MAJOR PAPER

Estimation of Gadolinium-induced T_1 -shortening with Measurement of Simple Signal Intensity Ratio between the Cochlea and Brain Parenchyma on 3D-FLAIR: Correlation with T_1 Measurement by TI Scout Sequence

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Purpose: T_1 -shortening of labyrinthine fluid on 3-dimensional fluid-attenuated inversion recovery (3D-FLAIR) has been reported in many inner ear disorders. Although semi-quantitative assessment by simple signal intensity ratio between cochlear fluid and brain tissue has been tried, its feasibility using a multi-channel phased-array head coil with an inherently inhomogeneous sensitivity distribution has not been fully evaluated. We evaluated the feasibility of measuring simple signal intensity ratio by correlating rapid T_1 measurements using an inversion time (TI) scout sequence.

Materials and Methods: We evaluated 10 patients with Meniere's disease and 4 patients with sudden deafness. Nine of the patients with Meniere's disease received a unilateral intratympanic injection of Gd-DTPA; the tenth patient received bilateral injections. The 4 patients with sudden deafness received a double-dose intravenous injection. Magnetic resonance (MR) images were obtained 24 hours after intratympanic injections and 4 hours after intravenous injections at 3 tesla using a 32-channel head coil. We measured the ratio (CM ratio) between the signal intensity of the perilymph in the cochlea (C) and that of the medulla oblongata (M) and correlated it with the null-point inversion time (TI_{null}) obtained with the TI scout sequence. The TI scout consisted of 85 images obtained with TI values between 132.5 and 3087.5 ms at increments of 37.5 ms.

Results: The correlation coefficient between TI_{null} and the natural logarithm of the CM ratio was -0.88 ($P < 0.01$). There was significant negative linear correlation.

Conclusions: Measurement of the simple signal intensity ratio between the cochlea and the medulla can be used for semi-quantitative analysis of 3D-FLAIR. The results of this study may facilitate clinical research of inner-ear disease using 3D-FLAIR.

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

Introduction

Three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) has been reported to detect subtle changes in lymph fluid composition that cannot be detected by T_1 -weighted images, such as slightly increased protein concentration, small hemorrhage, and faint Gd-DTPA (gadopentetate dimeglumine) enhancement.^{1,2} Various reports have described the utility of 3D-FLAIR images in eval-

uating inner ear disorders, such as sudden deafness,^{2,3} acoustic neurinoma,⁴ labyrinthine fistula with cholesteatoma,⁵ otosclerosis,⁶ enlarged endolymphatic duct and sac syndrome,⁷ and others.⁸⁻¹⁰ In studies correlating the signal intensity of cochlear lymph fluid on 3D-FLAIR and hearing level,^{3,4} semi-quantitative evaluation of cochlear fluid signal was performed by measuring the ratio between the signal of cochlear fluid and that of the brain, such as of the medulla oblongata⁴ or cerebellum,³ on pre- and post-contrast-enhanced 3D-FLAIR. However, these studies used multi-channel array head coils with non-uniform sensitivity for

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signal reception¹¹ and were performed at 3 tesla, where B_1 inhomogeneity sometimes degrades image uniformity.¹² More precise analysis requires a method without these limitations. One alternative would be T_1 measurement using multiple inversion recovery acquisitions with single spin echo and repetition time (TR) typically more than 5 times longer than the maximum T_1 value.¹² However, even for precise T_1 measurement, this method still takes too long for acquisition in a clinical setting. For more rapid assessment, the so-called Look-Locker sequence or inversion time (TI) scout sequence has been applied to determine the optimal TI to assess delayed enhancement of cardiac muscle viability.^{13–15} These quick methods are used to acquire multiple balanced steady-state free precession (b-SSFP) or true fast imaging with steady-state precession (FISP) images with variable TI after single inversion pulse. We evaluated the feasibility of using signal intensity ratio on 3D-FLAIR images to assess the composition of inner ear fluid by correlating the values obtained with the TI scout method.

