**MR Imaging of Ménière’s Disease after Combined Intratympanic and Intravenous Injection of Gadolinium using HYDROPS2**

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Endolymphatic hydrops (EH) in Ménière’s disease is currently evaluated by 3-dimensional (3D)-real inversion recovery (IR) sequence after intratympanic (IT) administration of gadolinium (Gd) or by heavily T2-weighted (hT2W)-3D-fluid-attenuated IR (FLAIR) sequence after intravenous (IV) injection of Gd. Unilateral IT injection is usually performed. We employed a method in which we simultaneously administered contrast into one ear intravenously (IV side) and into the other ear both intravenously and intratympanically (IT + IV side) to evaluate EH in 10 patients with Ménière’s disease. We then compared a HYDROPS2 image obtained by subtracting magnetic resonance cisternography from hT2W-3D-FLAIR with an image obtained by 3D-real IR and found that we could evaluate EH in all ears on the HYDROPS2 image but only in the IT + IV side on the 3D-real IR image.

**Keywords:** advanced imaging techniques, magnetic resonance imaging, Ménière’s disease, temporal bone disease, 3D imaging

**Introduction**

Visualization of endolymphatic hydrops (EH) in patients with clinically suspected Ménière’s disease (MD) is currently performed by 3-dimensional inversion recovery with real reconstruction (3D-real IR) imaging after intratympanic (IT) administration of gadolinium-based contrast material (GBCM)1,2 or by heavily T2-weighted (hT2W)-3D-fluid-attenuated inversion-recovery (FLAIR) sequence after intravenous (IV) administration of single-dose GBCM.3–6 The IT method usually provides higher contrast than the IV method and can predict the intralabyrinthine distribution of intratympanically injected gentamicin and steroids.7,8 However, IT administration of GBCM is off-label use and requires puncture of the tympanic membrane.9 Many patients with unilateral disease are reluctant to receive IT administration of GBCM in asymptomatic or ears with better hearing,10 so unilateral IT injection is usually performed even in cases when bilateral EH is suspected. Furthermore, in some patients, impaired permeability of the round window membrane prevents sufficient concentration of GBCM to visualize EH using the IT method.11 Intravenous administration permits simultaneous evaluation of both ears but requires sufficiently sensitive pulse sequences to detect very low GBCM concentration.12

Imaging parameters for the IT and IV methods differ. To simulate drug distribution in one ear and evaluate EH in the other, we have begun to administer contrast materials using a method that combines IT and IV administration (IT + IV). That is, we administer contrast only intravenously in one ear (IV side) and both intravenously and intratympanically in the other (IT + IV side). We have previously detailed the combined IT and IV administration of contrast and the difference in contrast enhancement between the IV and IT + IV sides.10

For the IT method, the use of 3D-real IR images was proposed, and their use allowed separate visualization of the endolymph, perilymph, and bone
on a single kind of image. For the IV method, use of a HYDROPS2 (hybrid of reversed image of magnetic resonance [MR] cisternography and positive perilymph signal by heavily T2-weighted 3D-FLAIR) image was recently proposed to allow separate visualization of the endolymph, perilymph, and bone on a single kind of image.

The purpose of this study was to evaluate whether the use of HYDROPS2 images can obviate the need to use 3D-real IR images for IT + IV study.

Materials and Methods

Ten patients with clinically suspected Ménière’s disease (6 men, 4 women, aged 35 to 68 years) underwent scanning using a 3-tesla MR imaging unit (Verio, Siemens Medical Solutions, Erlangen, Germany) with a 32-channel array head coil. Experienced otolaryngologists diagnosed Ménière’s disease based on the 1995 diagnostic criteria of the American Academy of Otolaryngology-Head and Neck Surgery.

