The Assessment of Endolymphatic Hydrops with High-resolution 3D Real Inversion Recovery and 3D Fluid Attenuated Inversion Recovery Sequences

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Introduction

Since the initial study by Nakashima et al. [1] who demonstrated that endolymphatic hydrops in patients with Ménière’s disease can be visualized using MR imaging following an intratympanic injection of gadolinium, this topic has gained strong clinical interest internationally [2–13]. The two most common sequences used in the evaluation of endolymphatic hydrops are a 3D Fluid Attenuated Inversion Recovery with variable flip angles turbo spin echo sequence (3D SPACE FLAIR) and a 3D real inversion recovery sequence (3D real IR) [1–3]. However, the use of the two sequences varies across different countries. The aim of this study was to compare and contrast the two sequences in terms of the imaging results to best determine their use in clinical practice.

Methods

Patients who have received a diagnosis of Ménière’s disease or delayed endolymphatic hydrops from the otolaryngologist (in the period October 2013 to May 2014) were retrospectively identified and their MR images analyzed. Ménière’s disease was diagnosed according to the diagnostic criteria established by the Chinese Society of Otolaryngology of the Chinese Medical Association in 2006 [14] while delayed endolymphatic hydrops was diagnosed according to the criteria of Komatsuzaki et al. [15]. Patients must have undergone MR imaging of their endolymphatic system with no significant head movement during imaging and have no history of otitis media or inner ear surgery. 40 patients were identified; 26 males and 33 females ranging in age from 19 to 67 years (mean = 48 ± 13 years), with 52 affected ears. The main symptoms reported by the patients include dizziness, hearing loss, tinnitus and ear stuffiness.

All patients underwent MR imaging 24 hours following an injection of contrast media into the tympanum through the tympanic membrane. An otology clinician with long experience in auripuncture injected a Magnevist solution (Bayer Healthcare, Berlin, Germany) that has been diluted 8-fold with saline into the tympanum through the tympanic membrane of the patient. The injection was performed using a 23-G needle with a 1 ml syringe and approximately 0.4–0.5 mm of the diluted solution was injected. Following the injection, patients were advised to rest their head for an hour, speak as little and swallow as little as possible. Patients were imaged 24 hours later on a MAGNETOM Verio with a 32-channel Head coil (see Table 1 for sequence parameters).

The images were assessed for differences in signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) and also for the ability to visualize the presence of endolymphatic hydrops. Analyses for SNR and CNR were performed by

<table>
<thead>
<tr>
<th>Parameter</th>
<th>3D SPACE FLAIR</th>
<th>3D real IR</th>
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</thead>
<tbody>
<tr>
<td>Repetition time (TR) (ms)</td>
<td>6000</td>
<td>9000</td>
</tr>
<tr>
<td>Echo time (TE) (ms)</td>
<td>387</td>
<td>181</td>
</tr>
<tr>
<td>Inversion time (TI) (ms)</td>
<td>2100</td>
<td>1730</td>
</tr>
<tr>
<td>Echo train length</td>
<td>173</td>
<td>--</td>
</tr>
<tr>
<td>Voxel resolution (mm)</td>
<td>0.7 x 0.7 x 0.6</td>
<td>0.4 x 0.4 x 0.8</td>
</tr>
<tr>
<td>Field-of-view (FOV) (mm)</td>
<td>220 x 220</td>
<td>160 x 160</td>
</tr>
<tr>
<td>Acquisition time (TA) (mins)</td>
<td>6:26</td>
<td>14:32</td>
</tr>
</tbody>
</table>

Table 1: Imaging parameters of the 3D SPACE FLAIR and 3D real IR sequences.
first identifying the 3D real IR image where the vestibule is clearly visible and a circle region-of-interest (ROI) of 0.02 cm² was drawn in the perilymph within the perilymphatic space. The ROI was replicated on the corresponding 3D SPACE FLAIR image and manually matched in location. Similar ROIs were created in the cerebrospinal fluid (0.1 cm²) within the cerebellopontine angle and in the brainstem (0.5 cm²). SNR ratio was defined as:

\[
\frac{(S_{\text{vestibule}} - S_{\text{cerebrospinal fluid}})}{\sigma_{\text{brainstem}}} = \text{SNR}
\]

