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Detecting cortical lesions in multiple sclerosis at 7 T using white matter signal attenuation

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Abstract

Cortical lesions have recently been a focus of multiple sclerosis (MS) MR research. In this study, we present a white matter signal attenuating sequence optimized for cortical lesion detection at 7 T. The feasibility of white matter attenuation (WHAT) for cortical lesion detection was determined by scanning eight patients (four relapsing/remitting MS, four secondary progressive MS) at 7 T. WHAT showed excellent gray matter–white matter contrast, and cortical lesions were hyperintense to the surrounding cortical gray matter. The sequence was then optimized for cortical lesion detection by determining the set of sequence parameters that produced the best gray matter–cortical lesion contrast in a 10-min scan. Despite the B1 inhomogeneities common at ultra-high field strengths, WHAT with an adiabatic inversion pulse showed good cortical lesion detection and would be a valuable component of clinical MS imaging protocols.

Keywords

Cortical lesions; White matter; MRI; 7 T; Optimization

1. Introduction

Multiple sclerosis (MS) is one of the most common causes of neurological disability in young adults, afflicting approximately 400,000 people in the United States alone [1]. Demyelinated white matter (WM) lesions have historically been the focus of MS research; however, white matter lesion load as seen on MRI cannot account for the full extent of MS patients' neurological deficits [2]. Recent studies of post mortem MS brain specimens have shown that, on average, 25% of cortical gray matter is demyelinated in patients with long-standing disease, and cases with over 70% demyelination have been reported [3]. Thus, cortical pathology has been implicated as a more significant contributor to the patients' clinical symptoms and disease course [3,4].

It has been suggested that active inflammatory lesions in white matter are indicative of relapsing/remitting MS (RRMS), while more diffuse white matter damage and cortical lesions are associated with later-stage secondary progressive MS (SPMS) [3]. Cortical

lesions are classified according to their anatomical location: mixed gray–white matter lesions (Type 1); intracortical lesions (Type 2), which are typically small, round and centered around a blood vessel; subpial lesions (Type 3), which extend from the pial surface to cortical layer 3 or 4; and Type 4 lesions, which span the entire width of the cortex. The most common lesions are Type 3 [5].

In vivo imaging of cortical pathology has been hampered by small lesion size and low MR contrast to adjacent, normal-appearing tissue [6,7]. Since conventional MRI (T2-SE, FLAIR and pre- and post-contrast T1-weighted imaging) is not well suited for cortical lesion depiction, there have been several recent attempts at improving MRI methods for cortical lesion imaging, including double inversion recovery (DIR) [8], thin-section 3D T1-weighted MRI [9] and 7 T T2*-weighted gradient-echo imaging [10,11].

The increased signal-to-noise ratio (SNR) and image resolution achievable with 7-T MRI are ideal for cortical lesion depiction. It was recently demonstrated that an inversion recovery turbo field-echo (IR-TFE) sequence, which uses an inversion time selected such that white matter signal is nulled, achieves excellent gray–white matter contrast [12]. The first purpose of this pilot study was to explore this sequence for cortical lesion detection. The second objective of this study was to determine the optimal sequence parameters that result in maximum SNR efficiency per scan time and contrast.

2. Methods

2.1. Sequence

White matter attenuation (WHAT) is achieved using an IR-TFE sequence with the acquisition parameters adjusted such that the center of k -space is acquired as the white matter longitudinal magnetization crosses zero during relaxation back to equilibrium. Fig. 1 shows a schematic of the WHAT sequence with the main sequence parameters indicated. The shot interval, TS, is the time between successive 180° inversion pulses. The inversion time, TI, is the time between the inversion pulse and the center of k -space (using centric phase encoding). The delay time, TD, is the duration between the last k -space line and the next inversion pulse. The repetition time, TR, is the time between adjacent α -pulses; and the turbo field-echo factor, TFE, is the number of α -pulses during the turbo field-echo readout. The echo time, TE, is the time that elapses between each α -pulse and the resulting turbo field echo.

Since sequence contrast is dependent on a multitude of interdependent parameters, sequence optimization was done by a series of numerical simulation and confirmatory experiments, including preliminary studies of patients with multiple sclerosis for initial assessment of the WHAT sequence for cortical lesion detection.