All patients received IT administration of 8-fold-diluted gadopentetate dimeglumine (Magnevist, Bayer Co. Ltd., Osaka, Japan) into one ear 24 hours prior to MR scan and single dose (0.1 mmol/kg) IV administration of gadodiamide hydrate (Ominiscan, Daiichi-Sankyo Co. Ltd., Tokyo, Japan) for both ears 4 hours prior to MR scan. We have previously described the procedure for IT contrast injection. Because recent study protocols in our institution employ gadopentetate dimeglumine for IT use and gadodiamide hydrate for IV study, we employed them for the present study.

The parameters for heavily T2-weighted 3D-FLAIR (hT2W-3D-FLAIR) were: repetition time (TR), 9000 ms; effective echo time (TE), 544 ms; inversion time (TI), 2250 ms; variable refocusing flip-angle echo train, initial flip angle of 180° rapidly decreased to a constant 120°; echo train length, 173; matrix size, 384 × 322; 104 axial, one-mm slice thickness with 180 × 150-mm field of view (FOV); GRAPPA acceleration factor, 2; voxel size, 0.5 × 0.5 × 1 mm; number of excitations (NEX), 4; scan time, 14 min 26 s; readout bandwidth, 434 Hz/pixel; and echo spacing, 5.6 ms.

The parameters for MR cisternography (MRC) by heavily T2-weighted SPACE (sampling perfusion with application-optimized contrast with different flip-angle evolutions) were the same as those used for hT2W-3D-FLAIR except: TR, 4400 ms with driven equilibrium pulse; NEX, 1.8; and scan time, 3 min 15 s.

The parameters for 3D-real IR were: TR, 6000 ms; effective TE, 181 ms; TI, 1650 ms; 180° flip angle (constant throughout echo train) for the conventional turbo-spin-echo refocusing echo train; echo train length, 27; matrix size, 384 × 384; 30 axial, 0.8-mm-thick slices covering the labyrinth with a 160 × 160 mm FOV; GRAPPA acceleration factor, 2; voxel size, 0.4 × 0.4 × 0.8 mm; NEX, one; scan time, 14 min 32 s; readout bandwidth, 213 Hz/pixel; echo spacing, 13 ms; and reconstruction mode, real.

We obtained MRC for an anatomical reference of total lymph fluid, hT2W-3D-FLAIR to visualize enhancement of the perilymph while the endolymph showed low signal (i.e., positive perilymph image [PPI]), and 3D-real IR images for separate visualization of the perilymph, endolymph, and bone on a single kind of image.

By subtracting MRC from PPI, we could obtain an image with 3D-real IR-like presentation after IV, an image we termed HYDROPS2. In this study, we generated HYDROPS2 images by subtracting MRC multiplied by 0.05 from PPI on the scanner console according to the method we described previously.

Our medical ethics committee approved this study, and all patients gave written informed consent. We used the data regarding difference in contrast enhancement between the IV side and IT + IV side of these 10 patients in the previously published study. In the current study, we generated HYDROPS2 images and compared them with 3D-real IR images.

In consensus, 2 neuroradiologists graded contrast enhancement of the perilymph in the cochlea, vestibule, and 3 semicircular canals (SCCs) and the degree of EH. They evaluated the presence of contrast enhancement in each semicircular canal separately.

EH was scored as none (0), mild (1), and significant (2) according to the reported criteria. The presence or absence of significant motion between hT2W-3D-FLAIR and MRC was also evaluated. The apparent double contour of the labyrinth on a HYDROPS2 image was considered the result of motion between scans.

Results

Table summarizes the patients and results of EH grading.

Enhancement of cochlear and vestibular perilymph was recognized in all ears in HYDROPS2 images but only in the IT + IV side in 3D-real IR images, and enhancement of only 22 of 30 semicircular canals could be recognized in the IT + IV side in the 3D-real IR images. In all IV-side ears,
3D-real IR failed to detect the enhancement of the perilymph in the cochlea, vestibule, and 3 semicircular canals. HYDROPS2 detected perilymph enhancement in all cochleas and vestibules and 58 of 60 semicircular canals but did not demonstrate enhancement in the superior and posterior semicircular canal of the IV side in one patient.

