Clinical applications

7T MRI research in neurology: initial results and future research applications

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The C.J. Gorter Center for High Field Magnetic Resonance Imaging (MRI) at the Leiden University Medical Center was established within the Department of Radiology in late 2007. The aim of the center is the development of new methods and protocols for high field clinical MRI in a variety of patient populations, in parallel with performing studies of correlative disease models in animals. In particular, the Center has recently installed a Philips Achieva 7T whole-body MRI system, one of only two in the Netherlands.

Strong collaborations exist within the Virtual Institute for Seven Tesla Applications (VISTA), a Dutch initiative of researchers from the University Medical Centers in Leiden, Utrecht and Nijmegen, and from the FC Donders Center for Cognitive Neuroimaging in Nijmegen. The 7T system presents major technical challenges to be able to achieve the full advantages of the high magnetic field. This article summarizes progress in neurological applications during the first year of research with the 7T scanner at Leiden.

Background

The past twenty years have seen a steady increase in the magnetic field strengths used for clinical MRI. If one compares, for example, 7T vs. 3T, the major advantages of the high field can be summarized as:

- an increased signal-to-noise (S/N) allowing higher spatial resolution or reduced scanning times
- a significantly increased sensitivity to differences in tissue magnetic susceptibility at the micro/mesoscopic scale, essentially introducing a new contrast mechanism
- an increased spectral resolution for localized MR spectroscopy.

The major challenges include:

- far greater signal inhomogeneity within the patient due to the interaction of high frequency (298 MHz) electromagnetic energy with the body
- higher energy deposition, as measured by the specific absorption ratio (SAR), in the patient with the potential of localized “hotspots”
- a greater degree of image artifacts from macroscopic static field (B0) inhomogeneities at tissue/air and tissue/bone boundaries.

In addition, tissue T1 relaxation times are longer at 7T and T2 values decrease, which reduces some of the improvements in S/N from the high field. Currently, there are also many practical issues, for example the lack of radiofrequency (RF) coils in general at 7T and the lack of a body coil in particular.

The Philips 7T Achieva system installed in Leiden, shown in Figure 1a, weighs 32,000 kg and has linear dimensions of 3.7 x 2.4 x 2.6 m (length x width x height). The 5 gauss line would be about 22.5 m from the magnet isocenter. The setup at Leiden, similar to many elsewhere, has about 400 tonnes of steel for passive magnetic shielding that brings the 5 gauss line to about 6 m from magnet isocenter. For neurological

Figure 1a. The Philips Achieva 7T system installed in Leiden in 2007.
applications, the system is delivered with a quadrature birdcage transmit coil and a 16 channel receive array, as shown in Figure 1b.

The current gradient configuration has a maximum strength of 33 mT/m with a slew-rate of 166 mT/m/ms. Two radiofrequency (RF) channels are available for proton and carbon experiments, each channel being driven by a 4 kW RF amplifier. Table motion for patients is currently only possible manually, and in the horizontal direction. The Philips system has a very simple hardware interface, illustrated in Figure 1c, which enables the use of custom-built RF coils via a standard type-N connector. One such example, constructed in Leiden, a simple transmit and receive surface coil for localized brain imaging, is shown in Figure 1d.

Based upon the advantages of high field outlined above, our current approach to developing protocols of clinical neurological relevance concentrates on three specific areas:

- high-resolution MR angiography and diffusion tensor imaging
- susceptibility and phase imaging with quantitative assessment of the distribution of the magnetic susceptibility
- localized proton MR spectroscopy.

High-resolution magnetic resonance angiography and diffusion tensor imaging

Enhanced spatial resolution is of most benefit when the dimensions of the structures of interest are very similar to that of the improved resolution. One example of direct clinical significance is high-resolution magnetic resonance angiography (MRA). Current clinical protocols at 3T typically acquire three-dimensional time-of-flight (TOF) angiograms at a spatial resolution of 1 x 1 x 1 mm and, therefore, much of the fine branching structure, which may be disrupted in vascular disease, is not visible.

