REVIEW

High-field MRI of the Central Nervous System: Current Approaches to Clinical and Microscopic Imaging

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Introduction of clinical high-field MRI has raised interest in the use of clinical imaging—the efficacy of which has not yet been fully established—in daily practice. A high signal-to-noise ratio and profound susceptibility effects can improve the spatial resolution and image contrast of clinical imaging, whereas the heating effects of the radio frequency tend to prolong acquisition time. As well, inhomogeneities in the static or local magnetic fields can have a negative effect on image quality. The T_1 prolongation may affect T_1 contrast yet improve the enhancement effect of gadolinium chelate and the inflow effect of MR angiography. High-contrast imaging, such as the short inversion-time inversion recovery technique, can provide excellent intra- and extracerebral contrast comparable to microscopic or macroscopic specimens. High-field systems can also be applied to microscopic imaging. High-field MRI is expected to have an increased clinical impact in the near future. Technological advances tailored to high-field systems, as well as the accumulation of scientific evidence, will be necessary to establish its predominance over conventional MRI.

Keywords: *high-field MRI, 3 tesla, central nervous system, short inversion-time inversion recovery, MR microscopy*

Introduction

High-field magnetic resonance imaging (MRI) is a recent advance in medical imaging. Following the U.S. Food and Drug Administration's approval of brain and whole-body imaging at 4 tesla or less, nearly 100 high-field scanners have been installed worldwide, and many have already been used in daily practice as well as in experimental situations. In Japan, interest in and expectations for the clinical impact of high-field MRI have been growing significantly since the Pharmaceutical Affairs Council of the Japanese Ministry of Health, Labor, and Welfare approved brain imaging at 3 tesla (3T) in February 2003.

The advantages of high-field MRI as a tool for neuroscientific research have already been established, especially in the area of functional imaging, which comprises functional MRI (fMRI).^{1,2}

However, its efficacy in clinical practice remains unclear, mainly because of the paucity of scientific evidence indicating its priority at 3 to 1.5 tesla (1.5T).^{3–7} In this review, we discuss the impact of high-field MRI on clinical imaging of the central nervous system (CNS) by describing the basic knowledge of high-field MRI and morphological imaging techniques at 3T in daily practice. We also briefly introduce magnetic resonance (MR) microscopic imaging, a recent area of interest in high-field MRI.

Influence of a Static Magnetic Field

Developing a full understanding of the advantages as well as the disadvantages of high-field MRI requires knowledge of the influences of a static magnetic field (B_0) on MR images.⁸ It is well known that a high signal-to-noise ratio (SNR) is a major—and possibly the major—advantage of high-field MRI. The SNR is said to rise roughly in proportion to B_0 because the MR signal is propor-

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tionate to B_0 squared (the combined effect of increasing excess protons and the Larmor frequency), whereas the noise is proportionate to B_0 . The high SNR at 3T, which is about twice that at 1.5T, provides images with a high spatial resolution and short acquisition time. The strong susceptibility effects at 3T can enhance the blood oxygen level dependent (BOLD) effects in fMRI^{1,2} and in BOLD MR venography;⁹ the negative enhancement effects of gadolinium chelate in perfusion MRI; and the low signal intensity of iron-containing lesions in routine images. On the other hand, image distortions and other susceptibility artifacts are pronounced, especially with echo planar imaging (EPI) techniques such as diffusion-weighted imaging (DWI) and fMRI. Parallel imaging, line scan and non-EPI techniques are necessary to minimize image deterioration in DWI and diffusion tensor imaging. An increase in the chemical shift in proportion to B_0 can improve spectral resolution of MR spectroscopy at 3T,⁷ whereas in comparison to 1.5T, spatial misregistration of fatty tissues is doubled and the echo time at in-phase between water and fat is halved. The heating effect of the radio frequency (RF) is increased at B_0 squared. The high specific absorption rate (SAR) at 3T, which is four times that at 1.5T, tends to place some limits on clinical imaging. To maintain the SAR under the limit for patient safety, it is usually necessary to compromise scanning parameters by reducing the number of slices, reducing the echo train length or lengthening the repetition time (TR). The T_1 relaxation time is said to be dependent on B_0 . At 3T, the T_1 of brain tissues is generally 1.1 to 1.3 times longer than that at 1.5T.¹⁰ On the other hand, T_2 relaxation is independent of B_0 , although it is somewhat related to T_1 relaxation. However, the apparent T_2 values of tissue and lesions, especially iron-containing nuclei, are shortened, mainly due to diffusion-mediated microscopic susceptibility effects. The nonuniformity of the RF magnetic field (B_1) is also dependent on B_0 , because the penetration of RF into the subjects is decreased at high frequency.¹¹ At 3T, the B_1 inhomogeneity and different flip angles between the surface and center of the subjects are not negligible, sometimes resulting in uneven distribution of the signal intensity. Other characteristics of the high magnetic field include strong motion artifacts, increased acoustic noise, the possibility of transient vestibular stimulation, and tremendous magnetic traction power.

