

## MAJOR PAPER

# Visualization of Endolymphatic Hydrops after Intratympanic Injection of Gd-DTPA: Comparison of 2D and 3D Real Inversion Recovery Imaging

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**Purpose:** Endolymphatic hydrops of Ménière's disease has been visualized after intratympanic injection of gadopentetate dimeglumine (Gd-DTPA) using a 3-dimensional (3D) inversion-recovery sequence with real reconstruction (3D real IR). This technique enables differentiation of bone and endo- and perilymph space on a single image but requires 15 min of scan time. Therefore, we compared it with 2D real IR, which is faster.

**Materials and Methods:** We investigated 10 ears in 9 patients with suspected Ménière's disease. Twenty-four hours after intratympanic administration of 8-fold diluted Gd-DTPA, we obtained 3D and 2D real IR images as well as magnetic resonance (MR) cisternography at 3 tesla. Three radiologists independently graded the degree of endolymphatic hydrops according to previously proposed criteria. Contrast-to-noise ratio (CNR) between peri- and endolymph was measured.

**Results:** We could evaluate the degree of endolymphatic hydrops in 9 cochleas and 10 vestibules but not in a tenth cochlea, which was too faintly enhanced on both 2D and 3D real IR. Grading of all evaluated cochleas and vestibules agreed completely among the 3 radiologists. Evaluation on 2D real IR and 3D real IR also agreed completely. Mean CNR was significantly higher on 3D than 2D real IR ( $P < 0.05$ ), and CNR on both correlated significantly ( $r = 0.872$ ).

**Conclusion:** Endolymphatic hydrops in Ménière's disease can be evaluated with 2D as well as 3D real IR and in a shorter scan time.

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

## Introduction

Many patients suffer from the symptoms of Ménière's disease, with prevalence of the disease among the entire insured population of the United States recently estimated at 190 per 100,000.<sup>1</sup> Ménière's disease significantly impacts quality of life. Diagnosis of *Certain Ménière's disease* requires histopathologic confirmation besides diagnosis of *Definite Ménière's disease* according to American Academy of Otolaryngology Head and Neck Surgery (AAO-HNS) guidelines.<sup>2</sup> However, such histological confirmation is impossible in living human patients. An imaging diagnosis of endolymphatic hydrops has long been desired.<sup>3</sup> In-

tratympanic injection of gadolinium-based contrast media (GBCM) and 3-dimensional (3D) fluid-attenuated inversion-recovery (FLAIR) at 3 tesla enabled the first separate visualization of endo- and perilymph space in living human patients.<sup>4</sup>

A 3D inversion-recovery sequence with real reconstruction (3D real IR) at 3T then allowed the separate visualization of endolymph, perilymph, and bone using a single pulse sequence.<sup>5</sup> Labyrinthine structure is very complex. Because of the complexity of the labyrinthine structure, 3D real IR and 32-channel head coil at 3T have been used for 3D visualization of endo-/perilymph space.<sup>6</sup>

The previously reported 3D real IR method using 3D turbo spin echo (3D TSE) requires 15 minutes' scan time.<sup>5,6</sup> Wider use of the method will require shorter scan time. Software limitations of different manufacturers' scanners sometimes make it diffi-

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cult to duplicate the 3D real IR protocol. Some scanners have limited flexibility for setting parameters of 3D TSE. Therefore, imaging with 2D real IR may be a viable alternative because acquisition time is shorter, and it is more easily implemented on various manufacturers' scanners.

We compared visualization of endolymphatic hydrops by 3D and 2D real IR images after intratympanic administration of GBCM in patients with suspected Ménière's disease.

## Materials and Methods

### *Patients and injection procedure*

We evaluated 10 ears in 9 patients (7 men, 2 women, aged 28 to 68 years) with suspected Ménière's disease. Our institutional medical ethics committee approved the study, and all patients gave written informed consent.