2.2. Theory

The mathematical model was based off the IR-TFE (a.k.a. MPRAGE) signal equation developed and described by Deichmann et al. [13]. The MR signal with centric k -space encoding, S_c , is related to the tissue magnetization, M , by:

$$S_c = M_1 \sin(\alpha) \quad (1)$$

where α is the flip angle and M_1 is defined as:

$$M_1 = \frac{A_3 + A_2 B_3 + A_2 B_3 B_3}{1 - B_1 B_2 B_3} \quad (2)$$

with,

$$\begin{aligned} A_1 &= M_0 * \left(1 - e^{-\frac{\tau}{T_1^*}}\right) & B_1 &= e^{-\frac{\tau}{T_1^*}} \\ A_2 &= M_0 \left(1 - e^{-\frac{TD}{T_1}}\right) & B_2 &= e^{-\frac{TD}{T_1}} \\ A_3 &= M_0 \left(1 - e^{-\frac{TI}{T_1}}\right) & B_3 &= -e^{-\frac{TI}{T_1}} \end{aligned} \quad (3a)$$

$$M_0^* = \frac{1 - e^{-TR/T_1}}{1 - e^{-TR/T_1^*}} \quad T_1^* = \left[\frac{1}{T_1} - \frac{1}{TR} \ln(\cos \alpha) \right]^{-1} \quad (3b)$$

where M_0^* —the asymptotic limit of longitudinal magnetization during turbo field echo as the number of α -pulses is increased, T_1^* —the effective time constant for the approach to M_0^* , τ —the repetition time multiplied by the number of α -pulses ($TR \cdot TFE$ factor) and M_0 —the longitudinal equilibrium magnetization.

Proton density (PD) and T_2^* scaling can be included in the simulations with the additional term, $e^{-TE/T_2^*} \cdot PD$, modifying Eq. (1) to:

$$S_c = M_1 \sin(\alpha) \cdot e^{-TE/T_2^*} \cdot PD \quad (4)$$

The empirically determined tissue parameters T_1 and PD for WM, GM and cortical lesions (CL), and cerebrospinal (CSF) used in this study are listed in Table 1 [14]. Also listed are the average published T_2^* values for WM and GM [15,16]. Since the TEs were selected to be as short as possible (1.0–1.6 ms), the T_2^* term ($e^{-TE/T_2^*} \approx 1$) was neglected in the simulations.

2.3. Initial tests and parameter selection

Initial studies indicated that images with excellent GM-WM contrast are obtained when TI is selected such that WM signal is nulled [12]. Accordingly, our initial studies and simulations were aimed at finding conditions that nulled WM signal. Fig. 2 shows example calculations of the signal as a function of TI. Since initial experiments used the scanner default inversion pulse—an optimized, but nonadiabatic pulse—we simulated the effects of radiofrequency (RF) inhomogeneity by scaling both the inversion pulse and the readout flip angle, α , with a scaling factor, c_{rf} . The computations demonstrate that image contrast is extremely sensitive to RF inhomogeneity. For small RF inhomogeneity ($0.8 < c_{rf} < 1.0$), the TI that nulls WM shifts slightly downward (Fig. 2B); however, GM signal remains brighter than WM (Fig. 2A). With larger RF inhomogeneity ($0.67 < c_{rf} < 0.80$), the signal curves shift to even lower TI, and for $c_{rf} < 0.67$, GM signal is nulled, WM is brighter and the contrast is inverted (not shown).

Although RF inhomogeneity is a dominant determinant of image contrast, the TFE factor, TR and the readout flip angle, α , also affect the null point TI for WM. Fig. 3 shows example calculations for different TFE factors, TRs, and readout flip angles. In all cases, the WM-nulling TI shifts significantly for $TS < 4000$ ms. Smaller TFE factors, TRs and flip angles all increase the TI for nulling WM. In addition, the GM signal decreases with the flip angle, proportional to $\sin(\alpha)$, as well as with increasing TR and TFE.

Based on these initial tests, parameters were selected for a pilot study aimed at exploring cortical lesion detection with the WHAT sequence. However, it was evident that adiabatic

inversion pulses (which would stabilize inversion throughout the image volume) and subsequent further parameter optimization would be necessary to identify optimal conditions for cortical lesion detection.

