Three-dimensional Visualization of Endolymphatic Hydrops after Intravenous Administration of Single-dose Gadodiamide

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Endolymphatic hydrops can be visualized with high contrast-to-noise ratio even after intravenous injection of single-dose gadolinium-based contrast material (IV-SD-GBCM) using HYDROPS-Mi2 images. We applied 3-dimensional rendering software to process HYDROPS-Mi2 images of 15 ears with and without suspected Méniére’s disease and separately visualized the volumes of endo- and perilymph in patients with Méniére’s disease even after IV-SD-GBCM. Such dimensional visualization will aid understanding of the pathophysiology of Méniére’s disease.

Keywords: intravenous, magnetic resonance imaging, Méniére’s disease, 3D imaging

Introduction

Ménière’s disease is characterized by low frequency hearing loss, aural fullness, tinnitus, and acute attacks of vertigo interspersed with periods of quiescence. Endolymphatic hydrops (EH) was first visualized in patients with Ménière’s disease by magnetic resonance (MR) imaging using 3-dimensional (3D) fluid-attenuated inversion recovery (FLAIR) after intratympanic administration (IT) of gadolinium-based contrast material (GBCM).1 A relationship between EH distribution in the labyrinth and symptoms is reported. Endolymphatic hydrops is found in all patients with Ménière’s disease, most importantly in the pars inferior (cochlear duct and saccule).2 However, the structure of the labyrinth is very complex, so 3D visualization of the endo-/perilymphatic space is desirable for proper diagnosis and understanding of the pathophysiology of this disease. Volumetrically separate visualization of the endo-/perilymphatic space on a single volumetric image was first reported using histological sections3 in patients with and without Meniere’s disease and then in patients with Ménière’s disease using MR imaging with optimized 3D-real inversion recovery (IR) sequence and 32-channel head coil at 3T after IT administration of GBCM.4 However, intratympanic injection of GBCM is off-label use, punctures the tympanic membrane, and requires waiting 24 hours before image acquisition. To address these issues, a method for detecting EH by intravenous administration of single-dose GBCM (IV-SD-GBCM) was developed for wider use in the clinical field.

Visualization of EH in patients with Ménière’s disease was reported using heavily T2-weighted 3D-FLAIR (hT2W-3D-FLAIR) images 4 hours after IV administration of single-dose GBCM (IV-SD-GBCM), even with a far lower concentration of GBCM in the perilymph than that after IT-GBCM.5 Creation of a hybrid image by subtracting a positive endolymph image (PEI)6 from a positive perilymph image (PPI), referred to as a HYDROPS image (HYbriD of Reversed image Of Positive endolymph signal and native image of positive perilymph Signal),7 improved the method utilizing IV-SD-GBCM by allowing separate visualization of the endolymph, perilymph, and bone in a single image. A HYDROPS-Mi2 (HYDROPS image Multiplied with heavily T2-weighted MR cisternography) image was then developed that multiplies T2-weighted images onto the HYDROPS image to increase the contrast-to-noise ratio (CNR) between...
the endo- and perilymph more than 200 times.\textsuperscript{8}

To date, 3D visualization of the endo- and perilymphatic space by IV-SD-GBCM has not been reported. Therefore, we investigated whether we could use HYDROPS-Mi2 images obtained after IV-SD-GBCM to generate a single volumetric image that would separately demonstrate the endo- and perilymphatic space.

Materials and Methods

Patients

We evaluated 15 consecutive ears of 8 subjects (3 men, 5 women, aged 32 to 72 years; 10 ears of 5 patients with clinically suspected Ménière’s disease, 4 ears of 2 patients with tinnitus without vertigo, and one healthy ear of the contralateral side in a patient with unilateral acoustic tumor. We excluded the ear of the ipsilateral side with acoustic tumor because of extreme enhancement of the labyrinth.) All patients had undergone MR scanning 4 hours after single-dose (0.2 mL/kg or 0.1 mmol/kg body weight) IV administration of gadolinium-diethylenetriamine pentaacetic acid-bis (methylamide) (gadodiamide: Gd-DTPA-BMA; Omniscan, Daiichi-Sankyo Co. Ltd., Tokyo, Japan) to evaluate the degree of endolymphatic hydrops. Experienced otoneurologists diagnosed Ménière’s disease as definite, probable, or possible according to the guideline of the AAO-HNS (American Academy of Ophthalmology and Otologyngology Head and Neck Surgery).\textsuperscript{9}

