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# MRI Inner Ear Imaging and Tone Burst Electrocochleography in the Diagnosis of Ménière's Disease

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**Objective:** To compare the sensitivity of gadolinium MRI inner imaging with tone burst electrocochleography (EcochG) for diagnosing endolymphatic hydrops.
**Study Design:** A prospective study on patients who were to have an MRI scan to exclude retrocochlear pathology.
**Setting:** Tertiary care center.
**Patients:** One hundred and two patients: 57 patients with Possible, Probable, or Definite Ménière's Disease, 25 with asymmetrical hearing loss, 18 with sudden sensorineural hearing loss, and 2 with unilateral tinnitus had additional MRI inner ear imaging and click and tone burst stimulus EcochG testing.
**Intervention:** Diagnostic.
**Main Outcome Measure:** To compare the sensitivity of the two techniques.
**Results:** In 30 patients with symptom-based Definite Ménière's Disease, tone burst EcochG was positive in 25 (83%) and the click EcochG was positive in 9/30 (30%), and gadolinium MRI imaging diagnosed hydrops in 14 (47%). A positive result for either MRI imaging or tone burst EcochG was seen in 26 patients (87%). In 14 subjects with symptom-based Probable Ménière's Disease, 10 (71%) had either a positive EcochG or MRI. In 13 with Possible Ménière's Disease, four (31%) had a positive EcochG or MRI.
**Conclusion:** This study confirms the greatly enhanced diagnostic sensitivity of tone burst EcochG over click response in diagnosing endolymphatic hydrops in Ménière's disease. Even though adequate MRI imaging was achieved in 90%, tone burst EcochG was a more sensitive test. **Key Words:** Ménière's disease—MRI inner ear imaging—Tone burst electrocochleography.

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Ménière's disease is thought to be a result of endolymphatic hydrops, and typically symptoms are spontaneous episodes of vertigo, fluctuating low-frequency hearing loss, tinnitus, and sensation of aural fullness. Diagnosis and likelihood of disease presence have been dominated by the 1995 consensus statement of the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) (1). These criteria use only clinical criteria for classifying patients as Definite Ménière's Disease and require histological (postmortem) analysis for Certain Ménière's classification. Another validated Ménière's disease scoring system is the Gibson 10-point score for the clinical diagnosis of Ménière's disease (2). The current AAO-HNS Guidelines for the diagnosis and evaluation of therapy in Ménière's disease do not recognize the existence let alone the validity of any in vivo test that can confirm endolymphatic hydrops.

Gibson in 1977 (3) demonstrated that in transtympanic electrocochleography (EcochG), an enlarged summating potential component (SP) of an action potential (AP), using a click stimulus, could be an indication of endolymphatic hydrops and therefore useful in the diagnosis of Ménière's disease. Based on a variety of SP/AP ratios, numerous investigators found that a click stimulus was unreliable in predicting the presence of Ménière's disease

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and the test fell into disfavor (4). Subsequently, Gibson (5), Conlon and Gibson (6), and others (7) have shown that a tone burst stimulus dramatically increases the reliability and sensitivity of the test. Gibson (5) found a combination of SP responses (published voltage criteria [8] based on the Gibson score) to 0.5, 1, and 2 kHz tone bursts achieves an 88% sensitivity for diagnosing hydrops based on the likelihood of Ménière's disease (2) (Table 1).

In 2007, Nakashima et al. (9) used intratympanic (IT) gadolinium to produce clear images of endolymphatic hydrops in the inner ear of patients with Ménière's disease using a 3-T magnetic resonance imaging (MRI) scanner. The dose and timing of gadolinium administration and the safety have been established and a hydrops grading system proposed (10) (Table 2). There has been intense interest in this technique, raising hopes that visualization of the hydrops on a scan might be the gold standard test for Ménière's disease and the basis of comparison for any competing test.

There are very few studies which attempt to correlate MRI inner ear imaging with EcochG findings. Yamamoto et al. (11), using a click stimulus and canal electrode, could not find a consistent correlation between visible hydrops and the SP/AP ratio. Fukuoka et al. (12) found that in 20 patients with Definite Ménière's Disease found that transtympanic click EcochG and the glycerol test was less sensitive for diagnosing hydrops than MRI imaging with intratympanic gadolinium. There are no published studies comparing tone burst EcochG and gadolinium MRI in Ménière's disease patients.