2.4. Initial evaluation of WHAT for cortical lesion detection

Eight patients [four RRMS, four SPMS; mean age=42 years (range 24–58); three male/five female] were scanned at 7 T (Philips Healthcare, Cleveland, OH, USA) with a 16-channel phased-array head coil (NOVA Medical, Wilmington, MA, USA). The study was approved by the local IRB board, and written consent was obtained from each patient.

The sequence parameters for the axial WHAT sequence used to evaluate cortical lesion detection were as follows: TS=3700 ms, TI=550 ms, TR=4.1 ms, TE=1.6, TFE factor=165, FA=8°, FOV=220×165 mm², matrix=548×165, acquired voxel size=0.4×1.0×1.4 mm³, reconstructed voxel size=0.38×0.38×0.7 mm³, reconstructed slices=128, NSA=2, scan time=10:04 min. An axial B1 map was acquired using scanner tools [17] and used to mask regions where B1 dropped below the contrast inversion threshold. These regions were excluded from further analysis.

The WHAT images were read and analyzed independently by two experienced readers who were also blinded to the disease status of each patient. The readers were advised to mark and classify cortical lesions into two groups: leukocortical (Type 1) and intracortical (Types 2–4). A third reader tabulated the counting results and moderated a consensus reading of the images. A kappa statistic was used to evaluate inter-reader agreement of marked lesions.

2.5. WHAT parameter optimization

Once an adiabatic hyperbolic secant inversion pulse became available, further signal simulations and tests were done. First, the settings for the adiabatic pulse were optimized to achieve good inversion throughout the image volume. This was done by setting a control parameter nominal flip angle ranging from 750° to 2000°, corresponding to pulse lengths from 8.5 to 61 ms. Using this strong inversion pulse increased the shot interval, TS, due to specific absorption rate (SAR) limits and instituted an absolute minimum TS of 3500 ms. Next, the minimal TSs achievable for different voxel sizes were recorded. This included checking pulse sequence interdependencies on TR, α , TFE factor, image plane orientation and SAR settings. TI values for nulling WM were computed for these minimal TSs. From these tests, scan parameters achieving the highest SNR per scan time were selected. These are listed in Table 2. We opted to use 10 min as our reference scan time.

Finally, SNR and contrast-to-noise ratio (CNR) measurements were performed in eight healthy volunteers (mean age=39 years [range 20–56], 6 male/2 female). Subjects were scanned at 7 T with a 16-channel phased-array head coil with IRB approval and written informed consent. SNR measurements were obtained by repeating scans with RF on and off, or by repeating identical scans and subtracting the images. The SNRs for the selected tissue regions of interest (ROIs) were determined as the signal average of the two scans divided by the standard deviation of the same ROI in the noise image (the RF off or the difference image). SNRs were measured for different TS/TI settings and voxel sizes using the optimized parameters in Table 2. Parallel imaging was not used in these studies (SENSE factor=1).

The signal, S_c , was computed for each of these conditions according to Eqs. (1–4) and scaled to the experimentally measured SNR_{exp} using:

$$\text{SNR}_{\text{exp}} = f \cdot S_c \cdot \Delta x \Delta y \Delta z \sqrt{N_x N_y N_z (\text{NSA} / \text{BW}_{\text{read}})} \quad (5)$$

where f is the scaling factor matching the theoretical signal, S_c , to the measured SNR_{exp} .

3. Results

3.1. Pilot study demonstrating the utility of WHAT for cortical lesion detection

WHAT-TFE images showed excellent GM–WM and GM–CL contrast, with cortical lesions depicted as focal hyperintensities within the cortex (Fig. 4). Type 1 lesions were especially visible with this tissue contrast. In the eight MS patients, a total of 292 cortical lesions were identified, of which 209 were marked by both readers (72%), resulting in moderate inter-reader agreement ($\kappa=0.53$). A majority (62%) of the lesions marked by both readers were classified as Type 1 lesions.

In vivo SNR measurements of WM, GM and CLs confirmed the excellent tissue contrast noted by the readers: $\text{SNR}_{\text{WM}}=3.4\pm0.2$, $\text{SNR}_{\text{GM}}=11.6\pm0.2$ and $\text{SNR}_{\text{CL}}=15.3\pm0.1$, making the gray matter–cortical lesion $\text{CNR}=3.7\pm0.2$.