At 7T, in addition to the increased spatial resolution, background tissue suppression is improved compared to 3T because of the higher tissue T1 value. The relatively low flip angles in 3D TOF sequences mean that SAR is not a major issue. The use of TOF MRA at 7T was first analyzed by the group in Utrecht [1].

Figure 2 shows a series of 3D TOF angiograms acquired at a spatial resolution of 0.23 x 0.23 x 0.23 mm. The data acquisition protocol is based on one developed recently specifically for high field [2], but the use of parallel imaging and sequence optimization allowed us to improve the spatial resolution by approximately 50% in the slice-select dimension. The very high spatial resolution gives clear visualization of the lenticulostriatal arteries, and the branching points from the major feeding artery.

This high-resolution MRA protocol is now part of ongoing clinical research at the LUMC into a number of neurodegenerative diseases that have components of small vessel disease such as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL).

The second area in which the higher spatial resolution at 7T will be clinically relevant is diffusion tensor imaging (DTI) in which the size of the white matter fiber tracts is much smaller than the imaging voxels. The most important potential confounding factors in DTI at high field is the increased macroscopic susceptibility effect. Eddy current compensation is particularly important, and significant improvements were seen with Philips’ recent “blue-ball” method.
Figure 2. 3D TOF angiograms from a volunteer acquired using the 16-channel head coil with 0.23 mm$^3$ isotropic voxels acquired in 10 minutes.

Figure 2a. Overview of the transverse maximum intensity projection (MIP).

Figure 2b. Selected slab, thickness 5 cm, through the circle of Willis.

Figure 2c. Expansion of the circled area in Figure 2b showing the lenticulo striatal arteries that branch off from a main artery and enter the basal ganglion.

Figure 3. Results from DTI of a volunteer acquired at a spatial resolution of 1.5 x 1.5 x 1.5 mm in ten minutes.

Figure 3a. and Figure 3b. Show two fractional anisotropy maps at different levels in the brain.

Figure 3c. Shows a fiber tract map through the corpus callosum.
Although some distortions can be seen in areas close to air/tissue and bone/tissue interfaces, the overall fractional anisotropy (FA) maps are very similar to those acquired at 3T, but at significantly higher resolution (1.5 x 1.5 x 1.5 mm) compared to the standard imaging protocol (~2.1 x 2.1 x 2.1 mm) at 3T. An example is shown in Figure 3.

Susceptibility and phase imaging

Early work at 7T [3] showed that high field imaging was particularly sensitive to the very small differences in the magnetic susceptibility of different tissues in the brain. Furthermore, it was shown by Duyn et al. [4] that even greater tissue contrast could be generated by using the phase image rather than the standard magnitude image. An example from the 7T at Leiden is shown in Figure 4, in which fine structures within the gray matter can be visualized in the phase image, but not in the magnitude image.

The direct relevance of this type of “susceptibility-weighted” imaging is to diseases such as Alzheimer’s disease and multiple sclerosis, in which the detection of small plaques could potentially form the basis of neuroradiological diagnosis. In Alzheimer’s disease, many of these plaques are visualized as dark spots in the magnitude image, indicating the presence of iron or other metals within the plaque.

However, some plaques are virtually invisible on magnitude images but can be seen on the phase images, suggesting the absence of metal deposition, but such observations are still somewhat controversial. Quantification of susceptibility is therefore an important goal, and our approach at 7T has followed that of Jensen et al. at 3T [5] in calculating magnetic field correlation (MFC) maps using asymmetric spin echo (ASE) sequences.

These MFC maps represent measures of the spatial heterogeneity in the magnetic field susceptibility, with high values of the MFC having been shown to correspond to areas of the brain with high iron concentration. Since the MFC scales as the square of the magnetic field strength, measurement at 7T is much more sensitive than at 3T. Figure 5 shows an example of an MFC map obtained at 7T from a volunteer.

Currently, clinical studies are being performed on patients with Alzheimer’s and Huntington’s disease to quantify the deposition of iron in plaques in the former case, and the altered biodistribution of iron in different parts of the basal ganglia in the latter.