Materials and Methods

Patients

We evaluated 14 patients (5 men, 9 women, aged 26–70 years), 10 with Meniere's disease and four with sudden deafness. Nine of the 10 patients with Meniere's disease received unilateral intratympanic injection of 8-fold diluted Gd-DTPA (gadopen-tetate dimeglumine; Magnevist, Bayer, Osaka, Japan), and the other received bilateral injection because of suspected bilateral disease. After 24 hours, the 10 then underwent MR scan. The 4 patients with sudden deafness received double-dose intravenous injection of Gd-HP-DO3A (gadoteridol; ProHance, Eisai, Tokyo, Japan) and underwent MR scan 4 hours after injection. We evaluated all 28 ears, including the non-injected side of 9 patients with unilateral intratympanic injection, for further measurements. These patients were imaged for the assessment of endolymphatic hydrops.^{16,17}

Intratympanic gadolinium injection

A previous report¹⁶ detailed the methods for intratympanic gadolinium injection and found a delay of 24 hours between intratympanic gadolinium injection and MR imaging to be optimal to allow the wide distribution of gadolinium in the perilymphatic space of the labyrinth. Gd-DTPA was diluted 8-fold with saline (v/v 1:7) and injected through the tympanic membrane using a 23-gauge needle and a one-mL syringe with the patient su-

pine with head turned approximately 30° away from the sagittal line toward the healthy ear. Injection until a backflow of fluid into the external ear was observed through a microscope resulted in an injected volume of 0.4 to 0.5 mL per patient. Following injection, the patient remained supine for 60 min with head turned approximately 60° away from the sagittal line toward the healthy ear. Gentamicin or steroid was not injected at the same time. Intratympanic injection of Gd-DTPA is an off-label use.

Intravenous gadolinium injection

Enhancement of perilymph fluid has been reported 4 hours after intravenous injection of single-dose Gd-DTPA in healthy subjects, but contrast concentration has been insufficient to visualize endolymphatic space. We doubled the dose of contrast medium (0.2 mmol/kg, 0.4 mL/kg) to visualize endolymphatic hydrops in the patients with Meniere's disease, utilizing the highest dose approved in our country. We employed Gd-HP-DO3A because it is the only drug approved in our country for double-dose use in central nervous system imaging to detect metastatic brain tumor.

MR imaging

We performed all scans on a 3T MR system (Magnetom Trio, a Tim system, Siemens Medical Solutions, Erlangen, Germany) using a 32-channel array head coil.

We acquired 3D images in all patients: 3D-constructive interference in the steady state (CISS); 3D-FLAIR by conventional turbo spin echo (3D-FLAIR-CONV);^{1,16} 3D-FLAIR by variable flip angle turbo spin echo (3D-FLAIR-VFL);¹⁸ and 3D-inversion recovery with real reconstruction (3D-real IR)¹⁹ as well as TI scout images. To evaluate signal intensity, we analyzed 3D-FLAIR-VFL and TI-scout images because the 0.8-mm slice thickness of the 3D-FLAIR-VFL protocol is less susceptible to partial volume averaging artifact than the 2-mm slice thickness of 3D-FLAIR-CONV. However, 3D-FLAIR-CONV has been shown to have better visualization of endolymphatic hydrops of the cochlea. We did not use 3D-real IR, although it is good for separately visualizing the endolymph, perilymph, and bone¹⁹ because it is not as sensitive as 3D-FLAIR for detecting faint enhancement.²⁰ However, we did obtain 3D-real IR and 3D-FLAIR-CONV to evaluate endolymphatic hydrops for clinical needs, as stated. We referred to 3D-CISS images to set regions of interest (ROI) on 3D-FLAIR-VFL and TI scout images. Details of pulse sequence are described below.

The parameters for 3D-CISS were: 0.4-mm isotropic voxels; TR, 6.4 ms; echo time (TE), 3.2 ms; and flip angle, 50 degrees. Scan time was 3.5 min.