Grades of EH in the IT + IV side agreed completely between HYDROPS2 and 3D-real IR images (Figs. 1, 2). No case showed significant motion between scans.

Discussion

In our previous study, the signal intensity ratio of the cochlea against the brain parenchyma was 1.70 ± 0.60 on the IT + IV side and 0.42 ± 0.10 on the IV side, and enhancement was significantly stronger in the IT + IV-side ears than the IV-side ears \((P < 0.001)\).\(^{10}\) The standard deviation was larger for the IT + IV side than the IV side.

The TI value of 3D-real IR in the present study protocol was determined for stronger perilymph enhancement by IT administration.\(^3\) The TI value is determined to be the value between the null point of endo- and perilymph. The degree of contrast enhancement by the IT method varies among patients,\(^11\) so optimal TI value for 3D-real IR obtained after IT might also vary among patients. TI must be longer to compensate for the far weaker enhancement by IV administration. Therefore, a single TI value in 3D-real IR cannot be suitable for both the IT + IV side and the IV side.

The null point of endolymph is nearly constant because there is almost no distribution of GBCM in the endolymph. Therefore, the HYDROPS2 method, based on the subtraction of MRC from \(\text{hT}_{2\text{W}}\)-3D-FLAIR, is robust for both the IT + IV side and the IV side.

The high sensitivity of \(\text{hT}_{2\text{W}}\)-3D-FLAIR might also be valuable for potential cases that demonstrate impaired distribution of GBCM by the IT method, a problem reported in 18% of patients in one study.\(^11\) In the present study, there was no significant motion between \(\text{hT}_{2\text{W}}\)-3D-FLAIR and MRC, but subtraction is susceptible to motion be-

### Table. Evaluation of endolymphatic hydrops after intratympanic and intravenous injection of GBCM

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Side</th>
<th>Hearing level (dB)</th>
<th>EH in the cochlea</th>
<th>EH in the vestibule</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>44</td>
<td>F</td>
<td>Definite MD</td>
<td>R*</td>
<td>68</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>M</td>
<td>Definite MD</td>
<td>L</td>
<td>15</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>M</td>
<td>Definite MD</td>
<td>R*</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>47</td>
<td>M</td>
<td>Definite MD</td>
<td>R</td>
<td>55</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>49</td>
<td>M</td>
<td>Definite MD</td>
<td>R*</td>
<td>65</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>F</td>
<td>Definite MD</td>
<td>L</td>
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<td>2</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>F</td>
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<td>13</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>42</td>
<td>M</td>
<td>Definite MD</td>
<td>L</td>
<td>27</td>
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<td>1</td>
</tr>
<tr>
<td>9</td>
<td>35</td>
<td>M</td>
<td>Definite MD</td>
<td>R*</td>
<td>38</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>36</td>
<td>F</td>
<td>Definite MD</td>
<td>L</td>
<td>48</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

EH, endolymphatic hydrops (0 = none, 1 = mild, 2 = significant); GBCM, gadolinium-based contrast material; MD, Ménière’s disease
*side with intratympanic GBCM injection
Hearing level is an average of 3 frequencies of 500 Hz, 1 kHz, and 2 kHz.
This problem might be overcome by the registration program available on most 3D workstations.

Our study is limited by the small number of cases and because most patients had definite MD. Further study that includes more cases of probable and possible MD is necessary to confirm that HYDROPS2 can replace 3D-real IR even in cases with mild EH. Further study is also necessary to evaluate the diagnostic efficacy of HYDROPS2 images when the IV method is used.

Conclusions

The use of HYDROPS2 images might obviate the need for 3D-real IR images in cases utilizing an IT + IV protocol. HYDROPS2 images permit simultaneous evaluation of the IV side and IT + IV side, contributing to the significant shortening of total examination time and possibly reducing the possibility of examination failure due to weak enhancement by impaired permeability of the round window membrane in the IT + IV side.
Acknowledgements

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References