All patients received intratympanic injection of 8-fold diluted GBCM (Gd-DTPA; gadopentetate dimeglumine, Magnevist, Bayer, Osaka, Japan) according to the previously reported procedure.<sup>4</sup>

### *MR imaging*

Twenty-four hours after intratympanic administration of 8-fold diluted GBCM, 3D and 2D real IR images were obtained as well as magnetic resonance (MR) cisternography by 3D constructive interference in steady state (3D CISS) and 3D FLAIR images. All scans were performed on a 3T MR scanner (MAGNETOM Trio-TIM, Siemens Medical Solutions, Erlangen, Germany) using a commercially available 32-channel array head coil (Siemens).

Parameters for the 3D real IR protocol were: sequence type, conventional 3D TSE with constant flip angle of 180° for the TSE train; repetition time (TR), 6000 ms; echo time (TE), 182 ms; inversion time (TI), 1650 ms; slab-selective inversion pulse; echo train length, 27; echo spacing, 12.2 ms; field of view (FOV), 160 mm; matrix 384 × 384 without zero-fill interpolation (ZIP); 30 slices 0.8-mm thick with slice partial-Fourier factor of 6/8; bandwidth, 213 Hz/pixel; and reconstruction mode "real." Generalized autocalibrating partially parallel acquisitions (GRAPPA) imaging was employed with an acceleration factor of 2<sup>7</sup> and one excitation, and scan time was 15 min. Voxel size was 0.4 mm × 0.4 mm × 0.8 mm. "Real" reconstruction allows positive and negative signal intensity values.<sup>5</sup>

Parameters of 2D real IR were: sequence type, conventional 2D TSE with constant flip angle of 180° for the TSE train; TR, 6000 ms; TE, 267 ms; TI, 1650 ms; slice-selective inversion pulse, echo

train length, 60; echo spacing, 12.2 ms; FOV, 160 mm; matrix 320 × 320 without ZIP; 10 slices; slice thickness, 2 mm with 0.2-mm gap; bandwidth, 250 Hz/pixel; and reconstruction mode "real." We used GRAPPA with acceleration factor of 2 and 6 excitations, and scan time was 5.7 min (10 slices were covered by 3 times of 1.9 min scan covering 3–4 slices). Voxel size was 0.5 mm × 0.5 mm × 2 mm. "Real" reconstruction allows positive and negative signal intensity values.<sup>5</sup>

We performed 3D CISS imaging to obtain reference images of the labyrinthine fluid-space anatomy using parameters: 0.4-mm isotropic voxels with ZIP in the slice encoding direction; TR, 6.4 ms; TE, 3.2 ms; and flip angle, 50°. Scan time was 3.5 min.

Parameters for 3D FLAIR were: TR, 9000 ms; effective TE, 458 ms; variable flip-angle echo train with average flip angle, 120°; echo train length, 119; echo spacing, 3.72 ms; matrix size, 214 × 256 without ZIP; 48 axial 0.8-mm-thick slices with ZIP in the slice encoding direction; FOV, 15 × 18 cm; bandwidth, 592 Hz per pixel; and acceleration factor, 2, using GRAPPA. Voxel size was 0.7 mm × 0.7 mm × 0.8 mm, number of excitations, 2, and total scan time, 5 min 17 s.

### *Image evaluation*

#### **Qualitative evaluation**

On a picture archiving communication system (PACS) viewer (Rapideye, Toshiba, Tokyo, Japan), 3 radiologists with 22, 12, and 3 years' experience in neuroradiology independently graded the degree of endolymphatic hydrops from 0 to 2 according to the previously reported grading criteria,<sup>8</sup> with 2 indicating significant, 1, mild, and 0, no endolymphatic hydrops. Enhancement of the perilymph that was too faint to evaluate endolymphatic hydrops was graded as "faint." The 3 radiologists knew the patients had suspected Ménière's disease because intratympanic Gd-DTPA injection is usually performed for these patients. The 3 radiologists reviewed the 2D and 3D real IR image series in random order. After an interval of more than one month, each radiologist also evaluated 3D FLAIR images independently from the other 2 radiologists to grade endolymphatic hydrops.