Evaluations for the presence of endolymphatic hydrops in the inner ear, vestibule and the basal, middle and apical turns of the cochlea of all affected ears were performed. For each turn of the cochlea, the diagnosis was made according to the standards proposed by Nakashima et al. [16]. The absence of endolymphatic hydrops is defined by no displacement of Reissner’s membrane inside the cochlea (Fig. 1). The presence of cochlear endolymphatic hydrops is visualized by the significant expansion of the non-enhancing endolymphatic space relative to the contrast-enhanced perilymphatic area (Fig. 2). The vestibule is considered normal if the area of low signal in the vestibule is confined to a level above the horizontal semicircular canal; an extension of the low signal area downwards below the horizontal semicircular canal is considered to be indicative of endolymphatic hydrops [5]. When endolymphatic hydrops are seen in either the cochlea or vestibule, a positive diagnosis of endolymphatic hydrops is made for the inner ear.

**Results**

SNR of the 3D real IR (28.06 ± 12.71) was significantly higher than the 3D SPACE FLAIR (17.46 ± 6.38; t = 6.37, p < 0.05). CNR was likewise significantly higher for the 3D real IR (33.79 ± 13.52) compared to the 3D SPACE FLAIR (15.40 ± 6.04; t = 11.11, p < 0.05). In the 3D real IR images, the endolymphatic space (low signal), the perilymphatic space (high signal) and bone (intermediate signal) can be differentiated (Fig. 2B, D). In comparison, with the 3D SPACE FLAIR, it is more difficult to differentiate between the endolymphatic space and the surrounding low-signal bone (Fig. 2A, C).

![Figure 1: 3D SPACE FLAIR (1A) and 3D real IR (1B) imaging of a normal left inner ear. There are no indications of enlarged endolymphatic spaces and displacement of Reissner’s membrane.](image1)

![Figure 2: 3D SPACE FLAIR (2A, C) and 3D real IR (2B, D) imaging of the right ear of a patient with Ménière’s disease. The presence of endolymphatic hydrops (marked by arrows) can be visualized within the cochlea (2A and B) and within the vestibule (2C and D). While the presence of endolymphatic hydrops within the cochlea is visible on the 3D SPACE FLAIR image (2A), the 3D real IR image clearly shows a severe presence at each turn of the cochlea (2B). The presence of vestibular endolymphatic hydrops is visible as an enlarged area of low signal in the patient’s right vestibule on the 3D SPACE FLAIR (2C) and 3D real IR (2D). Note that in the 3D real IR image, there is clear differentiation between the endolymphatic space (low signal), the perilymphatic space (high signal) and the surrounding bone (intermediate signal) while it is more difficult to differentiate between the endolymphatic space from the surrounding low-signal bone in the 3D SPACE FLAIR image.](image2)
Comparing the 3D real IR to the 3D SPACE FLAIR, the detection rates of endolymphatic hydrops were identical for the vestibule while significantly higher in all turns of the cochlea for the 3D real IR (Table 2). In all cases, endolymphatic hydrops which could be detected in the 3D SPACE FLAIR could also be visualized in the 3D real IR (Figs. 2A–D). In addition, there were a significant number of cases where milder cochlear endolymphatic hydrops were visible only in the 3D real IR images (Figs. 3 and 4). In particular, detection rate for endolymphatic hydrops at the apical turn of the cochlea was much lower for the 3D SPACE FLAIR (19.2%) images compared to the 3D real IR images (88.5%; Fig. 4).

**Discussion and conclusions**

The two most commonly used MR sequences for imaging endolymphatic hydrops are the 3D SPACE FLAIR and 3D real IR. The 3D SPACE FLAIR, using variable flip angles, achieves high-resolution 3D imaging in relatively short scan times and enables differentiation between the low-signal endolymphatic space and the high-signal perilymphatic space. However, with this sequence, the endolymphatic space cannot be distinguished from the surrounding low-signal bone (Figs. 3 and 4). The 3D real IR sequence is an inversion-recovery turbo spin-echo (TSE) sequence with real reconstruction [2, 3]. Information about the magnetization polarity is preserved and the contrast reflects the real signal value instead of the absolute value. With the appropriate T1 (≈ 1700 ms for 3T), the endolymphatic space will be hypo-intense (negative value), the perilymphatic space will be hyper-intense (positive value) while the surrounding bone will be iso-intense (near 0), which enables differentiation between these three structures with a single scan. In addition, the higher resolution used for the 3D real IR may help in the differentiation of finer structures in the inner ear and have been adopted more in recent studies [2, 7, 9, 10]. To our knowledge, this is the first study, to date, which reports a systematic comparison of the diagnostic quality of these two sequences.