After a small pilot study in our department (13,14), it was decided to test a larger number of subjects to compare the sensitivity of gadolinium MRI inner ear imaging with tone burst EcochG, and click stimulus EcochG. The aim was to assess the sensitivity, specificity, and practicality of these tests in a wide range of patients with inner ear disease. A secondary focus was whether these tests could be clinically useful in the objective diagnosis of Ménière's disease.

## METHODS

### Subjects

Participants were recruited prospectively from patients presenting to the outpatient clinic at the Otolaryngology Department at Christchurch Hospital.

**TABLE 1.** *EcochG criteria for hydrops (5)*

| Stimulus | Intensity (dB HL) | SP more negative than (μV): | SP/AP ratio |
|---|---|---|---|
| 1 kHz Tone burst | <25 | −6 | |
| | 20–35 | −6 | |
| | 40–55 | −6 | |
| | 60–75 | −3 | |
| 2 kHz Tone burst | <25 | −9 | |
| | 20–35 | −7 | |
| | 40–55 | −5 | |
| | 60–75 | −5 | |
| Click | | | 0.5 |

HL indicates hearing level; SP, summating potential; AP, action potential.

**TABLE 2.** *Endolymphatic hydrops: MRI grading system (10)*

| Location | Finding | Grade |
|---|---|---|
| Cochlea | No Reissner's membrane displacement | None |
| | Endolymph not exceeding perilymph | Mild |
| | Endolymph exceeds perilymph | Significant |
| Vestibule | Endolymph/perilymph ratio 1:3 | None |
| | Endolymph/perilymph ratio 1:3 to 1:2 | Mild |
| | Endolymph/perilymph ratio > 50% | Significant |

Inclusion criteria for the study were any patient who was clinically requiring an MRI to exclude vestibular schwannoma and who agreed to join the study. These patients were mostly episodic vertigo with AAO-HNS Guideline diagnosis of Definite, Probable, or Possible Ménière's Disease. Other patients had asymmetrical sensorineural hearing loss (SNHL), idiopathic sudden sensorineural hearing loss, or unilateral nonpulsatile tinnitus.

Exclusion criteria were patients who were pregnant, under the age of 18, had chronic middle ear disease, patients taking medications known to interact with gadolinium contrast agents (chemotherapy and HIV medications), tympanic membrane perforation, renal failure, previous allergic reactions to gadolinium contrast agents, metal foreign bodies (including cerebrovascular aneurysm clips), pacemakers, and claustrophobia.

A structured history was taken to allow calculation of the AAO-HNS score (1), Gibson score (2), the duration of symptoms, presenting symptom, and age at first presentation.

### Audiometry

Standard pure tone audiometry (PTA) was performed before EcochG on the day of contrast injection.

### Electrocochleography

Electrocochleography was carried out in the most affected ear of all patients following a standard protocol. Instruments used for the recording of EcochG signals were an electrodiagnostic system (Amplaid MK 15, Milan, Italy) and insulated transtympanic electrodes. A tiny drop of topical phenol was used for local anesthetic of the tympanic membrane. A sterilized transtympanic needle electrode was placed to rest in the round window niche (Fig. 1). Using a headphone sound source, tone burst and click stimuli were used. In addition, 100 dBnHL tone burst stimuli were presented at 0.5, 1, 2, and 4 kHz. The rise and fall time was 1 ms with a 14-ms plateau, with a total duration of 16 ms. Click stimuli were presented at 90 dBnHL with a duration of 100 μs and alternating polarity at a rate of 10 times per second. A total of 1,024 presentations per run were delivered for the tone burst stimuli and recorded, along with the response signals, with an analysis time window of 30 ms. A total of 256 presentations per run were delivered for the click stimuli and recorded, along with the response signals, with an analysis time window of 10 ms. Both the acoustic stimuli and the AER signals were filtered through a 32 band-pass filter, consisting of a low-pass filter at 3 kHz with a 12 dB per octave filter slope and a high-pass filter at 0.5 Hz with a 6 dB per octave filter slope.