Conventional Imaging

Fast spin-echo (FSE) techniques at 3T can easily

provide high-resolution proton-density weighted images (PDWI), T_2 -weighted images (T_2 WI), and fluid-attenuated inversion recovery (FLAIR) with a matrix size of 512×512 and slice thickness of 3 to 4 mm (Figs. 1a, b, d). A relatively long TR and short effective echo time (TE) would be suitable at 3T because B_1 heterogeneity effects are minimized and apparent T_2 shortening is compensated, respectively. Image contrast seems to be similar to that at 1.5T, but on T_2 WI and FLAIR the low signal intensity of iron-containing nuclei seems to be more prominent than at 1.5T because of pronounced susceptibility effects. When FSE techniques are used, the SAR limitation may considerably restrict parameter settings concerning the number of slices, echo train length or TR, resulting in a prolonged acquisition time. Parallel imaging or novel techniques utilizing lower flip angles such as TRAPS (transition between pseudo steady states) are believed to be effective at avoiding the RF heating issue in FSE sequences.¹²

At 3T, high resolution T_2 WI with a conventional spin echo (SE) technique is also available with an acceptable acquisition time (Fig. 1c). The SAR of this technique is so small that a sufficient number of slices to cover the entire brain can be obtained with a slice thickness of 3 to 4 mm. SE T_2 WI may be applicable as a routine imaging approach in daily practice at 3T. In addition, deep nuclei as well as white matter containing iron show remarkably low signal intensities as a result of apparent T_2 shortening due to diffusion-mediated susceptibility effects.¹³ The image contrast is comparable to that of iron-stained specimens (Figs. 2a, b). Iron-concentration weighted imaging at high spatial resolutions can be accomplished with the SE technique at 3T. T_2^* -weighted images obtained with gradient echo techniques are also promising at 3T. The detectability of microbleeding in arteriosclerosis or diffuse axonal injury is expected to be markedly improved.¹⁴

SE T_1 -weighted images (T_1 WI) seem to be unsuitable for routine imaging at 3T because of several shortcomings: the number of slices is too small to cover the entire brain due to the limitation of the SAR; the uneven signal distribution due to B_1 heterogeneity is prominent, especially at the center of the brain (Fig. 1e); and delay of magnetization recovery due to T_1 prolongation may cause deterioration of the SNR and reduce T_1 -dependent contrast under short TR conditions. As an alternative to SE T_1 WI, we usually use the 3D RF-spoiled gradient echo, which has a high SNR, lower SAR, less B_1 dependency, acceptable T_1 contrast, and multiplanar capability (Fig. 1f). The contrast

Fig. 1. Morphological brain images at 3T (healthy 31-year-old female) Axial images of the same section with a slice thickness of 4 mm, field of view of 22 cm, and matrix size of $512 \times 256 - 384$.

a: FSE proton-density weighted image, **b:** FSE T_2 -weighted image, **c:** SE T_2 -weighted image, **d:** FLAIR, **e:** SE T_1 -weighted image, **f:** reformatted image from 3D RF-spoiled gradient echo, **g:** fast STIR, **h:** video-inverted fast STIR (the same image as **g**, magnified), **i:** T_2 -reversed (the same image as **a**, video-inverted and magnified).

effects of gadolinium chelate may be enhanced at 3T, because the relaxivities of contrast agents R_1 and R_2 are largely constant in the range between 1.5T and 3T.³

