

Imaging of Endolymphatic Hydrops in Ménière’s Disease: A Clinical Update

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Introduction and Diagnosis of Ménière’s Disease

In 1861, Prosper Ménière described a series of patients with hearing loss and episodic vertigo before the French Academy of Medicine. He linked the condition to inner ear damage.¹

Since then, Ménière’s disease (MD) is known to affect 3.5–513 per 100,000 individuals worldwide.² It is a challenging condition for physicians to diagnose, as patients can have variable presentations. For the unfortunate, it can take years before the diagnosis is established, and hearing loss typically worsens.³ Apart from substantial morbidity, there is significant economic cost. The estimated annual loss of earning from MD in the United Kingdom totals GBP442.7 million.⁴

MD is a clinical diagnosis. The clinical classification created in 1995 by the American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNS), and revised in the 2015 International Classification of Vestibular Disorders by the Bárány Society, include the following two categories: Definite and Probable MD, as defined in Table 1.^{3,5} Apart from sensorineural hearing loss and episodic vertigo,

patients can experience tinnitus and fullness of the affected ear.^{3,6}

Aetiopathogenesis and Evolution of MR Imaging

Endolymphatic hydrops (EH) is a hallmark of MD, which has a complex aetiology that is likely multifactorial.^{7,8} There is propensity for EH to affect the apical turn of the cochlea that can account for low frequency sensorineural hearing loss. Eventually, there is excessive endolymph accumulating in the inner ear, causing damage to the spiral ganglion cells. Some pathology samples show microtears of the Reissner’s membrane,^{7,8} leading to postulation that the potassium-rich endolymph escapes and mixes with the perilymph, which is toxic to cochlear hair cells and vestibular sensory neurons of the 8th cranial nerve.

Development of niche magnetic resonance imaging (MRI) techniques to identify endolymphatic hydrops in the clinical setting began in 2007.⁹ Largely driven by Japanese radiologists in the early days,¹⁰ the technique has been further developed and adopted in hospitals internationally.^{11,12} Prior to this, endolymphatic hydrops

Table 1. Criteria for definite and probable Ménière’s disease (MD)^a

Definite MD	Probable MD
- Two or more spontaneous attacks of vertigo, each lasting 20 minutes to 12 hours	- At least 2 episodes of vertigo or dizziness lasting 20 minutes to 24 hours
- Audiometrically documented fluctuating low- to midfrequency sensorineural hearing loss in the affected ear on at least 1 occasion before, during, or after 1 of the episodes of vertigo	- Fluctuating aural symptoms (hearing loss, tinnitus, or fullness) in the affected ear
- Fluctuating aural symptoms (hearing loss, tinnitus, or fullness) in the affected ear	- Other causes excluded by other tests
- Other causes excluded by other tests	

^aBasura GJ, Adams ME, Monfared A, et al. Clinical practice guideline: Ménière’s disease executive summary. *Otolaryngol Head Neck Surg* 2020;162:415-34.

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was only identified in histopathological specimens and cadaveric studies.⁷

The role of endolymphatic imaging is acknowledged by the European Academy of Otolology and Neurotology, although visualisation of EH is not a requirement for the diagnosis of MD, and absence of endolymphatic hydrops does not exclude its diagnosis if the clinical criteria is met.¹² Other battery of tests available includes audiologic, vestibular assessments, and conventional MRI of the internal auditory meatus to exclude differential diagnosis.

Scientific literature in MRI of EH now includes imaging grading systems and differential diagnosis (Table 2). New imaging evidence bolsters the theories behind the pathoetiologies of MD.

Table 2. Conditions associated with endolymphatic hydrops

Primary
Ménière's disease
Vestibular migraine ^a
Recurrent peripheral vestibulopathy ^b
Congenital ear disease (e.g. Mondini dysplasia) ^{c,d}
Secondary^{c,d}
Vestibular schwannoma
Labyrinthitis, meningitis
Large vestibular aqueductal syndrome
Periductal otosclerosis
Trauma and post-surgical (e.g. cochlear implantation, endolymphatic ablation, stapedectomy for otosclerosis)
Semicircular dehiscence
Others
Asymptomatic ^e

^a Gürkov R, Kantner C, Strupp M, et al. Endolymphatic hydrops in patients with vestibular migraine and auditory symptoms. *Eur Arch Otorhinolaryngol* 2014;271:2661-7.

^b Attyé A, Dumas G, Troprès I, et al. Recurrent peripheral vestibulopathy: Is MRI useful for the diagnosis of endolymphatic hydrops in clinical practice? *Eur Radiol* 2015;25:3043-9.

