# Round-Window Anatomical Considerations in Intratympanic Drug Therapy for Inner-Ear Diseases

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***Abstract:*** Our aim was to elucidate the importance of anatomical aspects in planning local therapies for inner-ear diseases. The study undertakes the anatomical evaluation, from a surgical-approach perspective, of the relationship between the false and true round-window membranes. As our design, we chose a human temporal bone dissection study, for which we used 20 fresh temporal bones. After an exploratory tympanotomy and atticotomy, we drilled the anterosuperior (promontory) edge of the round-window niche until the true round-window membrane was completely exposed. We registered the presence or absence and the extent of the false round-window membranes on the round-window niche. We found false round-window membranes obstructing the round-window niche partially or completely in five temporal bones (25%). Complete obstruction was present in one temporal bone (5%). We found mucoperiosteal folds obstructing the round-window niche partially or completely in a significant proportion of the ears. These anatomical particularities could account, at least partially, for the great variability of the results of intratympanic therapies for inner-ear diseases.

***Key Words:*** drug therapy; round-window anatomy; topical administration

Intratympanic administration of drugs for inner-ear disease therapy started when Schuknecht [1,2] presented the results of this novel treatment for vertigo in Ménière's disease in eight patients, using the ototoxic drug streptomycin. That study started a new era of interest about the round window and round-window membrane, particularly in aspects related to permeability of the membrane by several substances and pathogens [3].

Today, we know that the round-window membrane is involved with several physiological aspects of the ear's function. First, in its auditory function, it serves as a compensatory area of the bony labyrinth, permitting movement of inner-ear fluids in association with movement of the stapedial footplate. Second, the round-window membrane has a definite role as a soft-tissue barrier between the middle and inner ear, and permeability of the membrane to substances can be altered drastically by diseases, particularly otitis media. Third, the round-window membrane can be the place of delivery of drugs influencing inner-ear activity, either as a primary or as an iatrogenic effect.

During the almost 50 years since the publication of the Schuknecht study, intermittent enthusiasm has occurred for methods using intratympanic administration of an agent to treat an inner-ear disease, particularly because of the variable results obtained with the use of any drug, either in abating the symptoms or in deleterious effects on hearing. A natural consequence is to investigate the reasons why standardization of these techniques has not yet been obtained.

Several studies emphasized the importance of anatomical conditions of the round-window niche in the variability of responses to local therapies for the treatment of inner-ear diseases [4,5]. A great variability in the middle-ear anatomy—particularly in the round-window niche opening—and three-dimensional configuration is easily documented in the images of the most important anatomical textbooks [6]. Surely that morpho-

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logical variability will have consequences in administering drugs intratympanically to the inner ear, independent of the method or the device used for the application.

The purpose of our study was to investigate the importance of anatomical aspects in planning local therapies for inner-ear diseases. The study undertakes the anatomical evaluation, from a surgical-approach perspective, of the relationship between the false and true round-window membranes.

## MATERIALS AND METHODS

We dissected 20 fresh temporal bones obtained in the pathological unit of the Department of Otolaryngology, Hospital de Egas Moniz, Lisbon, Portugal. The dissection started with an exploratory tympanotomy and atticotomy, exposing the tympanic cavity that included the oval and round-window regions. We documented the absence of middle-ear pathology (e.g., otosclerosis or chronic otitis media) in the medical records and confirmed it by inspection of middle-ear structures.

After exposure of the round-window niche (Fig. 1), we drilled the promontory in the vicinity of the round-window opening (anterosuperior edge of the round-window niche) until the round-window membrane was completely exposed (Fig. 2). In each case, we registered the absence or presence and the extent of the mucoperiosteal folds or veils (false round-window membranes) on the round-window niche. Additionally, we registered the relationship between the mucoperiosteal folds and the true round-window membrane

## RESULTS

We found mucoperiosteal folds partially or completely obstructing the round-window niche in five temporal bones (25%; Fig. 3). Complete obstruction was present in one temporal bone (5%).

A remarkable result of our study is the demonstration of the proximity of the true membrane to the false membrane in the anterior edge of the window. This proximity renders making a clear distinction between the two very difficult from a surgical approach.

