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# Comparison of enhancement of the vestibular perilymph between gadoterate meglumine and gadobutrol at 3-Tesla in Meniere's disease

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**KEYWORDS**
Inner ear;
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Gadolinium-based contrast agent;
Magnetic resonance imaging (MRI)

**Abstract**
*Purpose:* To compare the degree of enhancement of the perilymph between two macrocyclic gadolinium-based contrast agents (gadobutrol and gadoterate meglumine) in patients with Meniere's disease at 3-T magnetic resonance imaging (MRI).
*Materials and methods:* The MRI examinations of 20 patients with Meniere's disease obtained 4 hours after a single intravenous dose of macrocyclic gadolinium-based contrast agents were retrospectively compared. Ten patients (median age: 58.5 years; median body mass index [BMI]: 25) have received a single intravenous dose of gadoterate meglumine and 10 patients (median age: 45.5 years; median BMI: 25.4) have received a single-dose of gadobutrol. Two radiologists independently measured the signal intensity ratio (SIR) by using region of interest analysis and performed a visual assessment in order to evaluate the perilymph of each semicircular canal and of the vestibule.
*Results:* No differences in SIR of the symptomatic ear were found between gadobutrol (median SIR: 1.58) and gadoterate meglumine (median SIR: 1.3) ($P = 0.18$). The SIR of the contralateral

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asymptomatic ear was significantly greater with gadobutrol (median: 1.62) than with gadoterate meglumine (median: 1.21) ($P = 0.009$). No differences in endolymphatic structures visualization were found between gadobutrol and gadoterate meglumine in the symptomatic ears ($P = 0.27$) but gadobutrol allowed a better assessment of endolymphatic structures and semicircular canals in the asymptomatic ear ($P < 0.001$).

*Conclusion:* Gadobutrol and gadoterate meglumine provide similar degrees of enhancement of the symptomatic ear in patients with Meniere's disease but gadobutrol provides better anatomical details regarding endolymphatic space and semicircular canals of asymptomatic, contralateral ear.



The diagnosis of endolymphatic hydrops (EH) with magnetic resonance imaging (MRI) relies on inversion-recovery sequences after intratympanic or intravenous administration of gadolinium-based contrast agents. The intratympanic administration provides a higher inner ear contrast [1], yet requires 24 hours before the imaging acquisition and may induce substantial inflammatory reactions in the inner ear [2]. Visualization of the endolymphatic space after single-dose intravenous injection of gadolinium-based contrast agents has been reported to be possible in Meniere's disease (MD) when the administration of contrast media occurs at least 4 hours before images acquisition [3—5].

Gadolinium-based contrast agents physiologically cross the blood-perilymph barrier thus the perilymph appears hyperintense while the endolymph remains hypo-intense because gadolinium chelate does not pass the blood-endolymph and the perilymph-endolymph barriers due to the presence of tight junctions [6,7].

It is well known that the physiochemical properties of gadolinium-based contrast agents are determining factors to cross the round window after intratympanic administration [2]. One can hypothesize that the passage of the blood-labyrinth barrier also depends on biochemical properties of contrast agents. The perilymph enhancement is particularly important to distinguish saccule from utricle and these inner ear structures were recently used to classify MD patients with imaging [4,5]. Enhancement of the semicircular canals is useful to evaluate location of hydrops in the lateral semicircular canal [8]. To our knowledge, no studies have evaluated the differences in inner ear enhancement between two contrast agents after an intravenous administration in humans.

The purpose of this study was to compare the degree of enhancement of the perilymph obtained with two different macrocyclic gadolinium-based contrast agents (gadobutrol and gadoterate meglumine) in patients with MD at 3 T MRI.

## Materials and Methods

### Patients

This was a single center parallel-group imaging study. Twenty patients with a unilateral definite, probable or possible clinical diagnosis of MD based on the AAO-HNS guidelines [9] were recruited between December 2016 and April 2017. The side of the symptomatic ear was defined based on the clinical examination and/or the results of the electrophysiological tests. The patients did not have renal function impairment.

### MR imaging

Ten patients underwent MRI examination with delayed acquisition 4 hours after a single intravenous dose of gadoterate meglumine (Gd-DOTA, Dotarem®, Guerbet, Roissy-Charles de Gaulle, France) at a dose of 0.2 mmol/kg (0.5 mmol/mL) and 10 patients underwent MRI examination after a single dose of gadobutrol (Gd-DO3A-butrol, Gadovist®, Bayer Shering Pharma AG, Berlin, Germany) at a dose of 0.1 mmol/kg (1 mmol/mL). MRI examinations were carried out on a 3 T scanner (General-Electric Healthcare, Discovery®, Milwaukee, WI, USA) with a 16-channel head-neck-spine coil.

We performed a three-dimensional fluid attenuation inversion recovery (3D-FLAIR) MRI sequence with the CUBE® (General-Electric Healthcare) technique with the following parameters: TR: 8000 ms, TE: 130 ms, TI: 2059 ms, $288 \times 288$, variable flip angle and isotropic voxel size of 0.8 mm for acquisition and 0.4 mm for reconstructions. We employed the ARC parallel imaging technique with an acceleration factor of 2, nex: 1 and a scan time of 7 min 30 sec. This sequence was added to a T2-weighted spin-echo sequence with a whole-brain coverage and steady-state free procession sequence covering the labyrinth.

### Image analysis

For each patient, MR images were evaluated independently using Osirix MD® software by two readers blinded to clinical data. A quantitative assessment was performed using the region of interest (ROI) method as previously reported [10]. A 5 $mm^2$ circular ROI was placed in the basal turn of the cochlea and a 50 $mm^2$ circular ROI was placed at the same level in the medulla. The signal intensity ratio (SIR) was defined as the signal intensity of the basal turn divided by that of the medulla. The SIR was measured 3 times and the mean SIR value was calculated for each ear.

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