^c Ferster A, Cureoglu S, Keskin N, et al. Secondary endolymphatic hydrops. *Otol Neurotol* 2017;38:774-9.

^d Gürkov R, Pyykö I, Zou J, et al. What is Ménière's disease? A contemporary re-evaluation of endolymphatic hydrops. *J Neurol* 2016;263:71-81.

^e Nakashima T, Sone M, Teranishi M, et al. A perspective from magnetic resonance imaging findings of the inner ear: Relationships among cerebrospinal, ocular and inner ear fluids. *Auris Nasus Larynx* 2012;39:345-55.

The Role of Electrophysiological Tests in the Diagnosis of Ménière's Disease

Current diagnostic workup of MD relies on serial audiometric changes in pure tone audiometry or speech discrimination scores in relation to a vertiginous attack. Additional neurophysiological tests have attendant limitations and results need to be interpreted with caution.^{13,14}

Dehydration tests using glycerol and frusemide reduce endolymphatic volume and pressure, but further audio-vestibular tests are required. Significant hearing threshold improvement was evident in 31% of 32 patients (10dB or more at 2 frequencies or 12% speech discrimination improvement).¹⁵ Another study found 53% hearing improvement following a dehydration test, with 2 of the unaffected ears showing positive glycerol test.¹⁶ Standards to compare and determine the auditory thresholds may be prone to errors, more so with the fluctuating hearing pattern of MD.

Including tests such as vestibular evoked myogenic potential (VEMP) to document interval improvement, may add to cost.^{13,17} Sensitivity of dehydration tests varies as the disease fluctuates and progresses, positive pick-up being higher in early stages but lower in remission and advanced stages. Although cervical and ocular VEMPs offer objective quantitative measures of otolith functions relating to the saccule and utricle respectively, recent practice guidelines from the American Academy of Neurology concluded that there is inconclusive evidence whether VEMPs reliably diagnose MD.^{14,18}

Electronystagmography, a neurophysiological test of the lateral semicircular canal based on the vestibular-ocular reflex, may support the diagnosis of MD when peripheral weakness is found on caloric testing in the presence of hearing loss and normal video head impulse test findings.¹³

However, this is not perfect, as Casani describes normal caloric responses from 9–29% of his study population with unilateral Definite MD at various stages of hearing loss, and from 100% of patients with canal paresis when the loss is greater than 70dB.¹⁹ Furthermore, a valid objection to caloric testing is the aggravation of vertigo in patients with MD.

Electrocochleography uses extratympanic or invasive intratympanic electrodes to record electrical potentials generated in the auditory nerve (AP) and the cochlear summing potential (SP) after a sound stimulus. Enlarged SP/AP amplitude ratios correlate with expanded endolymphatic volume in cochlear EH, but

again, fluctuating symptoms limit their applicability as a diagnostic tool in the early course of disease.^{14,20}

Fukuoka et al. compared MRI, electrocochleography and the glycerol dehydration test in 20 patients diagnosed with definite MD. The latter two techniques yielded positive results in 11 and 12 patients, respectively, and in 15 patients overall on at least one of the two neurophysiological tests. In comparison, MRI was positive for hydrops in 19 patients.²¹

In another paper, Laureline Kahn et al. performed a retrospective study of 31 definite MD patients who were imaged with 3D fluid-attenuated inversion recovery (FLAIR) MRI sequence. They reported no significant correlation between the presence of saccular hydrops versus cervical VEMP, utricular hydrops versus ocular VEMP, and ampullar hydrops versus video head impulse test. However, the severity of endolymphatic hydrops on MRI was correlated with the degree of hearing loss.²²

MRI Technicalities and Radiological Assessment

Current state-of-the-art techniques for imaging of MD require gadolinium-based contrast medium to be introduced into the perilymph either via the intravenous or trans-tympanic routes. Initial studies were carried out via trans-tympanic contrast administration.¹⁰ The advantage of this mode is the smaller dose of diluted contrast locally introduced (<0.1% ordinarily given via intravenous route),²³ reducing systemic contrast exposure. This method has the dual advantage of concurrent assessment of the feasibility of trans-tympanic gentamicin therapy for MD, with regards to access to the entire membranous labyrinth. However, this is invasive with tympanic membrane puncture, and requires additional radio-otological coordination for imaging 12 to 24 hours later, when the contrast reaches the perilymph in the entire labyrinth.^{9,10,24} There are also logistical challenges with tight MR scheduling.