MR imaging

All MR imaging was performed on a 3T MR imaging unit (Verio, Siemens, Erlangen, Germany) using a 32-channel array head coil. In all 15 ears, 4 hours after IV-SD-GBCM, heavily T\textsubscript{2}-weighted MR cisternography (MRC) was obtained as the anatomical reference of total lymph fluid, and heavily T\textsubscript{2}-weighted (hT\textsubscript{2}W)-3D-FLAIR with inversion time (TI) of 2250 ms (PPI) and hT\textsubscript{2}W-3D-inversion recovery with TI of 2050 ms (PEI) were obtained as the clinical protocol of our hospital for the evaluation of EH. Parameters were set according to the previous report.\textsuperscript{5}

Detailed scan parameters for MRC were: variable flip angle 3D turbo spin echo technique (SPACE: sampling perfection with application-optimized contrasts by using different flip angle evolutions); repetition time (TR), 4400 ms; echo time (TE), 544 ms; initial 180\textdegree refocusing flip angle rapidly decreased to 120\textdegree constant flip angle for the refocusing echo train; echo train length, 173; restore magnetization pulse (fast recovery pulse); frequency-selective fat-suppression pre-pulse; matrix size, 322 \times 384; 104 axial slices of 1.0-mm thickness covering the labyrinth; field of view (FOV), 15 \times 18 cm; generalized autocalibrating partially parallel acquisition (GRAPPA); acceleration factor, 2; number of excitations (NEX), 1.8; and scan time, 3 min.

Detailed scan parameters of hT\textsubscript{2}W-3D-FLAIR for PPI were: SPACE sequence; TR, 9000 ms; TE, 544 ms; TI, 2250 ms; frequency-selective fat-suppression pre-pulse; initial 180\textdegree refocusing flip angle rapidly decreased to 120\textdegree constant flip angle for the refocusing echo train; echo-train length, 173; matrix size, 322 \times 384; 104 axial slices of 1.0-mm thickness covering the labyrinth; FOV, 15 \times 18 cm; GRAPPA parallel imaging technique with acceleration factor of 2; NEX, 4; and scan time, 14.5 min.

Inversion time was shorter for PEI (2050 ms) than PPI (2250 ms). MRC, PPI, and PEI employed identical FOV, matrix size, and slice thickness to facilitate comparison.

Image processing

HYDROPS images were generated on the scanner console by subtracting the PEI from the PPI, saved, and transferred to a PACS server as a separate series. For subtraction result, negative signal value was allowed. HYDROPS-Mi2 images and 3D surface-rendering images were generated on a free DICOM viewer (OsiriX image software, ver. 3.0.2. 32 bit; downloadable at http://www.osirix-viewer.com/index.html). HYDROPS and MRC images were transferred by CD-ROM to a MacBook PC (Apple Computer, Inc, Cupertino, CA, USA) with OsiriX software. We manually segmented the unilateral labyrinth on the axial thick-slab MIP (maximum intensity projection) image of MRC and copied the region of interest (ROI) of this MIP image onto the HYDROPS-Mi2 image and segmented the labyrinth on the HYDROPS-Mi2 image using this ROI. A 3D surface-rendering (SR) images were generated first from MRC data; then 3D-SR images were generated from the HYDROPS-Mi2 data. The thresholds for segmentation of the endo- and perilymph were subtly and subjectively adjusted with reference to the 3D-SR image generated from MRC data, taking into account labyrinthine shape and size (morphological proportion) on the SR image revealing the entire labyrinthine lymph fluid space. On HYDROPS-Mi2 images, endolymph shows negative signal intensity, and perilymph shows positive signal intensity. The absolute value of signal intensity of the endo- and perilymph is quite large when the MRC is multiplied. On the other hand, the signal intensity value of surrounding bone is near zero. Al-
though the segmentation of negative endolymph signal and positive perilymph signal is straightforward, the shape and size of the 3D-SR image is still susceptible to the changes in threshold. On 3D-SR images, we assigned the color blue to the perilymph and yellow to the endolymph according to the previous study.\textsuperscript{3,4}

