist’.

There has been a worldwide concern about the declining number of stapes operations available for training. Reports in the literature are confusing. Many report the results of stapes surgery performed by residents in a residency programme to be less favourable [3–6]. Others claim that the results of the residents could be as good as their trainers’, provided they were under very close supervision [10–13]. These reports were all based on retrospective studies and did not give details on what stage the trainers intervened during the operation. It is possible that many stapes operations were started off by the trainees...
and completed by their trainers. Indeed this is commendable if the welfare of the patients is the first priority.

To create a better match between trainers and trainees, the authors recommend that there should be more co-ordination and flexibility within the training programme. We believe that trainees who wish to become career otologists, and have shown the necessary skill and temperament should be offered targeted training by regional trainers who have the appropriate capacity, preferably at the tertiary referral centres for stapes surgery. Alternatively, these trainers can participate in a national fellowship programme for a selected number of trainees.

Many trainees find themselves turning into trainers when they become consultants. It could be argued that they can only be effective trainers when they have completed their own learning curves. Stapes surgery is an ideal operation to investigate the learning curve of surgery. It is conceptually simple but technically different. Once the technique is mastered, the results of stapes surgery are predictably good. Furthermore, the outcome of the operation is easily measurable and the ‘gold standard’ of stapes surgery is well documented.

If the current trend of decline in stapes surgery continues, it will take the whole working life of some otolaryngologists to complete their learning curves. It must be recognised that the learning curve should also apply to the other members of the team involved in the patient care. For example, the operating theatre staff should be familiar with the instruments and prostheses. The laser operator should be familiar with the ear laser. One possible solution is that hospitals and otolaryngologists should form networks to share resources and combine their surgical experiences for the benefit of patients and trainees, similar to the delivery of cancer services.

References


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