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High-Resolution Phased-Array MRI of the Human Brain at 7 Tesla: Initial Experience in Multiple Sclerosis Patients

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Abstract

Recent advancement for magnetic resonance imaging (MRI) involves the incorporation of higher-field strengths. Although imagers with higher magnetic field strengths were developed and tested in research labs, the direct application to patient MR studies have been extremely limited. Imaging at 7 Tesla (7T) affords advantages in signal-to-noise ratio and image contrast and resolution; however, these benefits can only be realized if the correct coils exist to capture the images. The objective of this study was to develop optimized high-resolution 7T MRI techniques using high sensitivity, specialized phased-array coils, for improved gray matter (GM) and white matter differentiation, in an effort to improve visualization of multiple sclerosis (MS) lesions in vivo. Twenty-three subjects were enrolled in this preliminary study, 17 with clinically definite MS (11 females, 6 males; mean age 43.4 years; range 22–64 years) and 6 healthy controls (2 females, 4 males; mean age 39.0 years; range 27–67 years). MR imaging of MS patients at 7T was demonstrated to be safe, well tolerated, and provided high-resolution anatomical images allowing visualization of structural abnormalities localized near or within the cortical layers. Clear involvement of the GM was observed with improved morphological detail in comparison to imaging at lower-field strength.

Keywords

Multiple sclerosis; cortical lesions; 7T; high-resolution

Introduction

Magnetic resonance imaging (MRI) was introduced for clinical diagnostic imaging in the early 1980s, and has evolved through a rapid series of technological and application-driven advances since that time.¹ The inherent advantages that MR possesses over other medical imaging technologies has secured MRI a position in medicine and science. The continued technical progress with the software and hardware of these systems has allowed for expansion of the MR field with image quality improvements and new applications continually emerging. A

recent area of advancement for MRI involves the incorporation of higher-field strengths. Although imagers with higher static magnetic field strengths were developed and tested in research labs for the past 2 decades, the direct application to patient MR studies has been extremely limited.²⁻⁶

The development of high-field strength imaging systems requires technological advances in coil design. Imaging at 7 Tesla (7T) affords advantages in signal-to-noise ratio (SNR) and image contrast and resolution; however, these benefits can only be realized if the correct coils exist to capture the images.⁷ There are many challenges with high-field signal excitation and reception, not limited to radio-frequency (RF) field homogeneity, high RF power requirement, and coil-specific issues such as element coupling, tuning, matching, and cable interactions.^{5, 8-10} These engineering issues have been theoretically and experimentally investigated by several of the leading high-field research groups. Recently, phased array coils at 7T have provided more uniform reception and increased sensitivity, allowing for the visualization of small anatomic structures not previously appreciated at lower magnet field strengths.¹⁰⁻¹² However, the value of these high-resolution 7T MRI techniques have not yet been well established for patient studies.

The advances in high-field MRI and application to the study of multiple sclerosis (MS), a condition whereby MR technology is frequently used for diagnosis and clinical surveillance, may provide further insights into the disease not previously appreciated at lower magnet field strengths. MS is a multifocal, inflammatory, heterogeneous demyelinating condition traditionally regarded as a disorder of white matter (WM). However, postmortem pathologic studies revealed significant involvement of the gray matter (GM) affecting principally the cingulate gyrus, frontal, parietal, and temporal lobes.¹³⁻¹⁵ WM lesions are detected easily in vivo at the conventional field strength of 1.5T, and with even better resolution at 3T. However, cortical GM lesions are poorly detected at these field strengths due to their small size and the technical limitations associated with achieving proper spatial and contrast resolution in vivo. Depending on the classification system proposed, cortical MS lesions can involve just a few cortical layers referred to as Type 1 (deeper layers) and Type 3 (superficial layers), all cortical layers (Type 2), involving all cortical layers and extending in the sub-cortical WM region (Type 5), while Type 4 lesions affect only the subcortical U-fibers.¹³ Fluid-attenuated inversion recovery (FLAIR) and double inversion-recovery images slightly improve cortical lesion detection in vivo at low-field strength without providing intracortical detail and certainty of sub-cortical WM involvement.¹⁶⁻¹⁷ At 7T, the SNR increase improves spatial resolution and should allow the visualization of smaller anatomical structures, in addition to providing morphological details.

The objective of this study was to develop high-resolution 7T MRI techniques using high sensitivity, specialized phased-array coils, with optimized acquisitions for improved GM and WM differentiation, in an effort to improve visualization of MS lesions in vivo.