**Image analysis**

First, an experienced neuroradiologist reviewed MRC, PPI, PEI, and HYDROPS images and subjectively graded endolymphatic hydrops of the cochlea and vestibule as significant, mild, or absent according to previously proposed criteria. On the HYDROPS-Mi2 image, the same reviewer subjectively determined the presence or absence of misregistration artifact. Apparent double contour of the labyrinth was considered positive for misregistration, in which case the ear was excluded from 3D processing.

After more than a month, the same neuroradiologist generated and evaluated 3D-SR images for all 15 ears. On 3D-SR images from HYDROPS-Mi2, the reviewer subjectively determined the presence or absence of endolymphatic space in the cochlea and vestibule. For the cochlea, endolymphatic space exceeding one turn was considered positive for presence. For the vestibule, visualization of the endolymph was considered positive if the longer diameter of its mass was larger than the caliber of the semicircular canal. The medical ethics committee of our institution approved this retrospective study, with informed consent waived.

**Results**

None of the 15 ears demonstrated misregistration artifact, so 3D-SR images were generated in all ears. On 3D-SR images, endolymphatic space was visualized in the cochlea of all ears with endolymphatic hydrops and none without and in the vestibules of all ears with or without EH. Table summarizes the patients and results of visualization on 3D-SR images for each ear. Figures 1 to 3 show representative images.

**Discussion**

The HYDROPS image has enabled recognition of the endolymphatic space on a single image, even after clinically feasible IV-SD-GBCM,\textsuperscript{7} and the HYDROPS-Mi2 image has increased CNR between the endo- and perilymph more than 200-fold on average, further facilitating recognition of endolymphatic hydrops.\textsuperscript{8} On the HYDROPS and HYDROPS-Mi2 images, perilymph shows positive

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**Table.** Summary of patients and results of visualization of endolymphatic space on 3D-SR images

<table>
<thead>
<tr>
<th>Patient#</th>
<th>Age</th>
<th>Sex</th>
<th>Side</th>
<th>Clinical diagnosis</th>
<th></th>
<th>Cochlea</th>
<th>Vestibule</th>
<th>Cochlea</th>
<th>Vestibule</th>
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<td>58</td>
<td>f</td>
<td>Right</td>
<td>Right probable MD</td>
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<td>0</td>
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<td>positive</td>
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<tr>
<td>2</td>
<td>72</td>
<td>f</td>
<td>Right</td>
<td>Bilateral probable MD</td>
<td></td>
<td>2</td>
<td>2</td>
<td>positive</td>
<td>positive</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>f</td>
<td>Right</td>
<td>Bilateral probable MD</td>
<td></td>
<td>2</td>
<td>2</td>
<td>positive</td>
<td>positive</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>m</td>
<td>Left</td>
<td>Left probable MD</td>
<td></td>
<td>1</td>
<td>0</td>
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<td>positive</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>f</td>
<td>Right</td>
<td>Left definite MD</td>
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<td>2</td>
<td>positive</td>
<td>positive</td>
</tr>
<tr>
<td>6</td>
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<td>m</td>
<td>Right</td>
<td>Bilateral tinnitus</td>
<td></td>
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<td>1</td>
<td>positive</td>
<td>positive</td>
</tr>
<tr>
<td>7</td>
<td>63</td>
<td>f</td>
<td>Right</td>
<td>Bilateral tinnitus</td>
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<td>positive</td>
</tr>
<tr>
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<td>Right acoustic tumor</td>
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<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