The parameters for 3D-FLAIR-VFL were: TR, 9000 ms; effective TE, 458 ms; variable flip-angle echo train with an average flip angle of 120 degrees; echo-train length, 119; echo spacing, 3.72 ms; matrix size; 214×256 ; 48 axial 0.8-mm-thick slices covering the labyrinth; field of view (FOV), 15×18 cm; bandwidth, 592 Hz per pixel, and acceleration factor, 2; generalized autocalibrating partially parallel acquisition (GRAPPA) parallel imaging technique;²¹ voxel size, $0.7 \times 0.7 \times 0.8$ mm; and 2 excitations. Total scan time was 5 min 17 s. We used non-selective inversion pulses and slab-selective excitation pulses. The features of this variable flip-angle sequence have been reported elsewhere.^{18,22} This sequence allows the use of very long echo-train lengths, in the range of 100–200, without severe blurring, while maintaining contrast similar to that of 3D-FLAIR-CONV, even with a long effective echo time.

Scan parameters for TI scout images were: 2D-true FISP sequence with inversion recovery pulse; TR, 35.0 ms; TE, 1.9 ms; flip angle, 35 degrees; FOV, 16.3×25.6 cm; matrix, 104×256 ; 5-mm thickness; no parallel imaging technique. After ap-

plying the inversion pulse with cardiac pulse triggering, true FISP data were acquired with inversion times of 132.5 to 3087.5 ms at increments of 37.5 ms. Eight lines in k-space were filled per one inversion pulse. The intervals between inversion pulses were longer than 16 s. We obtained 85 images with different inversion times in the approximately 3-min scan time.

Because multi-channel array coils inherently produce images of inconsistent intensity, we applied a correction based on a 3D sensitivity map for the 32-channel head coil. For each patient, the scanner automatically computed a sensitivity map based on two 3D references scans, one measured with the built-in body coil (nearly homogeneous sensitivity across the head) and another, with the multi-channel coil. The receiver gain was fixed and not modified among patients.

ROI analysis

We measured cochlear signal intensity on 3D-FLAIR-VFL by setting a circular ROI in the perilymph space of the basal turn of the cochlea, referring to 3D-CISS images. We set a circular ROI of one-mm diameter in the cochlear perilymph space and one of 6-mm diameter in the center of the medulla oblongata on 3D-FLAIR-VFL (Fig. 1a). We defined the CM ratio as the signal intensity

Fig. 1. An example of region of interest (ROI) setting. A 68-year-old man with left Meniere's disease. **a)** On 3-dimensional fluid-attenuated inversion recovery by variable flip angle turbo spin echo (3D-FLAIR-VFL) image, ROI #1 was set at the center of the medulla oblongata with a diameter of 6 mm, and ROI #2 was set in the scala tympani of the basal turn of the cochlea with a diameter of one mm. The ratio of the signal intensity of the perilymph in the cochlea with that of the medulla oblongata (CM ratio) was given as the signal intensity value of the ROI in the cochlea divided by that in the medulla oblongata. Note that the enlarged endolymphatic space is visualized as an area of low signal intensity (arrow). **b)** On the first inversion time (TI) scout image (TI = 132.5 ms), the ROI was set in the basal turn of the cochlea with a diameter of one mm (circle #2). The inversion time giving the minimum signal intensity value of the ROI was selected for the null-point inversion time (TI_{null}). Note a band-like susceptibility artifact with low signal (arrow).

value of the cochlear ROI divided by that of the ROI of the medulla oblongata.

We also measured the cochlear signal on TI scout images. We set a circular ROI of one-mm diameter in the cochlea and measured the signal intensity for each image with a different TI. We selected a particular TI of the image showing minimum signal intensity for the null-point inversion time (TI_{null}).

One of the authors (S.N.) performed all ROI measurements on PACS viewer (RapidEye, Toshiba, Tokyo, Japan).

The TI_{null} and natural logarithm ($\ln$) (CM ratio) were correlated using Spearman's rank correlation coefficient.