#### **Quantitative evaluation**

The radiologist with the longest experience measured the contrast-to-noise ratio (CNR) between the endolymph and perilymph for 2D and 3D real IR and 3D FLAIR images. A circular region of interest (ROI) was drawn in the vestibular endolymph and perilymph, where usually, a larger ROI can be

drawn than in the cochlea. The ROI was first drawn on the 3D real IR image, then copied on the corresponding 2D real IR and 3D FLAIR images. In the case of any misregistration between 2D real IR, 3D FLAIR, and 3D real IR images, ROI placement was manually adjusted. The diameter of the ROI was 2 mm for the endolymph and one mm for the perilymph. If the vestibular endolymph was very large and there was no surrounding perilymph in the vestibule, the ROI was placed in the lateral semicircular canal. Noise was estimated as the standard deviation of the ROI drawn in the ipsilateral cerebellar peduncle; we considered the cerebellar peduncle to be the most uniform structure near the inner ear. The diameter of this ROI was 3 mm. We defined the CNR as the difference in signal intensity between the perilymph and endolymph divided by the standard deviation of the ROI in the cerebellar peduncle. We performed analysis of variance (ANOVA) to determine significant difference among CNR values by 2D and 3D real IR and 3D FLAIR, with  $P < 0.05$  considered significant, and then performed Fisher's protected least significant difference *post hoc* test to compare all pairs of 2 sequences. We also obtained the correlation coefficient between CNR values on 2D and 3D real IR.

**Results**

There was no side effect from intratympanic Gd-DTPA administration. Table details patient char-

acteristics, results of hydrops grading, and CNR values.

*Qualitative evaluation*

The 3 radiologists completely agreed in their grading of all evaluated cochleas and vestibules. Their evaluation on 2D and 3D real IR also agreed completely (Fig. 1). We could evaluate the degree of endolymphatic hydrops in 9 cochleas and 10 vestibules on 2D and 3D real IR images, but faint enhancement in one cochlea on both 2D and 3D real IR images prevented its evaluation (Fig. 2). In this particular cochlea, only 3D FLAIR visualized significant endolymphatic hydrops. In another patient, mild cochlear endolymphatic hydrops visualized on 2D and 3D real IR images could not be recognized on 3D FLAIR images.

*Quantitative evaluation*

The mean CNR between the perilymph and endolymph was  $17.0 \pm 7.8$  (mean  $\pm$  standard deviation) on 3D real IR,  $11.2 \pm 6.0$  on 2D real IR, and  $6.7 \pm 3.0$  on 3D FLAIR. CNR values differed significantly between 2D and 3D real IR and between 3D real IR and 3D FLAIR but not between 2D real IR and 3D FLAIR. There was significant linear correlation of CNR values between 2D and 3D real IR ( $r = 0.872$ ).

**Table.** Summary of patient characteristics, results of grading, and contrast-to-noise ratios

Patient	Age (years)	Sex	Side	3D real IR			2D real IR			3D FLAIR		
				cochlea	vestibule	CNR	cochlea	vestibule	CNR	cochlea	vestibule	CNR
1	68	F	R	2	2	9.5	2	2	5.4	2	2	3.1
2	49	M	R	2	0	31.0	2	0	19.5	2	0	8.0
3	61	M	R	2	2	15.6	2	2	15.0	2	2	8.0
4	28	M	L	1	2	22.6	1	2	16.8	0	2	8.6
5	62	F	L	2	2	24.7	2	2	17.0	2	2	9.8
6	60	M	R	2	2	16.2	2	2	11.3	2	2	4.8
7	54	M	L	faint	1	5.5	faint	1	2.3	2	1	2.3
8	56	M	L	2	2	17.5	2	2	13.0	2	2	11.5
9	41	M	R	2	2	18.5	2	2	5.4	2	2	4.8
			L	2	1	8.7	2	1	6.1	2	1	5.8