### IT Gadolinium

An 8-fold dilution of 0.5 M solution of gadobenate dimeglumine (MultiHance; Bracco Diagnostics, Germany) with normal saline was used as the contrast agent. With the patient positioned with the head extended and the tested ear elevated, 2 ml

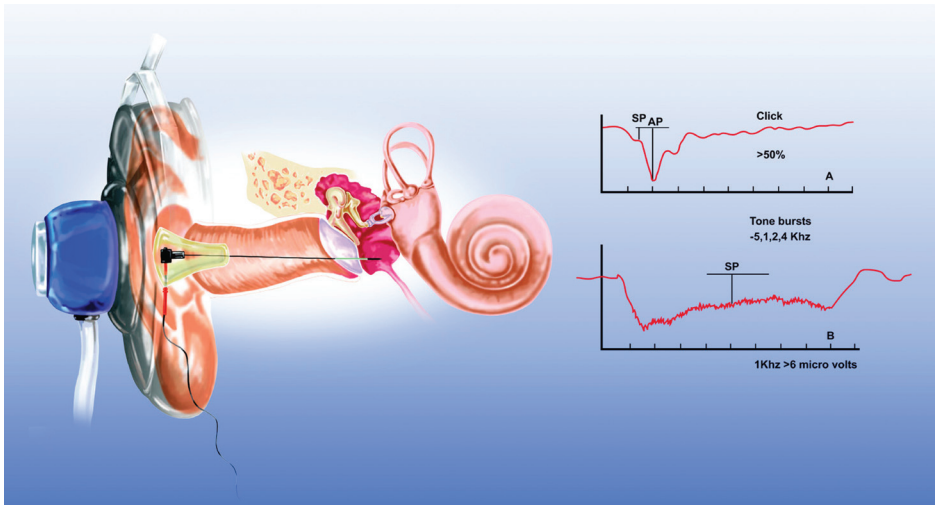


**FIG. 1.** Insulated transtympanic needle contacting the cochlea in a right round window niche. Recording response to a click and a 1-kHz tone burst. Reproduced by permission from Hornibrook J, George P, Gourley J. Vasopressin in definite Ménière's disease with positive electrocochleographic findings. *Acta Otolaryngol* 2011;131:613–7.

was injected through the transtympanic needle site over 30 minutes with a 23g spinal needle.

### MRI

MRI scans were obtained 24 hours after contrast injection using a 3-T scanner (General Electric HDX). In addition to routine 3D Fiesta imaging of the inner ear and IAMs, two inversion recovery sequences were obtained with inversion times of T1 1000 (endolymph) and 2500 (perilymph). The scans were reported by one of the two head and neck specialist radiologists who were blinded to all audiology results and had a minimal amount of clinical information as was required on the radiology requesting documentation (which was completed before the audiological testing).

Using a scale prescribed by Nakashima et al. (10), the scans were graded into none, mild, or significant endolymphatic hydrops (Table 2).

Initial follow-up was at 2 weeks and further appointments depending on clinical requirements.

The study protocol was reviewed and approved by the Southern Regional Ethics Committee. Written informed consent was obtained from all patients before their participation in the study.

### Statistical Analysis

Data were analyzed using SPSS software v. 19.0 (IBM Inc., Armonk, New York, USA). A $p$ value less than 0.05 was defined as the level of significance.

## RESULTS

One hundred two participants underwent PTA (bilateral), click and tone burst EcochG on their most affected side, and MRI of the temporal bone with previous gadolinium instillation. Mean age at the time of scanning was 58 years, with mean age at first symptoms 54 years. There were 49 males (48%) and 53 females (52%). Ninety-seven percent were NZ European in ethnicity.

The presenting diagnosis and reasons for scanning were Ménière's disease 56% (57/102), asymmetrical SNHL 25% (25/102), sudden SNHL 18% (18/102), and unilateral tinnitus 2% (2/102).

Of the Ménière's cohort, 30 were clinically scored as AAO-HNS Definite (Gibson score >7), 14 as Probable, and 13 as Possible (Gibson score <7). Test results are summarized in Table 3.

Ten percent (10/102) of participants had inadequate gadolinium diffusion into the inner ear perilymph to be able to make any comment on hydropic status. Sixty-one percent (62/102) had good gadolinium entry and 29% (30/102) had suboptimal gadolinium entry but adequate to assess for hydrops. For further analysis reasons, inadequate gadolinium cases are classed as negative results.

In 14/102 (14%) patients, EcochG tone burst traces were unobtainable because of profound hearing loss in six patients and severe hearing loss in eight patients. For further analysis reasons, cases where EcochG traces were unobtainable are classed as negative results.