The intravenous route is less invasive and more convenient for the patient as MR imaging is performed only 4 hours after contrast injection.²⁵ In addition, both ears are assessed simultaneously after a single intravenous injection, whereas the trans-tympanic route requires separate punctures when both sides are to be assessed. If the scan is meant to assess for diseases associated with EH by destruction of the stria vascularis, such as circulatory disturbances and trauma, the intravenous route is also more suited.²³

Contrast causes the perilymph in the scala vestibuli and tympani to be enhanced. Due to the intact endolymph–blood barrier, the endolymph in the scala

media does not enhance, appearing dark (hypointense) against the bright (hyperintense) perilymph within the labyrinth on the MR images (Figs. 1 and 2).

Several MRI sequences have been developed to identify EH. Two commonly used ones are 3D FLAIR, and 3D Inversion Recovery with real reconstruction (3D real IR). 3D FLAIR is more sensitive than T1-weighted imaging to faint gadolinium enhancement. Moreover, heavily T2-weighted 3D FLAIR with a long effective echo time specifically heightens sensitivity to low gadolinium concentrations, enabling the use of single-dose intravenous contrast

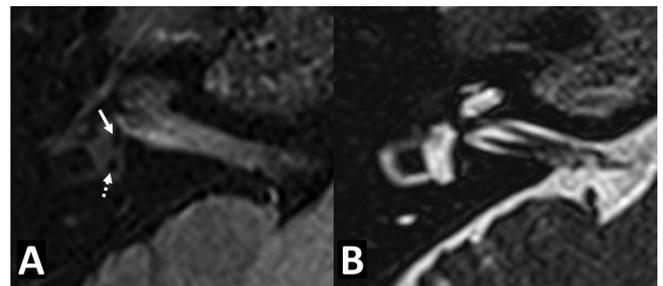


Fig. 1. Axial (A) 3D real inversion recovery post-contrast and (B) cisternographic constructive interference in steady state (CISS) images of the healthy ear show normal-size saccule (white arrow) and utricle (white-dashed arrow) as small black dots within the bony vestibule, yielding saccule to utricle area ratio inversion (SURI) <1 score. The perilymph is mildly enhancing and there is no endolymphatic hydrops.

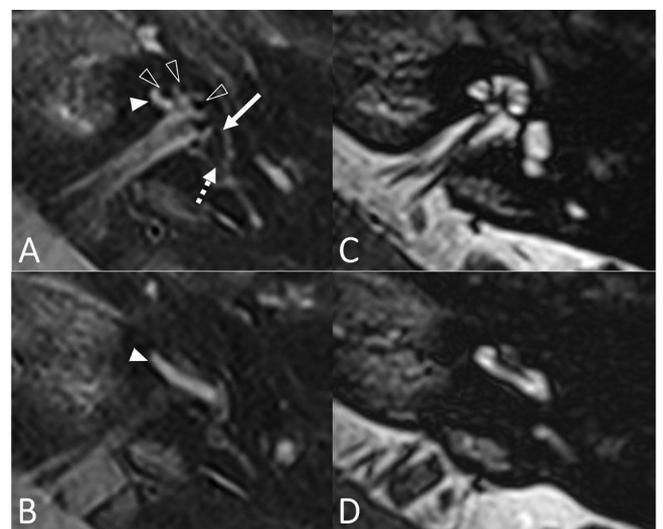


Fig. 2. Axial (A, B) 3D real inversion recovery post-contrast and (C, D) cisternographic constructive interference in steady state (CISS) images of the diseased ear in a patient with left-sided Ménière's disease. The distended hypointense saccule (arrow) nearly fills the entire bony vestibule, and is larger than the utricle (dashed arrow), yielding a grading of SURI >1. Thin enhancing rim of perilymph is still visible, congruent with grade 1 vestibular hydrops by Barath grading. Abnormally prominent perilymph enhancement in the cochlea (solid arrowheads) well depicts the non-enhancing, hypointense, distended cochlear duct (open arrowheads) that completely obstructs the scala vestibuli, compatible with grade 2 cochlear hydrops.

injection.²⁶ It is noteworthy that shortening inversion times in 3D FLAIR can suppress the gadolinium signal in the perilymph and produce endolymph hyperintense images instead, allowing for semi-quantitative assessments using endolymph: perilymph ratio. However, reproducibility is sensitive to optimal inversion time selection.^{18,19} Various image post-processing techniques—through fusion by image subtraction or multiplication involving MR cisternographic images and heavily T2-weighted 3D FLAIR images—enhance the contrast-to-noise ratio between the endolymph, perilymph and bone.^{27,28} However, 3D real inversion recovery using phase-sensitive reconstructions to delineate the EH boundary from the surrounding bone and air suffices, and precludes the need for additional image processing and mis-registration pitfalls.^{10,27}