Materials and Methods

Research Participants

Adult patients with an established diagnosis of clinically definite multiple sclerosis (CDMS) evaluated by the Multiple Sclerosis Center at the University of California, San Francisco, were invited to participate. Healthy, age-matched control subjects were also studied. A total of 23 subjects were enrolled, 17 with CDMS (11 females, 6 males; mean age 43.4 years; range 22-64 years) and 6 healthy controls (2 females, 4 males; mean age 39.0 years; range 27-67 years). The clinical MS subtype for all 17 patients was relapsing-remitting. The concomitant use of disease-modifying therapies for MS was permitted. The protocol was approved by the

Committee on Human Research at the University of California, San Francisco, and informed consent was obtained from all participants.

Image Acquisition

All patients were scanned on a GE EXCITE 7T scanner (General Electric Healthcare Technologies, Waukesha, WI). Excitation was performed using a commercial volume transmit head-coil with a shielded, high-pass birdcage coil design (NOVA Medical, Wilmington, MA). An in-house, custom-made, 8-channel phased-array surface coil was used for signal reception in 9 patients and 4 controls. A commercially available 8-element volume receive coil (NOVA Medical) was used in the other 8 patients and controls.

A low-resolution, 3-plane localizer was followed by a series of gradient echo acquisitions to obtain T2*-weighted images with different resolutions and orientations. Two axial series were acquired, one with a reduced field of view [FOV] and less gap between slices for higher-resolution images. The sequence parameters for each of the series are shown in Table 1. Axial slices were prescribed with the most inferior slice along the anterior commissure to posterior commissure (AC-PC) line and the rest superior to that in order to cover the corpus callosum and above. The prescriptions used in this work did not result in full brain coverage; the Axial-1 protocol (slice thickness 2 mm, skip 4 mm) covered a range of 54 mm, and the Axial-2 (slice thickness 2 mm, skip 1.5 mm) covered 31.5 mm. Sagittal series were collected in 5 patients. The sagittal series was prescribed with the center slice aligned with the mid-sagittal image from the localizer, and dividing the remaining slices to both the right and left hemispheres of the brain. This sagittal prescription (slice thickness 2 mm, skip 1.5 mm) covered a brain volume of 31.5 mm.

Optimization of TE

In addition to very high spatial resolution, one objective of the T2*-weighted GRE sequence was to maximize the contrast resolution between GM and WM in the brain, while maintaining excellent SNR. To determine the image parameters that best accomplished this, a series of GRE sequences were acquired on a single volunteer using the custom-made phased-array coil (Fig 1). Each acquisition had the same sequence parameters, except the TE was varied from 12-24 ms, at intervals of 3 ms. Contrast to noise (CNR) and SNR were calculated for each of the image sets and the echo time (TE) that provided the best gray/white differentiation was chosen. SNR in the WM and GM was calculated by region of interest (ROI) analysis, with manually defined small representative sections (approximately 5 mm × 5 mm) of each tissue type and the background noise outside the brain. Noise was estimated as the standard deviation of the background ROI divided by .7, a factor that accounts for the fact that noise was measured from magnitude images collected using a phased array with 8 coils.¹⁸ The SNR was calculated by the mean magnitude of the tissue ROI divided by the noise, and the CNR was the difference in signal between GM and WM ROIs divided by the noise of interest.

Image Processing

The high-resolution phased array 7T images were reconstructed on the scanner and subsequently transferred off-line to a Sun Ultra20 workstation for image processing. High coil sensitivity on the brain periphery resulted in images that are very bright at the edge, and darker in the center of the brain. In order to compensate for this signal heterogeneity, the brain images were masked from the background noise and an edge-filled low-pass filtering algorithm was used to achieve a more uniform signal profile.¹⁹ All SNR and CNR calculations were performed via ROI analyses of the images before the image-processing was applied.

Results

TE Optimization

The results of the SNR and CNR calculations used to determine the optimal TE are presented in Table 2. The data suggest for a TE of 12 and 15 ms, the SNR of the GM and WM are similar, with the 15-ms TE being less than 2% lower in each case than the 12-ms echo time. This minimal change lead to the CNR being approximately the same in both the 12- and 15-ms TE cases, although the CNR is slightly lower with the increased TE. As the TE increases beyond 15 ms the SNR, and corresponding CNR, drop to a greater extent. In addition to quantitative criteria, the TE decision was also based on the qualitative image inspection by a neurologist and neuroradiologist. These two factors resulted in 15 ms being chosen as the optimal TE for the T2*-weighted GRE sequence.

Coil Sensitivity

The custom fabricated phased array coil provided a 2.5-fold increase in SNR at the cortex and 30% increase in deep brain parenchymal structures compared to the commercially available 8-channel phased-array coil. The increased sensitivity at the cortex resulted in image brightness at the edges, as seen in Figure 2A. The low-pass filtering produced images with a more uniform signal intensity profile, as shown in Figure 2B. This post-processing facilitates visual inspection and qualitative analysis of the images. The images in Figure 2A, as well as Figure 3, demonstrate darkening in the anterior frontal regions. This darkening is due to the geometry of the custom-developed coil. This coil wraps around the head, and fastens in the frontal region. The coil arrays at this point are not as close together as on the rest of the array, and result in a region that is lower in signal than the rest.