Twenty-one percent (21/102) of patients had a positive click EcochG (SP/AP ratio >50%). Fifteen of these were patients being assessed for Ménière's disease, and all of

**TABLE 3.** *Results of MRI and EcochG in each clinical category*

| Clinical category | Number | Gadolinium MRI positive (%) | Tone burst EcoG (%) | Click EcoG (%) |
|---|---|---|---|---|
| Definite Ménière's | 30 | 14 (47) | 25 (83) | 9 (30) |
| Probable Ménière's | 14 | 4 (29) | 8 (57) | 4 (29) |
| Possible Ménière's | 13 | 1 (8) | 4 (31) | 2 (15) |
| Asymmetric SNHL | 25 | 2 (8) | 7 (28) | 4 (16) |
| Sudden SNHL | 18 | 1 (6) | 5 (28) | 2 (11) |
| Asymmetric tinnitus | 2 | 0 | 0 | 0 |

**TABLE 4.** *Distribution of hydrops as demonstrated by gadolinium MRI*

| Distribution of hydrops | Number in study | EcochG positives |
|---|---|---|
| Vestibule only | 6 | 6 |
| Cochlea only | 10 | 7 |
| Vestibule and cochlea | 6 | 4 |

these patients recorded a positive tone burst EcochG. In 30 clinically Definite Ménière's patients, the tone burst EcochG was positive in 25 (83%) and the click EcochG was positive in 9 (30%) patients.

In the group of 30 clinically Definite Ménière's patients, gadolinium MRI was positive in 14 (47%). If the two patients with a profound hearing loss in the test ear were excluded (EcochG unobtainable), then a positive yield for EcochG testing was 89%. A positive result for either EcochG or MRI was seen in 26 patients (87%). Excluding profound hearing loss patients gives positive results in 26 of 28 patients (i.e., 93%). See Table 4 for further breakdown of results. Figure 2 shows a normal (non-hydropic) ear. Figure 3 shows endolymphatic hydrops in Ménière's ear.

In the 14 cases of clinically Probable Ménière's Disease, eight had a positive tone burst EcochG with a negative MRI. Two patients had positive MRIs with negative EcochGs, and four had negative results for both. Overall, 10 (71%) patients had either a positive EcochG or MRI.

In the 13 cases of clinically Possible Ménière's disease, only one had a positive MRI with a positive EcochG; three others had positive EcochGs with negative MRIs. The other nine patients were negative for EcochG and MRI.

When looking at all Ménière's disease categories (57 patients), there were 37 (65%) positive EcochG patients. Definite Ménière's showed 25 of 30 (83%) positive cases, Probable Meniere's 8 of 14 (57%), and Possible Ménière's 4 of 13 (31%). Sensitivity for less than clinically definite cases cannot be quantified as there is a degree of alternate diagnosis potential.