At least 7 different imaging grading systems are available, and we summarise 4 that we use clinically in Table 3.²⁹⁻³² Most of these analyse the degree that the EH bulges into the scala vestibuli, similar to pathological grading employed.⁷ Others analyse volumetry, proximity to the round window, and the saccule-utricle comparison.^{32,33}

Radiological Findings

Concurring with pathological findings, *in vivo* MRI EH study demonstrates the tendency for severe EH to occur in the symptomatic ear.⁷ Findings of severe EH (grade 2) on imaging are more specific for Ménière's disease (Table 3, Nagoya Scale),¹¹ while mild hydrops can be present in clinically asymptomatic ears, and are as yet of uncertain clinical significance.^{7,11} Evidently, the longer the duration of MD, the more marked is the EH.¹¹ In addition, vestibular hydrops is also a more distinctive primary imaging finding in MD than cochlear hydrops.¹⁶

The saccule to utricle area ratio inversion (SURI) classification is founded on the fact that the saccule is smaller than the utricle in a healthy ear,³⁴ whereas the saccule is often dilated compared to the utricle in MD.^{7,32} Understandably, the SURI classification is not applicable when the saccule and utricle appear fused in the scan. Additionally, if the saccule is not visualised in a patient with MD, it has been postulated that the saccule has collapsed or ruptured/fistulised,^{11,35} and enhancement of the endolymphatic duct in such a case will support the premise of a ruptured Reissner's membrane.^{23,36}

Greater perilymph enhancement secondary to blood-labyrinth barrier breakdown is associated with the pathological ear in MD, a higher functional level on

audiologic tests at the time of MR assessment than those without breakdown, and duration of disease.^{30,33}

The imaging findings also need to be interpreted in correlation with the clinical picture (Table 2), given that not all differentials for endolymphatic hydrops can be diagnosed radiologically, and mild hydrops are reported in asymptomatic individuals.

Clinical Impact

The earlier AAO-HNS 1995 guideline for MD included the definition of "certain MD" that was removed in the 2015 guidelines.⁵ This removal referred to its need for histopathologic confirmation, which is now deemed of little clinical utility since it entailed surgical resection or autopsy. Furthermore, while MRI of EH was unavailable in 1995, it is accessible in specialised imaging centres today.

MRI endolymphatic hydrops may facilitate earlier diagnosis for MD, and is part of the clinician's armamentarium in evaluating patients with profound hearing loss, when functional tests such as electrocochleography and glycerol test cannot be reliably used.²³

Endolymphatic hydrops imaging with intratympanically administered contrast may also be used in assessing the suitability of trans-tympanic treatment.⁹ Prospective MRI studies to determine if patients with unilateral disease and bilateral endolymphatic hydrops are susceptible to developing symptoms in the asymptomatic ear will deepen our understanding of inner ear pathologies. The definitive role of EH imaging in the evaluation of related disorders such as recurrent peripheral vestibulopathy, vestibular migraine or sudden deafness remains to be determined in further clinical studies.^{24,25}

EH imaging is performed in tandem with the conventional internal acoustic meatus MRI. The latter excludes important differential diagnosis of endolymphatic hydrops in the imaging diagnostic workup of patients with MD presentation (Table 2). Naturally, this increases the total duration of the study and entails additional cost. Thus, appropriate patient counselling and engagement for this workup also need attention.

Hospitals and radiology departments with interest in this area need to develop a workflow, fine-tune the MRI sequences on their systems that meet clinical needs, and organise a validated clinical pipeline for radiological reporting. Dedicated radiologists familiar with the delicate anatomy of the temporal bone structures and differentials of MD and EH are critical. Continual