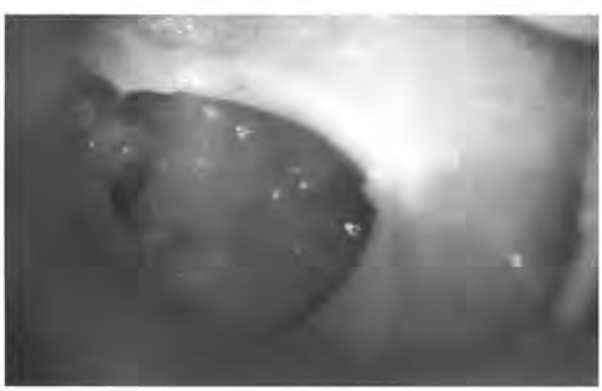

**Figure 1.** When the round-window region is exposed by the tympanomeatal flap approach, the round-window niche is only partially exposed, and the round-window membrane is not visible.

**Figure 2.** Only after extensive drilling on the anterosuperior (promontory) edge of the oval-window niche can the oval-window membrane be seen clearly.

## DISCUSSION

When promised clinical results do not materialize suitably, sometimes investigation must come back to basics.

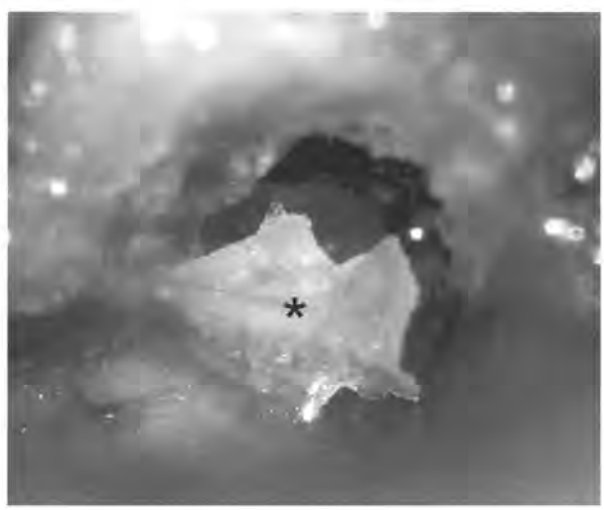

**Figure 3.** The round-window niche is completely obstructed by a mucoperiosteal fold. When the edge of the round window was dissected, the false membrane was disrupted, and the round-window niche and membrane were then exposed.

As to the intratympanic administration of drugs to treat inner-ear diseases, anatomical particularities of the round-window niche had been mentioned as one factor accounting potentially for variability of responses [5]. Nomura [7] described investigations of human temporal bones in which the round-window niche was found to be limited by mucoperiosteal folds in 70% of specimens (the so-called false round-window membrane). In the same study, in 30% of the temporal bones, the round-window niche was completely occluded by these folds.

The first and only study directly addressing the implications of the round-window patency for perfusion of the inner ear via intratympanic instillation of medications was published by Silverstein et al. [4] in 1997. In that study, endoscopic evaluation of the round-window niche obstruction through a tympanostomy hole was performed in 41 ears before inner-ear perfusion. The authors found that the round-window niche was partially obstructed in seven ears (17%) and completely obstructed in five ears (12%).

Our study undertook the anatomical evaluation, from a surgical-approach perspective, of the relationship between false and true round-window membranes. We started with the temporal bone in the usual surgical position, where the round-window content is almost completely hidden, and we ended with the complete exposure of the round-window membrane. The results of our study confirmed the results of previous studies, wherein mucoperiosteal folds partially or completely obstructing the round-window niche were found in a significant proportion of ears.

The delivery of drugs to the inner ear via intratympanic administration will always be very different from other routes of drug administration (e.g., oral or intravenous routes) in which bioavailability can easily be measured. Anatomy has to be considered in dealing with local therapies for inner-ear diseases. Anatomical particularities of the round-window niche account, at least partially, for the great variability of the results of these treatments. The relationship between the degree of round-window niche obstruction and the results of inner-ear perfusion should be addressed in future studies so as to standardize the techniques of local therapy for inner-ear diseases.

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