3.2. WHAT sequence parameter optimization

Fig. 5 shows the significant improvement achieved with the adiabatic hyperbolic secant pulse when compared to the default inversion pulse in a healthy subject. With the adiabatic pulse, the chosen GM–WM contrast was achieved throughout the image volume. Significant contrast inversion between GM and WM occurred due to lower than 180° inversion pulses with the default pulse. Testing different settings for the adiabatic inversion pulse showed a GM signal increase from 8.7 (1200° ; 21.9 ms pulse length) to 11.1 (1600° ; 38.9 ms pulse length) and 13.3 (2000° ; 61 ms pulse length). The 2000° pulse was selected as the best compromise between optimal inversion and SAR limitations.

The signal simulations in Fig. 2A show that best bright GM –black WM contrast is achieved when TI is selected to null WM. Fig. 2B shows the TS/TI pairs that null WM signal. GM signal increases with increasing TS (Fig. 3D–F). Thus longer TSs are favorable in terms of increasing GM and cortical lesion SNR. Fig. 6 confirms this with experimental data. However, long TS also increases scan times beyond clinically acceptable lengths, especially for very high spatial resolution. Scan parameters were thus further evaluated to find conditions with optimal scan efficiency, providing the highest SNR per unit scan time with particular emphasis on high spatial resolution imaging —important for cortical lesion imaging. This optimization involved testing feasible settings based on scanner limitations and numerical signal simulations.

For axial brain scans, the best scan efficiency is achieved for a rectangular field of view (FOV) when the TFE factor equals the number of in-plane phase encoding steps, N_y (all in-plane phase encode steps are acquired in one-shot interval TS). Alternatively, two-shot intervals could be used to acquire the data, but this method would only be worthwhile if the minimum shot interval, TS, for $\text{TFE}=N_y/2$ is half of the minimum TS for $\text{TFE}=N_y$. The minimal achievable TS depends on SAR limitations, phase encoding order and $\tau=\text{TR}*\text{TFE}$. TR, in turn, depends on voxel size, TE, the readout bandwidth (BW) and the image plane orientation. We chose to assess scan efficiency for a range of near isotropic voxel sizes, making slice thickness twice the in-plane resolution, $\Delta x=\Delta y=2\Delta z$. With a FOV of 220×180 mm (suitable for most head sizes), minimal TS, TR and TE were determined for each voxel size using maximal SAR and gradient strengths (Table 2). Also included in Table 2 is the maximal number of slices, N_z , that can be acquired in 10 min for the listed minimum TS,

including the scanner default slice direction oversampling of $N_{\text{shot}}/N_z=1.28$ used to prevent slice aliasing.

The range of TFE, TR, TE, flip angle and BW was then further evaluated to determine whether further scan time efficiency could be achieved. First, Fig. 3D indicates that the GM signal changes little with TFE. Minimal TSs were determined for $\text{TFE}=N_y/2$, but, in all cases, they were larger than half the minimal TS for $\text{TFE}=N_y$. We explored the feasibility of using larger readout segment flip angles to increase GM signal [Eq. (1), Fig. 3E]. However, because the minimal TS is SAR limited, the flip angle cannot be increased without increasing TS. For low spatial resolution (>0.7 mm in-plane), TS and FA could be further balanced to increase SNR; however, for high-resolution scans, increasing the flip angle is not possible or advantageous. Finally, SNR can be increased by decreasing the readout bandwidth. However, this will increase TE and, in turn, TR, and result in decreased GM and cortical lesion signal (Fig. 3F).

Fig. 7 shows the measured cortical GM SNR for different spatial resolutions using a flip angle of 8° and the optimized parameters listed in Table 2. Also shown is the computed GM SNR based on signal calculations [Eqs. (1–4); GM: $S_c=0.033$] and scaling for the resolution parameters according to Eq. (5), with a scaling factor=22 to match the experimental SNR. Also shown is the computed SNR for cortical lesions (CL: $S_c=0.058$). The flip angle may be further increased to 15° , increasing the computed GM and cortical lesion signal to 0.041 and 0.072, respectively. The estimated $\text{CNR}_{\text{GM-CL}}$ values listed in Table 2 also indicate that lower resolution scans have higher GM-CL contrast.