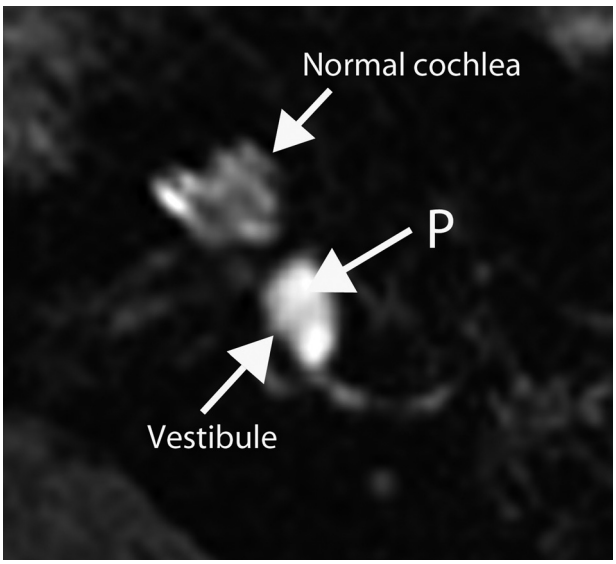


**FIG. 2.** MRI of a normal (non-hydropic) left inner ear. P = perilymph, E = endolymph.

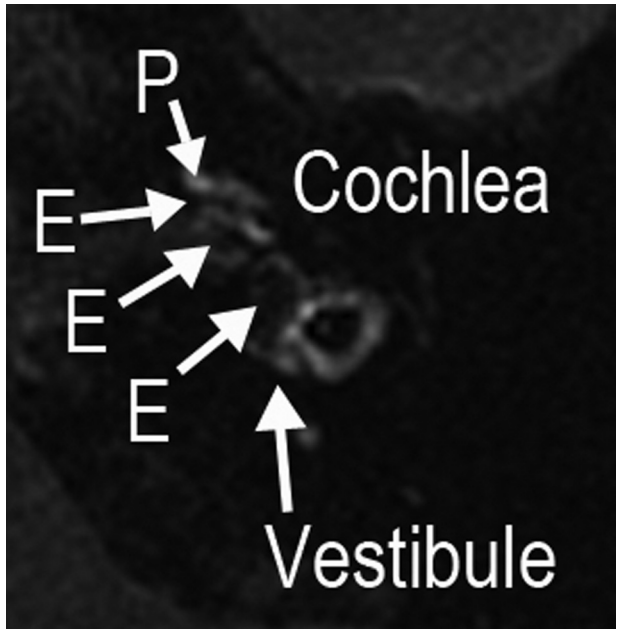


**FIG. 3.** Magnetic resonance imaging of the left inner ear of a Ménière's patient. The perilymph sequence demonstrates enlargement of the endolymphatic compartment in the cochlea and endolymph filling the vestibule. P = perilymph, E = endolymph.

When comparing the clinically Definite Ménière's Disease patients with a combined group of Probable and Possible patients, there was a statistically significant difference in the clinical groups for the likelihood of a positive tone burst EcochG ($\chi^2$ test with $p < 0.005$). The odds ratio of 5.56 (1.7–17.8) at $p$ less than 0.004 demonstrates that a positive EcochG patient has greater odds of being in the clinically Definite Ménière's group. For either a positive EcochG and/or positive MRI, the groups are again statistically different but with a lower odds ratio ($\chi^2$ test with $p < 0.005$). The odds ratio was 5.20 (1.6–17.4) at $p$ less than 0.02. But the groups show barely statistically significant difference ($p = 0.05$) when looking at just the positive MRI results, likely due to the low numbers.

Asymmetric SNHL patients totaled 25. Seven patients had positive EcochGs, with one of these cases also having a positive MRI. One patient had a positive MRI but negative EcochG. The other 17 had negative tests.

Sudden SNHL patients totaled 18. Five patients had positive EcochGs and one patient had positive MRI with the other 12 patients having negative results.

The two unilateral tinnitus patients both had negative MRI and EcochG results.

The distribution of endolymphatic hydrops as demonstrated by the gadolinium MRI was categorized as vestibular only, cochlea only, or both vestibule and cochlea (see Table 4). Twelve patients showed vestibular hydrops (11 with Ménière's and 1 with asymmetrical SNHL). Of these, 10 had a positive tone burst EcochG. Six had vestibular hydrops only on MRI and all of these had a positive

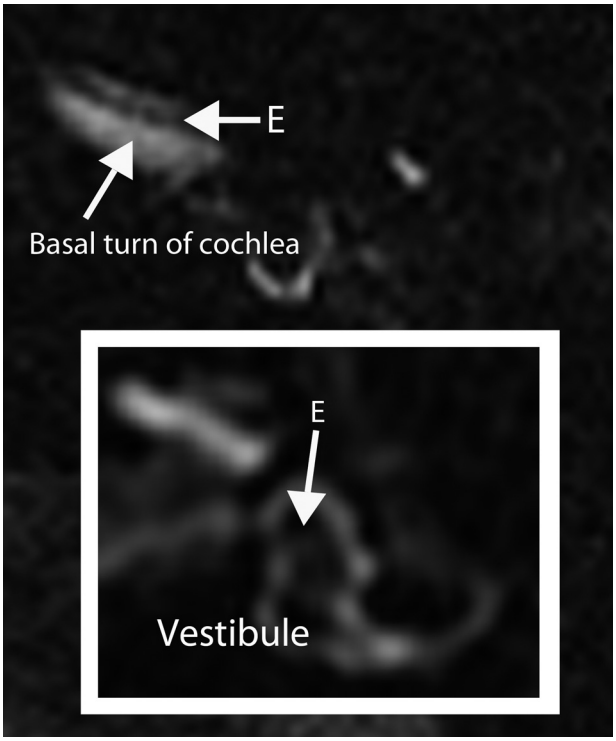


**FIG. 4.** Left inner ear MRI of a subject with a positive EcochG and no visible cochlear hydrops but hydrops in the vestibule. P = perilymph, E = endolymph.