We determined that TI_{null} was equal to $0.693 T_1$. After an inversion pulse, longitudinal recovery occurs along an *exponential* curve with time constant T_1 . In the present study, the repetition time between the inversion pulses of 3D-FLAIR was 9 s and that of the TI scout, 16 s. These repetition times are long enough compared to the inversion time and to the T_1 values of Gd-containing cochlear fluid and of the medulla. Therefore, we used the natural logarithm of the CM ratio to evaluate the correlation with TI_{null} .

The medical ethics committee of our institution approved this study, and we obtained written informed consent from all patients.

Results

In all ears, we could determine TI_{null} based on TI scout images, although we observed susceptibility artifacts and signal inhomogeneity in the field of view (Fig. 1b). The correlation coefficient between TI_{null} and the natural logarithm of the CM ratio was -0.88 ($P < 0.01$). There was a significant negative linear correlation, as shown in Fig. 2.

Discussion

Even using a multi-channel phased array head coil, with non-uniform signal sensitivity in the FOV,¹¹ there was a significant correlation between CM ratio and quick null point measurement by TI scout sequence. This was perhaps attributable to the relative position of the inner ear and medulla oblongata in the head coil and the normalized filter map, neither of which may have differed greatly among patients. Another important reason would be that the T_2 -value of cochlear perilymph fluid might be little altered because of the low concentration of Gd-DTPA in the present study. In addition, b-SSFP or true FISP pulse sequences generally introduce only a little perturbation of the relaxation curve compared to conventional fast gradient echo sequence, such as turbo-fast low-angle shot

Fig. 2. Correlation of null-point inversion time (TI_{null}) and the ratio of the signal intensity of the perilymph in the cochlea with that of the medulla oblongata (CM ratio). The natural logarithm of the CM ratio was set on the horizontal axis, and the null-point inversion time (TI_{null}) was set on the vertical axis. Data points are well distributed on the line with the correlation coefficient of -0.88 ($P < 0.01$). Note that the points of the ear with intravenous (iv) contrast injection distributed between the cluster of the ear without contrast injection (no Gd) and that with intratympanic (it) contrast injection.

(FLASH).¹⁵

The low spatial resolution of TI scout may have allowed a partial volume averaging effect, and TI scout images suffer from susceptibility artifact. However, even with these drawbacks, the 2 measurements correlated well, and our results support the feasibility of measuring signal intensity ratio on 3D-FLAIR as reported regarding acoustic tumor.⁴

Recent MR imaging frequently uses parallel imaging techniques,²¹ which are inappropriate for measuring noise in regions of air and, therefore, for measuring signal-to-noise and contrast-to-noise ratios. Measurement of simple signal intensity ratio in a single image, however, makes such evaluation quite easy. Our results may open the way for the semi-quantitative analysis of inner ear disease using 3D-FLAIR in a routine clinical setting.

Our study was limited by the absence of ears with hemorrhage or by the increased concentration of protein in lymph fluid without gadolinium. We also may have excluded ears with moderate contrast alteration by evaluating ears with relatively high concentrations of contrast from intratympanic Gd-DTPA injection or double-dose intravenous injection and the contralateral ears with no contrast. As seen in Fig. 2, data points between -0.5 and 0 of $\ln$ (CM ratio) is not so dense. Further study is necessary to determine whether data points with moderate contrast changes would be well on correlation line.

Neither did we evaluate the reproducibility of the 2 measurement methods by scanning the same patients at different occasions, on different scanners, and with different coils. Reproducibility should be assessed to spread the CM ratio measurement method widely among many institutions.

TI-scout sequence used in the present study might have some partial volume averaging effect due to low spatial resolution. A rapid high resolution 3D T_1 mapping method using variable repetition times has been reported,¹² but scan time is longer than that used in the present study.

As shown in Fig. 2, contrast enhancement by intravenous administration seems to be weaker than that by intratympanic administration, but the visualization of endolymphatic hydrops by intravenous administration is promising.¹⁷

In conclusion, the measurement of signal intensity ratio is a feasible semi-quantitative method for analyzing 3D-FLAIR images of the inner ear and will facilitate clinical research of diseases of the inner ear.

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