The improved image quality of 3D time-of-flight MR angiography (MRA) at 3T is remarkable because of the high SNR and increased in-flow effects resulting from prolonged T_1 relaxation of the blood.⁴ Minute vessels such as anterior choroidal arteries and perforators are clearly visualized (Fig. 3). However, the SAR of magnetization transfer contrast (MTC) pulses is so high that TR should be significantly extended to reduce SAR under this limitation. Recently, novel techniques in which MT pulses apply only around the center of the k-space have succeeded in minimizing TR elongation by significantly reducing the SAR.^{15,16}

High-contrast Imaging

In daily practice, MRI examinations are performed with a combination of several kinds of images, including T_1 WI, T_2 WI, PDWI/FLAIR, DWI, and MRA. They provide complicated but useful data on lesion detection and characterization. However, the anatomical details of CNS structures in such images are sometimes lacking. It is therefore preferable that a new imaging technique be established that is capable of visualizing almost all the clinically required morphological information. To our knowledge, this was first proposed by Fujii and Nakada.¹⁷⁻¹⁹ They developed video-inverted high-resolution PDWI (4000/17), known as T_2 -reversed imaging (T_2 R), as a routine 3T imaging technique (Fig. 1i). T_2 R has superb contrast and spatial resolution mimicking gross

Fig. 2. Susceptibility effects in SE and FSE images at 3T

a: SE T₂-weighted image (healthy 31-year-old female). The globus pallidus shows low signal intensity (arrows), as do the putamen, anterior limb of the internal capsule, dorsomedial nucleus, and pulvinar.

b: Coronal SE T₂-weighted image (the same volunteer as in **a**). The emboliform nucleus can be clearly identified (arrow) superomedial to the dentate nucleus.

c: Fast STIR image (ruptured cavernous hemangioma, 51-year-old female).

A low signal intensity suggesting a hemosiderin rim is evident. The fresh intratumoral hemorrhage shows the fluid-fluid level between the high and low signal intensity areas.

Fig. 3. 3D time-of-flight MR angiography with optimized magnetization transfer pulses at 3T (healthy 39-year-old female)

Visualization of cortical branches is excellent (**a**). Anterior choroidal arteries (**b**: arrows) and perforating arteries (**c**: arrows) are also clearly depicted.

specimens, which makes it possible to visualize minute intracerebral and extracerebral structures because of the inherently high SNR and contrast of PDWI as well as the improved conspicuity provided by video-reversal processing.

As an alternative to T₂R, we proposed a fast short inversion-time inversion recovery (STIR) technique.^{20–22} The STIR sequence is widely known as a fat suppression technique, but it has high contrast resolution because the proton density and T₁ and T₂ relaxations have synergetic effects on image contrast. The SNR, which is considered relatively low, can be increased by utilizing FSE technique with a longer TR and shorter inversion time. T₁ prolongation of brain tissues at 3T also

contributes to an improved SNR. Acquired images show excellent intracerebral contrast nearly identical to that of the myelin-stained specimens (Fig. 1g). We can identify minute intracerebral structures such as the subthalamic nucleus, intrathalamic structures, and intrahippocampal components, which are not well identified by MRI (Fig. 4). Under reversed video, the fast STIR technique can successfully mimic T₂R (Fig. 1h). Visualization of cerebral vessels and other extracerebral structures is excellent. The contrast of pathological lesions is also superb, because T₁ and T₂ relaxations additively affect signal alteration. Even hemorrhagic lesions can be identified thanks to strong susceptibility effects under 3T (Fig. 2c).

Fig. 4. High-resolution fast STIR images at 3T

a, b: Coronal contiguous images (healthy 54-year-old female). The subthalamic nucleus (s) is clearly identified as a low signal intensity area below the ventral thalamus (vt). The circuit of Papez including the mamillary body (m), mamillothalamic tract (mt), and anterior thalamic nucleus (a) is visualized. Other intrathalamic substructures, including the internal medullary lamina (im), dorsomedial nucleus (dm), ventrolateral nucleus (vl), lateral dorsal nucleus (ld), lateral posterior nucleus (lp), and ventral posterolateral nucleus (vpl), can also be seen. n: substantia nigra, p: cerebral peduncle.

c: Oblique coronal images perpendicular to the long hippocampal axis (healthy 57-year-old female). Intra-hippocampal structures, such as the molecular layer of the cornu ammonis (arrow) and residual cavity of hippocampal sulcus (arrowhead), are well depicted. f: fimbria, n: substantia nigra, r: red nucleus.