Significantly higher signal-to-noise and contrast-to-noise ratios were found for the 3D real IR sequence compared to the 3D SPACE FLAIR sequence. The higher contrast-to-noise ratio reflects the difference in signals between the endolymphatic space and the perilymphatic space, with the 3D real IR sequence being clearly superior.

<table>
<thead>
<tr>
<th>Ear</th>
<th>Rate (%)</th>
<th>Ear</th>
<th>Rate (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affected side’s inner ear¹</td>
<td>41</td>
<td>78.8</td>
<td>49</td>
<td>94.2</td>
</tr>
<tr>
<td>Vestibule</td>
<td>39</td>
<td>75.0</td>
<td>39</td>
<td>75.0</td>
</tr>
<tr>
<td>Basal turn of the cochlea</td>
<td>33</td>
<td>63.5</td>
<td>46</td>
<td>88.5</td>
</tr>
<tr>
<td>Middle turn of the cochlea</td>
<td>37</td>
<td>71.2</td>
<td>46</td>
<td>88.5</td>
</tr>
<tr>
<td>Apical turn of the cochlea</td>
<td>10</td>
<td>19.2</td>
<td>46</td>
<td>88.5</td>
</tr>
</tbody>
</table>

Table 2: Detection rate for endolymphatic hydrops in the affected ears (n = 52).

¹Noted as positive if endolymphatic hydrops were detected in any part of the inner ear.
As endolymphatic hydrops occurs mainly in the cochlea and balloon and less frequently in the utricle and semicircular canal [17, 18], our assessment was limited to the cochlea and the vestibule. A significantly higher detection rate for endolymphatic hydrops in the cochlea, especially in the apical turn, was achieved for the 3D real IR sequence relative to the 3D SPACE FLAIR while detection rates were the same in the vestibule.

The cochlear structure is small and highly detailed; there are 2.50–2.75 turns, and the diameter of each turn is very small (the diameter of the basal turn is about 1.4 mm) [21]. In the early stage of Ménière's disease, endolymphatic hydrops start in the apical turn of the cochlea and will grow downward when the extent of the hydrops increases. For the 3D SPACE FLAIR sequence, the detection rate of hydrops was much lower in the apical turn (n = 10) compared to the middle (n = 37) and basal (n = 33) turns, which is inconsistent with the known clinical evolution of this disease. In contrast, the detection for the 3D real IR sequence was consistent across the three turns and better reflects the evolution of the disease (Figs. 3 and 4).

There are two reasons as why it is more difficult to visualize hydrops at the apical turn of the cochlea with the 3D SPACE FLAIR sequence. First, the endolymphatic space is virtually indistinguishable from surrounding bone which makes it extremely difficult to visualize hydrops in small structures such as the apical turn. Secondly, the signal-to-noise ratio and the resolution of the sequence are lower, again making it difficult to appreciate the smaller structures of the inner ear.

The 3D-real IR sequence has a higher CNR and resolution with a contrast that provides strong advantage in the display of endolymphatic hydrops. However, the scan time of the 3D real IR is significantly longer, generally taking around 12 to 16 minutes, which has limited its use on a wider clinical basis. With further optimization of the sequence parameters and the development of new MR hardware, this problem is expected to be resolved in the near future.

In conclusion, the 3D real IR sequence is superior to the 3D-FLAIR-VFL sequence for the MR assessment of endolymphatic hydrops and may help in the early diagnosis of Ménière's disease and other diseases of the inner ear.

References
3 Naganawa S, Ishihara S, Iwano S, Sone M, Nakashima T. Three-dimensional (3D) visualization of endolymphatic hydrops after inversion-recovery turbo spin-echo (TSE) sequence and application of a 32-channel head coil at 3T.