MD, Ménière’s disease
3D-SR, 3-dimensional surface rendering
n.a., not applicable
endolymphatic hydrops: 2, significant; 1, mild; 0, no hydrops
信号，内淋巴显示负信号，周围骨显示信号接近零。图像对比度类似于IT-GBCM获得的3D-IR图像。通过增加内淋巴和外淋巴信号之间的CNR，HYDROPS-Mi2图像使3D内淋巴性水肿的可视化成为可能，如图所示。

尽管内淋巴性水肿的严重程度与MR图像的听觉发现之间的关系已经报道过，但是内淋巴性水肿分布模式的3D模式和听觉发现之间的广泛关系尚未得到广泛认识。

图1. 一位34岁女性，左内淋巴性水肿。三维表面渲染（SR）图像由（a、c）磁共振室壁造影（MRC）和（b、d）HYDROPS-Mi2（HYDROPS图像乘以重T2加权MRC）数据生成。（e）HYDROPS-Mi2原始图像和（f）内淋巴区域分割图像。注意背景信号在内淋巴区域分割之前是均匀的。3D-SR图像（b、d）的生成考虑了由MRC图像计算得到的内淋巴性水肿的三维空间图像。在这一耳朵中，显著的内淋巴性水肿在右耳（短箭）和前庭（长箭）中可视化（a）。右耳中的内淋巴性水肿通过分割处理并易于在3D图像中观察。黄色，内淋巴；蓝色，外淋巴。

图2. 一位32岁女性，双侧可能的内淋巴性水肿。三维表面渲染（SR）图像由（a）右耳和（b）左耳的HYDROPS-Mi2（HYDROPS图像乘以重T2加权MR室壁造影）数据生成。（a）右侧耳显著内淋巴性水肿。在左侧耳中，轻微的内淋巴性水肿（b）。在左耳中，未见扩张的内淋巴。虽然在源HYDROPS-Mi2图像中观察到的类似移位是呈箭头状的，但通过在3D-SR图像中更易于观察。

图3. 一位40岁男性，右听神经瘤。三维表面渲染（SR）图像由（a）正常左耳的HYDROPS-Mi2（HYDROPS图像乘以重T2加权MR室壁造影）数据生成。（a）足部视图，（b）左视图。原始HYDROPS-Mi2图像中未见内淋巴性水肿。仅在上部前庭（箭头，a和b）中可见正常大小的内淋巴性水肿。黄色，内淋巴；蓝色，外淋巴。
A pathological study reported the importance of EH in the pars inferior (cochlear duct and saccule) in patients with Ménière’s disease, with possible distention of the saccule into the lateral semicircular canal resembling herniation in severe cases. Therefore, knowledge of the 3D distribution of endolymphatic hydrops in the very complex labyrinthine anatomy provided by 3D-SR images is important.

The mechanism underlying vertigo attacks in patients with Ménière’s disease is still unknown, though sudden flow of endolymph from the cochlea to the vestibule has been suggested. It might be interesting to compare the 3D size and shape of endolymphatic hydrops before and after attack using 3D-SR images.

Our study has several limitations. First, setting the threshold for segmentation of the endo- and perilymph is subjective. Although the absolute value of signal intensity of the endo- and perilymph on HYDROPS-Mi2 images is quite large by the multiplication of MRC images onto HYDROPS images, the 3D-SR image is still susceptible to the threshold value setting. Second, total scan time as long as 32 min to obtain a HYDROPS-Mi2 image presents greater risk of patient motion than the 15 min required for the 3D-real IR sequence used in the IT method. Third, we did not visualize nondilated cochlear endolymph on 3D-SR images, probably because of the smaller size of cochlear than vestibular endolymph in a healthy state; such visualization would require increased spatial resolution. Fourth, our number of study patients was small. Correlation of clinical symptoms and otological tests in a larger patient population is needed to evaluate the appropriateness of the 3D-SR images generated from HYDROPS-Mi2 images for evaluating endolymphatic hydrops.

Conclusions

Use of HYDROPS-Mi2 images obtained after IV-SD-GBCM allows separate visualization of the volumes of endo- and perilymphatic space on a single volumetric image in patients with endolymphatic hydrops. Further clinical study is warranted to establish the utility of 3D-SR images.

References