4. Discussion

In summary, cortical lesion detection at 7 T is feasible by using a white matter attenuation (WHAT) sequence that produces high contrast between white matter, gray matter and cortical lesions. SNR efficiency was maximized as a function of spatial resolution (Table 2) through testing a wide range of parameters and signal simulations.

In our study, two independent readers detected 209 lesions in eight patients (26 lesions per patient on average). This lesion detection rate is high in comparison to previously published work even though much of the imaged volume had to be excluded due to RF inhomogeneity with the nonadiabatic pulses in our pilot study of MS patients.

In comparison, Mainero et al. [11] recently published a study using a T2*-weighted FLASH sequence for cortical lesion detection at 7 T and reported detection of 199 lesions in 16 patients (average of 12 lesions per patient). Our study detected mostly Type 1 lesions; however, Mainero et al. [11] reported cortical lesion type distributions mirroring those reported in histology literature [5,18]. Cortical lesion studies at 1.5 and 3 T using DIR or T1-weighted sequences report much lower lesion detection rates of six to eight lesions per patient [9,19–21].

DIR sequences use two inversion pulses timed such that the signal from both WM and CSF is eliminated, thus generating high contrast for gray matter. This enhances subtle gray matter abnormalities and reduces partial volume artifacts, and DIR studies of MS patients at 1.5 and 3 T show very promising results for cortical lesion assessment [8,9,19–23]. However, DIR suffers from inherently low SNR and is susceptible to flow-related artifacts, which may lead to false-positive lesion identification [9]. Additionally, only DIR turbo spin-echo (TSE) sequences have been implemented, but due to high SAR requirements of the TSE acquisition, this sequence is not favorable for use at 7 T. Thin-section 3D T1-weighted imaging improves image SNR and spatial resolution compared to DIR. Both 3D-magnetization-prepared rapid acquisition with gradient echo (3D MP-RAGE) at 3 T [9] and

T1-weighted 3D-spoiled gradient echo (3D SPGR) at 1.5 T [23] have shown promise in cortical imaging where lesions are dark compared to adjacent GM.

Since it is impossible to validate in vivo cortical lesion counts in the same way as MRI/histological comparisons are used for postmortem specimens [24], reader bias is a significant issue. In this study, readers were trained in cortical lesion detection via repeated exposure to both MS specimen images with histologically confirmed lesions and in vivo images of MS brains with various levels of lesion activity. Although the MRI appearance of formalin-fixed and living tissue is different [25], repeated and sustained exposure to both is currently the best way to guide future reader training.

The WHAT sequence is very promising for cortical lesion detection; nevertheless, it has several shortcomings. Since cortical lesions and CSF appear hyperintense, it can be difficult to differentiate them. Type 3 lesions manifest at the cortical GM–CSF boundary and can be easily obscured or mimicked by similar GM and CSF signal intensities. Similarly, small vessels show inflow enhancement and it may be difficult to distinguish vessels and small Type 2 lesions. Furthermore, WHAT image contrast is solely based on tissue T1 differences, unlike FLAIR and DIR which are based on TSE sequences using long TEs, introducing T2 contrast. Further studies are needed to assess the importance of T2 effects in enhancing contrast between cortical lesions and adjacent GM. Finally, our study only evaluated SNR and CNR efficiency, which decrease with increasing spatial resolution (Fig. 7). It is known that lesion detection depends on both CNR and spatial resolution [25]. However, the best balance between CNR and voxel size — including the relative advantage of isotropic resolution vs. high in-plane resolution with thicker slices — has yet to be determined. Future studies testing different resolutions with fixed SNR and CNR are needed.

Table 2 and Fig. 7 show that, for high spatial resolution (voxel sizes smaller than $0.5 \times 0.5 \times 1.0 \text{ mm}^3$), SNR efficiency and GM–CL contrast cannot be further optimized by sequence parameter optimization alone. Thus, no increase in scan efficiency can be achieved by collecting the phase encoding steps in two, rather than in one, TS intervals. This also showed that the minimal achievable TS is SAR limited due to the adiabatic inversion pulse. Better adiabatic pulses requiring less RF power or multichannel transmit could help overcome RF inhomogeneity problems [26]. Further improvement may also be achieved with larger numbers of receiver arrays. For lower spatial resolutions, SNR is high and additional optimization options are available. Scan time can be reduced by using parallel imaging and/or by using the turbo field-echo readout train not only for in-plane but also for slice phase encoding.