Fig. 5. Lower convexity meningioma (52-year-old female)

a, b: Fast STIR images at 3T, **c:** FSE T_2 -weighted image at 1.5T.

On fast STIR images at 3T, intratumoral textures, tumor vessels, and surrounding cerebral vessels and cerebral parenchyma are clearly visualized, revealing much more information than is available in images obtained at 1.5T.

As a preoperative means of assessing brain tumors, fast STIR can provide useful information concerning the tumor itself, tumor vessels, and surrounding vascular and parenchymal structures (Fig. 5). Fast STIR seems to be an all-round imaging technique at 3T and can replace other conventional images in some situations of daily practice.

Microscopic Imaging

High-field MRI has the potential to achieve microscopic imaging. Recently, this field has marked several innovations. A perfusion technique

using fixatives containing gadolinium chelate has allowed us to obtain high-resolution *in-vitro* volume images with a relatively short acquisition time.^{23,24} With this technique, the SNR of small animal brains can be dramatically increased by up to eight times. The image contrast depends mainly on the vasculature of tissues and resembles that of the above-mentioned STIR images (Fig. 6). Free unchelated manganese is utilized as a contrast agent or a neuroaxonal tracer.^{25,26} *In-vivo* visualization of beta-amyloid plaque in transgenic mouse brains has been accomplished with iron-labeled peptides.²⁷

Fig. 6. MR microscopic imaging at 3T

MR microscopic images of the rat (**a**, **b**) and cat (**c**) after perfusion by fixatives containing 5% and 2% Gd-DTPA. 3D T₁-weighted FSE, voxel size: 0.3 × 0.3 × 0.3 mm, acquisition time: 1.5 hours.

Conclusions

High-field MRI is a promising technique not only for scientific research, but also for clinical imaging of the CNS. Its clinical impact is expected to increase in the near future. However, its efficacy in diagnostic performance, patient outcome, and societal aspects has not yet been fully established. Optimization of imaging techniques and the accumulation of scientific evidence is clearly essential to future development.

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References

- Kim S, Ashe J, Georgopoulos AP, et al. Functional imaging of human motor cortex at high magnetic field. *J Neurophysiol* 1993; 69:297–302.
- Turner R, Jezzard P, Wen H, et al. Functional mapping of the human visual cortex at 4 and 1.5 tesla using deoxygenation contrast EPI. *Magn Reson Med* 1993; 29:277–279.
- Nobauer-Huhmann IM, Ba-Ssalamah A, Mlynarik V, et al. Magnetic resonance imaging contrast enhancement of brain tumors at 3 tesla versus 1.5 tesla. *Invest Radiol* 2002; 37:114–119.
- Bernstein MA, Huston III J, Lin C, Gibbs GF, Felmlee JP. High-resolution intracranial and cervical MRA at 3.0T: technical considerations and initial experience. *Magn Reson Med* 2001; 46:955–962.
- Hunsche S, Moseley ME, Stoeter P, Hedehus M. Diffusion-tensor MR imaging at 1.5 and 3.0T: initial observations. *Radiology* 2001; 22:550–556.
- Wang J, Alsop DC, Li L, et al. Comparison of quantitative perfusion imaging using arterial spin labeling at 1.5 and 4.0 Tesla. *Magn Reson Med* 2002; 48:242–254.
- Gonen O, Gruber S, Li BSY, Mlynarik V, Moser E. Multivoxel 3D proton spectroscopy in the brain at 1.5 versus 3.0T: signal-to-noise ratio and resolution comparison. *AJNR* 2001; 22:1727–1731.
- Ugurbil K, Garwood M, Ellermann J, et al. Imaging at high magnetic fields: initial experiences at 4T. *Magn Reson Q* 1993; 9: 259–277.
- Barth M, Noebauer-Huhmann IM, Reichenbach JR, et al. High-resolution three-dimensional contrast-enhanced blood oxygenation level-dependent magnetic resonance venography of brain tumors at 3 Tesla: first clinical experience and comparison with 1.5 Tesla. *Invest Radiol* 2003; 38:409–414.
- Wansapura JP, Holland SK, Dunn RS, Ball WS. NMR relaxation times in the human brain at 3.0 Tesla. *J Magn Reson Imaging* 1999; 9:531–538.
- Alecci M, Collins CM, Smith MB, Jezzard P. Radio frequency magnetic field mapping of a 3 Tesla birdcage coil: experimental and theoretical dependence on sample properties. *Magn Reson Med* 2001; 46:379–385.
- Hennig J, Weigel M, Scheffler K. Multiecho sequences with variable refocusing flip angles: optimization of signal behavior using smooth transitions between pseudo steady states (TRAPS). *Magn Reson Med* 2003; 49:527–535.
- Schenck JF. Magnetic resonance imaging of brain iron. *J Neurol Sci* 2003; 207:99–102.
- Scheid R, Preul C, Gruber O, Wiggins C, von Cramon DY. Diffuse axonal injury associated with chronic traumatic brain injury: evidence from T₂*-weighted gradient-echo imaging at 3T. *AJNR*