EcochG (Fig. 4). So in these six cases, the EcochG was positive but any cochlear hydrops was not severe enough to be demonstrated on gadolinium MRI. There were 10 cases of hydrops demonstrated in the cochlea only and the EcochG was positive in 70% (7/10) with two of the negative cases being patients with unrecordable EcochG traces resulting from severe or profound hearing loss. There was no correlation of severity of symptoms and the distribution or severity (mild or significant) of hydrops as demonstrated by gadolinium MRI.

There were three patients in the study that had a positive gadolinium MRI but negative EcochG. Two patients had Ménière's disease (one Definite and one Probable) and the other patient had asymmetric SNHL. Age, gender, and duration of disease were not significant differing factors for these patients. The extent and distribution of hydrops as demonstrated by MRI was significant, and in all three patients it was present in the cochlea. The reason for this is unclear.

Complications: one patient had an episode of acute otitis media after the gadolinium injection with tympanic membrane perforation that healed spontaneously with return to pre-injection hearing levels.

## DISCUSSION

Gadolinium instilled in the middle ear 24 hours before a MRI scan gave adequate imaging contrast in more than 90% of cases. It was relatively well tolerated with very few complications.

In this study, tone burst EcochG correlates well with symptoms of Ménière's disease. It is more sensitive than gadolinium MRI scanning using these techniques. Using either positive tone burst EcoG or positive gadolinium MRI as an objective indicator for endolymphatic hydrops, 87% of our patients who met AAO-HNS criteria for clinically Definite Ménière's Disease were detected. This gives us a lot of confidence in our clinical diagnostic criteria. Our study confirms the previous findings of Gibson and others (6–8) that the use of tone burst EcochG dramatically increases the sensitivity of the test compared to click EcochG.

In histological studies, enlargement of the endolymphatic space (hydrops) is seen almost invariably in patients who had Ménière's disease, although the severity may not correlate clinically and not all those with endolymphatic hydrops have clinical symptoms of Ménière's disease (15). We think it likely that the tone burst EcochG detects electrophysiological changes from pathological basilar membranes in patients who have Ménière's disease with more sensitivity than the degree of hydrops that can be detected with gadolinium MRI. Future techniques using higher Tesla scanners or animal models may confirm this hypothesis.

Another area of possible utility of an ''objective'' test of endolymphatic hydrops is in the management of those patients without a full clinical diagnosis of Ménière's disease. Approximately half of the patients with clinically Possible or Probable Ménière's Disease had a positive EcochG or MRI. Some of these people may go on and develop the full clinical picture of Ménière's disease. One of our patients presented to the Department in 2010 with sensorineural hearing loss with no vertigo. He re-presented in 2012 with the addition of vertigo and clinically Definite Ménière's Disease. A longitudinal study of a cohort of such people would be required to determine the risk of a patient with positive EcochG or MRI going on to develop Ménière's disease.

Objective tests may also have a role in assessing the effects of therapeutic intervention, surgical or medical (16,17). Any investigation into the efficacy of treatment in Ménière's disease is of course complicated by the high rate of spontaneous symptom improvement and the unpredictable nature of the condition. Changes in the parameters of an objective test may give valuable information when assessing a therapeutic intervention and indeed when assessing spontaneous improvement in symptoms.

The distribution of endolymphatic hydrops has been shown to often include the cochlear and vestibule irrespective of cochlear only symptoms or vestibular only symptoms (18). Our study shows poor correlation of extent and distribution of hydrops on gadolinium MRI and patient severity of Ménière's symptoms. It has shown that some patients can have EcochG changes indicating endolymphatic hydrops in the cochlea but without changes being identified on gadolinium MRI. We think that this most likely is explained by electrocochleography being a

more sensitive indicator of inner ear dysfunction than MRI which is producing a relatively coarse image of a tiny organ.

Although click EcochGs with canal electrodes have been performed by audiologists, transtympanic electrode placement achieves significantly (10 times) greater responses. The measure from a click stimulus is an SP/AP ratio, whereas the SP from tone burst response is an absolute voltage measurement.

In summary, this study demonstrates high correlation between positive transtympanic EcochG with tone burst stimuli and clinical Ménière's disease and a lower rate of positive gadolinium-enhanced MRI scans. Although both tests have promise as objective tests in this condition, tone burst EcochG should be strongly considered by clinicians and researchers investigating Ménière's disease.

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