Our study focused on optimizing the IR-TFE sequence for WHAT. However, the IR-TFE sequence through selection of TI can be adjusted to give a multitude of different tissue contrasts. For example, TI could be adjusted to null cortex such that lesions would appear hyperintense. This may increase lesion conspicuity, but may not improve lesion–vessel or lesion–CSF differentiation. Alternatively, TI could be selected to null cortical lesion signal, which would allow differentiation of lesions and vessels, but may reduce GM–CSF contrast and hinder depiction of cortex boundaries. Finally, TI can be adjusted to give classic T1 contrast showing CSF black, WM hyperintense and GM with midrange signal. Cortical lesions would appear darker than surrounding GM, allowing differentiation from vessels. Finally, at least for moderate spatial resolution, it may be possible to implement a multi-contrast sequence, where readout segments for different effective TI are placed in the center of k -space and combined with some kind of view sharing. Optimization of all these different options can follow the methods outlined in this work, and initial estimation of SNR and CNR is possible using the results in Table 2 and Fig. 7.

5. Conclusion

White matter attenuated (or otherwise optimized IR-TFE) sequences are very promising for cortical lesion MRI. This approach may be especially promising at 7 T, since T1s are longer and spread further apart for different tissue types. Since IR-TFE is exclusively dependent on T1 tissue differences, WHAT and other IR-TFE sequences could be combined with T2*/phase-weighted gradient-echo images for evaluating different tissue characteristics such as iron content [24]. Pathophysiology of cortical lesions and their evolution with disease progression are not yet fully understood. Thus MRI with a combination of contrast mechanisms could play an important role as predictor for MS disease progression and/or monitoring treatment outcomes and is a valuable step forward in expanding MRI MS research.

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Fig. 1.

A 180° inversion pulse is followed by a train of turbo field-echo readouts. α =flip angle (FA), TE=echo time, TR=repetition time, TI=inversion time, TFE=turbo field-echo factor (number of α -pulses), TD=delay time and TS=shot interval. The cross-hatched boxes represent acquisition. Centric k -space encoding is used.

Fig. 2.

(A) Example simulation of the IR-TFE sequence signal as a function of TI for TS=3700 ms for WM (solid) and GM (dashed), and (B) computation of the TIs nulling WM (solid) and GM (dashed) signal as a function of TS. Computations used TFE=165, TR=4.1 ms, FA=8° and tissue parameters from Table 1. To simulate the effects of RF inhomogeneity, both the inversion pulse and the readout flip angle, α , were scaled by a scaling factor. For $c_{rf}=1$: $\alpha=8^\circ$, IR pulse=180° (black line); for $c_{rf}=0.80$: $\alpha=6.4^\circ$, IR pulse=144° (gray line). Note that the TI nulling WM decreases from 595 to 510 ms for $c_{rf}=1.0$ and 0.80 [indicated by two vertical dotted lines on the left of (A)], respectively. The TI nulling point also decreased GM from 900 to 790 ms [indicated by two vertical dotted lines on the right of (A)]. For the TS/TI pairs in (B), absolute GM signal is larger than WM signal. The horizontal dotted lines correspond to the nulling points in (A) and where they intersect a TS=3700 ms.

Fig. 3.

(A) WM nulling T1 values as a function of TS for different TFE factors: TFE=165 (dashed), TFE=244 (solid), TR=4.1 ms, $\alpha=8^\circ$; (B) different readout flip angles: $\alpha=8^\circ$ (solid), $\alpha=4^\circ$ (dashed), TFE=165, TR=4.1 ms; and (C) different TRs: TR=4.1 ms (dashed), TR=8.2 ms (solid), TFE=165, $\alpha=8^\circ$. In (D), (E) and (F), the computed GM (black) and cortical lesion signals (gray) for the condition in (A) through (C) are shown.

Fig. 4.