faint: enhancement too faint to be evaluated

2: significant endolymphatic hydrops

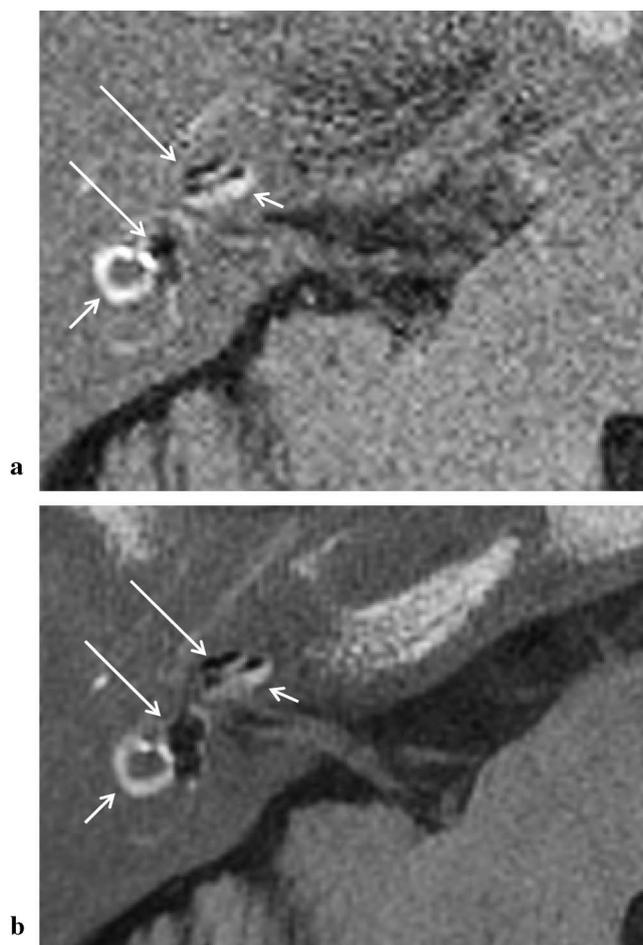
1: mild endolymphatic hydrops

0: no endolymphatic hydrops

CNR: contrast-to-noise ratio between perilymph and endolymph

FLAIR: fluid-attenuated inversion-recovery

real IR: inversion-recovery sequence with real reconstruction



**Fig. 1.** A 62-year-old man with right-side Ménière's disease. Images were obtained 24 hours after intratympanic injection of gadolinium-based contrast media (GBCM). Two-dimensional (2D) real inversion-recovery (IR) image (a) and 3D real IR image (b). (a) This 2D real IR image shows enlarged endolymphatic space (arrows) as negative signal and perilymph space as positive signal (short arrows). The 2D real IR image is noisier than (b) the 3D real IR image. All 3 reviewers graded endolymphatic hydrops as "significant" for both the cochlea and vestibule on both 2D and 3D real IR images.

## Discussion

We observed identical grades of endolymphatic hydrops for 2D and 3D real IR, and the scan time of 2D real IR was approximately one-third that of 3D real IR. When only the center of the labyrinth is scanned with 3 to 4 slices, scan time can be as short as 2 min, which is less than one-seventh the duration of 3D real IR.

CNR values were significantly lower by 2D than 3D real IR because of the shorter scan time and longer effective TE of 2D than 3D real IR and perhaps because of partial volume averaging effect due

to the thicker slices of 2D real IR.

In this study, we estimated noise as the standard deviation of the ROI in the cerebellar peduncle. Estimating noise on images obtained using parallel imaging is usually difficult in a clinical setting.<sup>9</sup> Error can result if noise is estimated for an ROI in the air area in the peripheral part of the field of view;<sup>10</sup> we selected the cerebellar peduncle as the most uniform structure near the inner ear in the field of view. Although this method may not be perfect for measuring CNR, we believe the significant correlation in CNR values by 2D and 3D real IR make it a reasonable choice.