Table 3. Commonly used grading systems for severity of endolymphatic hydrops

Grading System	Nagoya Scale 2008 ^a	Barath 2013 ^b	SURI 2017 ^c	4-Stage Vestibular Hydrops and Perilymphatic Enhancement 2019 ^d
Technique	3D FLAIR 3D-real Inversion Recovery Intratympanic contrast	3D Real Inversion Recovery Intravenous contrast	3D FLAIR Intravenous contrast	3D FLAIR
Study population	Patients with inner ear disease	Definite, Probable, Possible Ménière's disease	Definite Ménière's disease Healthy individuals	Definite and Probable Ménière's disease
Sensitivity/ Specificity of clinically diseased from non-diseased ear	* <i>Cochlear Hydrops</i> * All grades: 100%/29% Severe: 37–81%/67–87% * <i>Vestibular Hydrops</i> : All grades: 86%/62% Severe: 47–57%/70–90%	90%/78% [†]	<i>Vestibular hydrops</i> : 50%/100%	<i>Cochlear PE + 4-stage Vestibular EH</i> (Definite MD vs non-diseased ear): 84.6%/92.3%
Grades	No hydrops: <i>Cochlear</i> : No displacement of Reissner's membrane <i>Vestibule</i> : area ratio ≤ 33.3%		Grade 0: SURI <1	Normal: <i>Cochlear PE</i> : Less than contralateral ear
	Mild hydrops: <i>Cochlear</i> : Displacement of Reissner's membrane. Area of cochlear duct ≤ area of the scala vestibule <i>Vestibule</i> : 33% < area ratio ≤ 50%	Grade 1 hydrops: <i>Cochlear</i> : Mild dilation of the non-enhancing cochlear duct, sparing parts of the enhancing perilymph of the scala vestibuli <i>Vestibule</i> : Distention of the endolymph space of the sacculle or utricle or both with visible perilymphatic space along the periphery of the vestibule	Grade 1: SURI ≥1	<i>Cochlear PE</i> : Equal to the other ear Grade 1 Vestibular hydrops : Area of the sacculle: area of the utricle ≥1 (i.e. SURI grade 1)

^a Nakashima T, Naganawa S, Pyykkö I, et al. Grading of endolymphatic hydrops using magnetic resonance imaging. *Acta Otolaryngol* 2009;129:5-8.

^b Barath K, Schuknecht B, Monge Naldi A, et al. Detection and grading of endolymphatic hydrops in Ménière disease using MR imaging. *Am J Neuroradiol* 2014;35:1387-92.

^c Attye A, Eliezer M, Boudiaf N, et al. MRI of endolymphatic hydrops in patients with Ménière's disease: a case-controlled study with a simplified classification based on saccular morphology. *Eur Radiol* 2017;27:3138-46.

^d Bernaerts A, Vanspauwen R, Blaivie C, et al. The value of four stage vestibular hydrops grading and asymmetric perilymphatic enhancement in the diagnosis of Ménière's disease on MRI. *Neuroradiology* 2019;61:421-9.

* Attye et al.³² and Pai et al.¹¹ based on Nagoya Scale, using 3D FLAIR

† Calculated from the original paper

Table 3. Commonly used grading systems for severity of endolymphatic hydrops (Cont'd)

Significant hydrops	Grade 2 hydrops	Grade 2	Cochlear PE
<p><i>Cochlear</i>: Area of the cochlear duct exceeds the area of the scala vestibuli</p> <p><i>Vestibule</i>: area ratio >50%</p>	<p><i>Cochlear</i>: Scala vestibuli uniformly obstructed by distended cochlear duct</p> <p><i>Vestibule</i>: Bony vestibule entirely encompassed by dilated endolymphatic spaces</p>	No sacculle visible	More than the other ear
			<p>Grade 2 vestibular hydrops</p> <p>Distention of the endolymph space of the sacculle or utricle or both with visible perilymphatic space along the periphery of the vestibule (i.e. Barath grade 1)</p>
			<p>Grade 3 vestibular hydrops</p> <p>Bony vestibule entirely encompassed by dilated endolymphatic spaces (i.e. Barath grade 2)</p>

EH: endolymphatic hydrops; PE: perilymphatic enhancement; SURI: sacculle to utricle area ratio inversion

clinico-radiological engagement between radiologists and experienced ENT or neurology colleagues with expertise in assessment of vestibulopathy is crucial in improving patient management.

Future Directions

Using a 3D T2-weighted steady state free precession sequence to imaging MD obviates the need for contrast administration to enhance the perilymph for depiction of the EH altogether.^{37,38} This proposes direct visualisation of the sacculle for identification of its morphological changes; however, validation and reproducibility assessments await verification.³⁹ Further improvement in spatial resolution that could be achieved on ultra-high field MR imaging at 7 Tesla systems offers hope for improved linear quantification of fine intra-labyrinthine structures and lateralisation of the symptomatic ear. In addition, as demand for MR imaging in the diagnostic workup of MD and EH rises, deep-learning techniques also show promise in rapid, automated analysis.⁴⁰

We have reviewed the evolution and clinical implementation of specialised state-of-the-art high-resolution MR techniques to identify EH in MD. Engaging the relevant radiological and clinical teams is of paramount importance to translate these novel MR imaging into clinical practice and impact patient outcome.

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