Examples of Type 1, 2, 3 and 4 cortical lesions showing their appearance in WHAT images. Type 3 lesions are particularly difficult to detect because of partial voluming artifacts at the boundary of the CSF and because cortical layers can produce local contrast variations that can be mistaken for lesions. The Type 3 lesion indicated was identified by its having intermediate hyperintensity between normal-appearing cortex and CSF as well as existing within the first three to four cortical layers. The other hyperintensities in the zoomed-in section do not exhibit proper location, nor is the contrast at the boundaries as crisp — thereby suggesting that those are more likely local contrast variations than actual lesions.

Fig. 5.
(A) WHAT with default IR pulse compared to (B) WHAT image with a hyperbolic secant adiabatic pulse.

Fig. 6.

Measured WHAT SNR and simulated signal (lines) for fixed TFE=244 in a healthy volunteer for white matter (diamonds), cortical gray matter (triangles) and cerebrospinal fluid (squares). Measured data are for TS/TI pairs=6000/750, 5000/730, 4000/700, 3000/620 and 2000/470 ms, with respective scan times of 10:07, 8:26, 6:45, 5:04 and 6:49 min. Other parameters were TR=4.1 ms, TE=1.6 ms, FA=8°, FOV=220×170 cm, matrix=316×244, 40 slices (51 shots), voxel size=0.7×0.7×1.4 mm³, BW=600 Hz and NSA=2.

Fig. 7.

Experimental SNR per 10-min scan time for different resolutions. Shown are the measured WM ($\times$'s) and cortical GM (squares) SNR values for three healthy volunteers and the calculated GM and CL SNR using the theoretical signal computation with a readout flip angle of 8° , matching the measured data and parameters from Tables 1 and 2. The computed signals were corrected for voxel size, matrix and bandwidth according to Eq. (5), and scaled by a factor of 22 to match the measured data. The experimental GM signal measured for a $1 \times 1 \times 2\text{-mm}^3$ voxel size may be too large due to partial volume averaging with adjacent CSF. The dotted line shows the average for measured WM SNR and represents the measured background noise.

Table 1

Tissue T1, T2* and proton density (PD) values used in simulated IR-TFE (MPRAGE) tissue signal calculations

	T1 (ms) [14]	T2* (ms) [15,16]	PD [14]
White matter	890	27.9	0.63
Gray matter	1550	34.6	0.71
Cortical lesions	2420	–	0.86
Cerebrospinal fluid	4470	168	1.0

Table 2

SNR/CNR optimized WHAT sequence parameters at different resolutions for a 10-min scan

Voxel size (mm ³)	Matrix $N_x \times N_y$	N_z	FOV _z (mm)	TS _{min} (ms)	TR _{min} (ms)	TE _{min} (ms)	BW (Hz)	Calculated TI _{WM=0} (ms)	Expected TI _{WM=0} (ms) ^a	Calculated GM	Expected SNR _{GM} ^b	Estimated CNR _{GM-CL}
0.33×0.33×0.66	666×544	81	53	5820	5.4	1.6	560	595	–	0.034	–	3.4
0.35×0.35×0.7	628×514	90	64	5230	4.5	1.5	580	595	–	0.034	–	3.9
0.4×0.4×0.8	550×450	104	83	4550	3.5	1.4	665	595	600	0.034	11.4	4.7
0.5×0.5×1.0	440×360	117	117	4010	3.0	1.2	830	595	550	0.033	18.1	6.5
0.6×0.6×1.2	366×300	129	155	3660	2.7	1.1	990	590	–	0.032	–	8.5
0.7×0.7×1.4	314×254	135	188	3500	2.5	1.0	1155	590	–	0.031	–	10.3
1.0×1.0×2.0	220×180	135	270	3500	2.1	0.9	1660	595	600	0.033	79	18.2

FOV=220×180 cm; TFE factor= N_y ; minimal TR, TE and water/fat shift; partial echo; FA=8°; orientation orthogonal to gradient axes; and NSA=1. The number of slices, N_z was adjusted to give a total scan time of 10 min; this includes the scanner's default oversampling by a factor of $N_{shots}/N_z=1.28$.

^aThe experimental null was determined from scans of healthy subjects by changing TI=50–100 ms near the computed value and recording the TI value with minimal WM signal.

^bThe experimental SNR for GM was determined from a set of RF on/RF off scans under the listed conditions, except the number of slices which was reduced to shorten scan time for the SNR measurement. The listed experimental SNR was corrected by $\sqrt{N_z/N_{z,exp}}$ to account for using fewer slices in the acquisition.