- 2003; 24:1049–1056.
 15. Thomas SD, Al-Kwif O, Emery DJ, Wilman AH. Application of magnetization transfer at 3.0T in three-dimensional time-of-flight magnetic resonance angiography of the intracranial arteries. *J Magn Reson Imaging*. 2002; 15:479–483.
 16. Lin C, Bernstein MA, Gibbs GF, Huston III J. Reduction of RF power for magnetization transfer with optimized application of RF pulses in k-space. *Magn Reson Med* 2003; 50:114–121.
 17. Fujii Y, Nakayama N, Nakada T. High-resolution T₂-reversed magnetic resonance imaging on high magnetic field system. *J Neurosurg* 1998; 89:492–495.
 18. Nakada T. High-field, high-resolution MR imaging of the human indusium griseum. *AJNR* 1999; 20: 524–525.
 19. Harada A, Fujii Y, Yoneoka Y, Takeuchi S, Tanaka R, Nakada T. High-field magnetic resonance imaging in patients with moyamoya disease. *J Neurosurg* 2001; 94:233–237.
 20. Sasaki M, Oikawa H, Ehara S, Tamakawa Y. Ventral thalamus and subthalamic nucleus: MR findings using optimized fast short inversion-time inversion-recovery technique. *Radiology* 2000; 217(P):672 (abstract).
 21. Sasaki M, Oikawa H, Ehara S, Tamakawa Y. Internal structures of cerebral gray matter at 3 Tesla: MR imaging using fast short inversion-time inversion-recovery technique. *Radiology* 2001; 221(P):672 (abstract).
 22. Oikawa H, Sasaki M, Tamakawa Y, et al. The substantia nigra in Parkinson disease: proton density-weighted spin-echo and fast short inversion-time inversion-recovery MR findings. *AJNR* 2002; 23:1747–1756.
 23. Johnson GA, Cofer GP, Gewalt SL, Hedlund LW. Morphologic phenotyping with MR microscopy: the visible mouse. *Radiology* 2002; 222:789–793.
 24. Johnson GA, Cofer GP, Fubara B, et al. Magnetic resonance histology for morphologic phenotyping. *J Magn Reson Imaging* 2002; 16:423–429.
 25. Watanabe T, Natt O, Boretius S, Frahm J, Michaelis T. *In vivo* 3D MRI staining of mouse brain after subcutaneous application of MnCl₂. *Magn Reson Med* 2002; 48:852–859.
 26. Watanabe T, Michaelis T, Frahm J. Mapping of retinal projections in the living rat using high-resolution 3D gradient-echo MRI with Mn-induced contrast. *Magn Reson Med* 2001; 46:424–429.
 27. Pautler RG, Mongeau R, Jacobs RE. *In vivo* trans-synaptic tract tracing from the murine striatum and amygdala utilizing manganese enhanced MRI. *Magn Reson Med* 2003; 50:33–39.
 28. Wadghiri YZ, Sigurdsson EM, Sadowski M, et al. Detection of Alzheimer's amyloid in transgenic mice using magnetic resonance microimaging. *Magn Reson Med* 2003; 50:293–302.
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