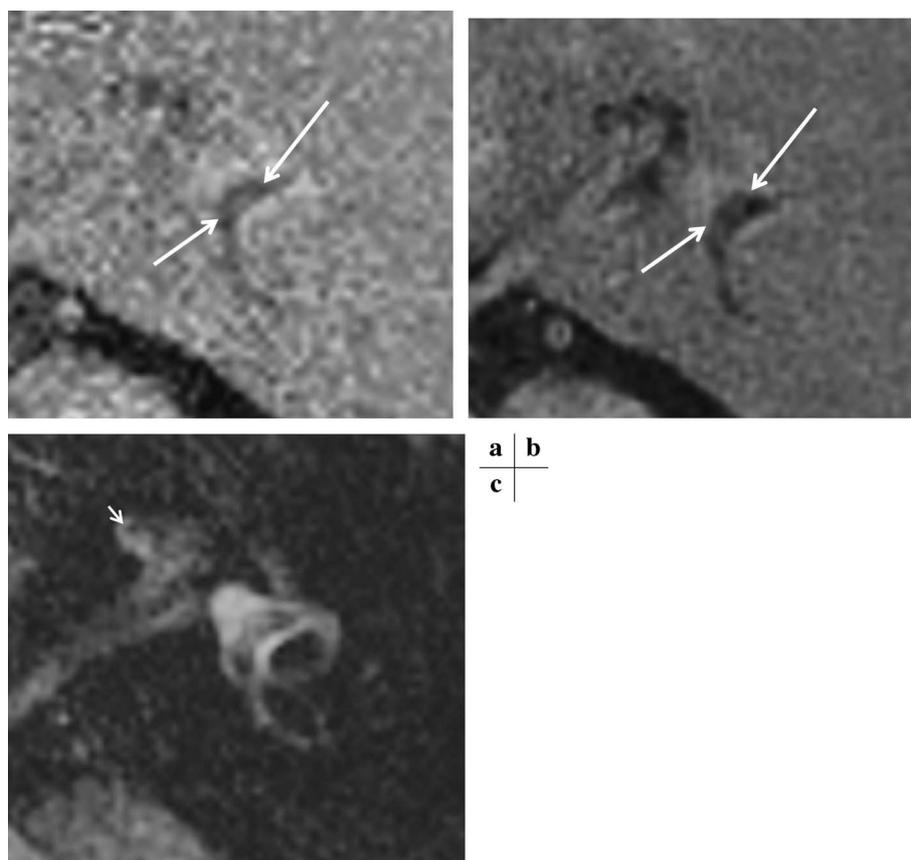
Two-dimensional real IR was noisier than 3D real IR with the current parameters. However, in a clinical setting, scan time of 15 min for 3D real IR can be too long for some patients. The lower risk of image degradation by patient motion for 2D than 3D real IR images suggests 2D real IR as a practical solution for restless patients. The scan time of 3D real IR might also be shortened by reducing matrix size or increasing slice thickness. Future study should compare the images acquired by the shorter version of 3D real IR protocol and those by 2D real IR protocol using similar scan times.

Our study has some limitations. In the case with faint enhancement of the cochlea, image quality was inadequate with 2D and 3D real IR, and we still needed 3D FLAIR. However, we used 3D FLAIR with variable flip angle echo train that caused blurring of the small endolymphatic space in the cochlea. In another patient, mild cochlear endolymphatic hydrops visualized on 2D and 3D real IR images was not visualized on 3D FLAIR images. Thus, 3D FLAIR and 3D or 2D real IR images still complement each other.

The absence of a reference standard for degree of endolymphatic hydrops prevents the comparison of sensitivity and specificity of grading endolymphatic hydrops by 2D and 3D real IR, although our grading results agreed completely between the 2 methods. Future comparison of the 2 methods in larger numbers of patients will require some standard of reference.

## Conclusions

In conclusion, we could evaluate the grade of endolymphatic hydrops using 2D as well as 3D real IR images and with shorter scan duration. Although 2D real IR images are noisier and have lower spatial resolution than 3D real IR images, we achieved identical grading of endolymphatic hydrops using either technique. We expect that 2D real IR images could be more widely used in the clinical setting for



**Fig. 2.** A 54-year-old man with left-side Ménière's disease. (a) Two-dimensional (2D) real inversion-recovery (IR) image, (b) 3D real IR image, (c) 3D fluid-attenuated inversion-recovery (FLAIR) image. On (a) and (b), cochlear enhancement is too faint to grade endolymphatic hydrops. Vestibular mild hydrops can be graded on both 2D and 3D real IR images (arrows). Evaluation of the cochlea requires a 3D FLAIR image (c), on which significant endolymphatic hydrops is visualized in the cochlea (short arrow).

grading endolymphatic hydrops.

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