Spatial Resolution

Based on the imaging parameters listed in Table 1, spatial resolution was $195 \times 260 \mu\text{m}$ or $215 \times 286 \mu\text{m}$, depending on the FOV for the particular image acquisition series. Figure 2B shows an axial slice from a control subject, which demonstrates that excellent image quality can be obtained even at the ultrahigh resolutions achieved with these imaging parameters. The image in Figure 2B illustrates the level of structural detail that it is possible to achieve using the combination of specialized phased-array coils and the optimized GRE acquisition.

Contrast Resolution

The T2*-weighted GRE acquisition allowed for excellent gray-white contrast as demonstrated in the axial slice of the control subject in Figure 2B. The images in Figure 3 illustrate the outstanding gray-white contrast in the cortex of an MS patient, as well as the lesion contrast that is achieved with this method. The patient images also highlight the appearance of vasculature when using this method due to susceptibility-based signal loss in the vessels.

From a qualitative perspective, the inspection of 7T patient images suggested that WM lesions were easily detected and better delineated from adjacent structures than lesions visualized on images at lower-field strengths (1.5 and 3T). The good contrast, in addition to the improvement in spatial resolution, allows for differentiation between juxtacortical WM lesions and cortical lesions possible (Fig 3B). Most strikingly, Figure 4 demonstrates the fine detail that can be visualized in a cortical lesion that originates from the pia and extends through the GM layers to the sub-cortical WM, visibly reflecting what Kidd et al¹³ have already described as a cortical MS lesion Type 2.

Sagittal Imaging

Figure 5 contrasts sagittal images from an MS patient with a sex- and age-matched control subject. These images demonstrate the extent of the coil coverage in the superior/inferior direction and also illuminate some deep WM structural differences. From these images we see that we can obtain excellent quality high-resolution sagittal images with coverage from the top of the brain down through the cerebellum. The arrowheads in the zoomed-in image from the MS patient highlight the dramatic thinning of the corpus callosum compared to control. The contrast resolution achieved with the T2*-weighted GRE sequence made it possible to view the extent of lesions in multiple regions of the corpus callosum in this particular patient.

Discussion

The application of structural neuroimaging for MS patients has proven to be an invaluable tool for the diagnosis, clinical surveillance, management, and the assessment of therapeutic efficacy in pivotal MS clinical trials. The implementation of advanced radiological techniques is providing more insight into MS pathology compared to conventional imaging metrics by enhancing lesion morphology and spatial distribution.

Very high-field MR imaging of all CDMS patients at 7T was demonstrated to be safe, well tolerated, and provided high-resolution anatomical images allowing for the visualization and differentiation of structural abnormalities localized near or within the cortical layers. Clear involvement of the GM was observed in 1 patient at 7T, with improved morphological detail, appreciated qualitatively, in comparison to imaging at lower-field strengths. These data clearly support that MS pathology is not limited to the WM regions. GM involvement could be the result of retrograde (Wallerian) degeneration from lesions originating in the WM structures. Recent data, however, suggests a dissociation between cortical demyelination and WM pathology, suggesting that MS patients possess both gray and WM demyelinating pathology independently.²⁰

To achieve ultra-high spatial resolution brain images in vivo, significant new technologies had to be developed and employed. New coils designed to be super-sensitive at the cortex were tested and the utility of the gain in SNR was investigated. Also, MR imaging sequences were optimized to produce images of the highest quality possible at this field strength. These developments allowed for high-quality images to be produced and emphasized the potential application to other patient populations.

Recent studies at 7T have demonstrated the utility of T2*-weighted imaging to the investigation of MS pathology, and have revealed new information on lesion location and relationships with brain vasculature.^{21,22} Also, new forms of lesion contrast have been achieved by looking at the signal phase information and its relationship to lesion characteristics.²³ The image collection in this work was optimized for gray/white contrast, with the best SNR at the cortex, and although this imaging methodology was useful to produce ultra high-resolution images to identify lesions in the gray, subcortical, and WM, it is not without limitations. When using T2*-weighting, both cerebrospinal fluid and lesions appear bright, thus making lesion identification in and near the cortex challenging. Previous work with double-inversion recovery (DIR) at 3T has shown the ability of DIR to improve lesion identification in many regions of the brain.²⁴ However, technical and safety limitations with the B1 field and production of 180° pulses on high-field systems make the implementation of this pulse sequence challenging at 7T.

Scanning at 7T provides several limitations from a clinical standpoint. With regard to patient safety and comfort, previous work has suggested that 7T is well tolerated by most subjects; however, the number of complaints was greater at 7T than at lower-field strengths.²⁵ With this

in mind, the imaging protocol used in this study was kept very short, ideally less than 35 minutes, to minimize possible discomfort, and the table was moved into the magnet bore very slowly to reduce the potential for sensation of vertigo. The short scan time limited the number of series that were done, as well as the coverage of each of the acquisitions. None of the T2*-weighted protocols resulted in full-brain coverage, but if the imaging session time allowed, full-brain coverage for the Axial-1, Axial-2, and Sagittal series could be achieved in approximately 16, 40, and 26 minutes, respectively. None of the patients enrolled in this study had to terminate the imaging session due to side effects, and only a small fraction reported disorientation when entering the magnet bore. Claustrophobia was no different than at lower-field strengths, and although patients commented on increased noise at 7T, it was not a limiting factor.

The coverage available using the optimized protocol is constrained not only by scan time, but also by the coils available for imaging at 7T. The 8-channel commercially available coil, as well as the coil developed in-house, have limited range in the S/I directions, and thus whole-brain coverage is difficult, if not impossible, to achieve. This limitation will be eliminated as more coils are specifically designed and tested for the 7T systems. Also, due to high coil sensitivity on the outer portion of the head, and the resulting brightness at the cortex, post-processing has to be carried out to get clinically useful images with uniform image intensity across the slice. Although this processing was done offline in this study, it can be completed in less than 1 second, and in the future could be included on the scanner if this were to be incorporated into regular clinical imaging.

The preliminary studies in MS patients indicated that very high-field MR imaging was well tolerated and provided ultra-high-resolution anatomical images allowing for the visualization of structural abnormalities associated with disease. These initial results show that scanning MS patients at 7T is not only feasible, but allows for the detection of lesions with adequate CNR at a higher spatial resolution than has been demonstrated at lower fields. MS lesions were clearly detected in both the white and cortical GM, with morphological details not fully appreciated at lower-field strengths. While still not applicable clinically in patient care, these advancements may allow for a more comprehensive understanding of multiple sclerosis, allowing for further investigation into the natural history and the in vivo delicate immune mediated systems responsible for the genesis of MS pathology in and around the cortical GM.

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Fig 1.

Axial 2D GRE images at 7T were acquired from a volunteer with varying TE to determine optimal T2* weighting for maximum image SNR and CNR between the GM and WM. From these optimization studies, a TE of 15 ms was selected for the MS patient exams.

Fig 2. Images collected using the Axial1 protocol ($215 \times 286\text{-}\mu\text{m}$ resolution) in a control subject demonstrating image intensity across a single slice before (left) and after image post-processing (right).

Fig 3.

7T T2*-weighted axial images from (A) an MS patient using the Axial1 protocol (in-plane resolution: $215 \times 286 \mu\text{m}$). Images demonstrate multiple foci of abnormality involving the deep WM structures, as well as the GM, WM, and lesion contrast achieved using this methodology, and (B) an MS patient with multiple lesions using the Axial2 protocol (in plane resolution: $195 \times 260 \mu\text{m}$), along with an enlarged image of highlighted selection which demonstrates sub-cortical WM lesions (arrows).

Fig 4.

(A) 3T axial T1-weighted SPGR image (in-plane resolution $938 \times 938 \mu\text{m}$) of an MS patient with a cortical GM lesion. (B) Axial T2*-weighted image ($195 \times 260 \mu\text{m}$) of the same patient at 7T. (C) Enlarged image of the highlighted selection from Figure 4B demonstrating fine detail within the cortical lesion. (D) Measurement of the cortical lesion. (E) Representative pathology section of a Type 2 lesion, along with cortical layer diagram (from Kidd et al¹³ with permission).

Fig 5. Sagittal T2*-weighted images from age- and sex-matched (A) healthy control and (B) an MS patient. Resolution: $215 \times 286 \mu\text{m}$. Note the dramatic thinning (arrowheads) and the presence of demyelinating lesions in the body and splenium of the corpus callosum (arrows).

Table 1

Imaging Parameters

	Axial-1	Axial-2	Sagittal
TR/TE (ms)	250/15	250/15	250/15
Flip angle	20 °	20 °	20 °
Slice thickness (mm)	2	2	2
Skip	4	1.5	1.5
NEX	2	3	2
FOV (cm)	22	20	22
Matrix size	1024 × 768	1024 × 768	1024 × 768
Number of slices	9	9	9
Imaging time	6:28	9:38	6:28

Table 2

Calculations of signal (SNR) and contrast (CNR) to noise ratios

	WM SNR	GM SNR	WM/GM CNR
TE = 12ms	16.4	25.3	8.9
TE = 15ms	16.1	24.9	8.8
TE = 18ms	13.7	19.3	5.6
TE = 21ms	11.8	18.7	6.9
TE = 24ms	11.0	13.9	2.9

WM = White matter; GM = Gray matter.