Localized proton spectroscopy

The range of metabolite resonance frequencies increases linearly with field strength and therefore, provided that the linewidths of the individual resonances are not broadened significantly at the higher field, the spectral resolution also increases linearly with field strength. Since metabolite T1 values and T2 values are not highly field dependent, one also expects a significant increase in S/N. This can be used to acquire spectra from smaller voxels, to improve spectral quantitation via increased S/N, or to reduce the data acquisition time, or a combination of all three.

The two most commonly used localized spectroscopy sequences are stimulated echo acquisition mode (STEAM) and point resolved spectroscopy (PRESS). Although PRESS has a theoretical factor of two higher S/N than STEAM, PRESS requires a much longer echo time and suffers from a higher chemical shift artifact than STEAM and so our current protocols use the STEAM sequence.

Ongoing studies include Huntington’s disease and familial hemiplegic migraine. Figure 6a shows a spectrum acquired from the frontal lobe of a healthy volunteer. In addition to the resonances from creatine, choline and N-acetylaspartate (NAA), which are observable at 3T (albeit at much lower S/N), metabolites such as GABA can be detected at 7T. This is due to the increased spectral resolution, as they are not observed at 3T. Figure 6b shows a spectrum from the migraine study, in which the high spectral quality allows the concentrations of several coupled and singlet resonances to be quantified using commercial software such as the LC-model.

The improved spectral resolution can also be used to address basic research questions. In collaboration with Dr. Itamar Ronen at Boston University, we are investigating the diffusion properties of NAA and NAAG to determine the ability to quantitate NAA diffusion at lower field strengths. At 1.5T and 3T, the spectral resolution is not sufficient to separate the NAA and NAAG peaks, and so the measured diffusion coefficient is a weighted average of the two metabolites.

At 7T the resonances from NAA and NAAG can be at least partially resolved, as shown in Figure 6, and therefore separate diffusion coefficients can be measured. Preliminary results suggest that the diffusion coefficient of NAA is approximately 30% lower than that of NAAG.
Figure 4. Enlargement of the temporal lobe of a volunteer.

Figure 4a. Image in magnitude mode. Fine details within the white matter can be seen due to small differences in magnetic susceptibility. The image is from a heavily T2*-weighted gradient echo sequence with a TE of 30 ms.

Figure 4b. The corresponding phase image shows even more information than the magnitude image, including substructures within the gray matter.

Figure 5. Calculation of an MFC map from 7T images obtained from a volunteer.

Figures 5a, b. Two slices from ASE sequence showing the following areas: (arrow 1) globus pallidus, (arrow 2) putamen, (arrow 3) red nuclei, (arrow 4) substantia nigra.

Figures 5c, d. Calculated MFC maps from the corresponding areas. A high value of the MFC is seen in all four areas. Total acquisition time for all the ASE images was eight minutes.
Although the images obtained are not yet of clinical quality, these new approaches show considerable promise for the future, since they may form alternatives to complicated transmit arrays at high fields.

Patient acceptance of 7T

Aside from protocol and technique development, it is also important that 7T MRI be compatible with patient studies in terms of patient acceptance of the entire procedure. The results of a survey of volunteers and patients who have undergone a 7T scan are shown in Figure 8. The time duration of a scan is currently limited to one hour by the Ethics Committee at the Leiden University Medical Center.

The majority of these studies have been neurological, but the development of in-house RF coils has enabled a number of cardiac and musculoskeletal studies to be performed. The results of the survey show that the most common effect is dizziness when entering the magnet, suggesting that very slow table motion should be used. Overall, there is very little difference among the experiences of volunteers and patients between having 3T and 7T scans.

Future clinical directions

As of 2009, 7T human MRI research is a field dominated academically by technical innovations in RF design, sequence optimization for both...
The use of 7T MRI is clearly not anticipated to replace that of 3T for general clinical diagnosis, but to supplement it for specific, well-defined types of scans.

Twenty years of intensive commercial and academic developments meant that the transition from 1.5T to 3T was essentially entirely comprehensive in terms of increased image quality. In large part, this was because no fundamental changes in hardware beyond those for 1.5T were needed. The situation is completely different when comparing 3T with 7T MRI. Patient dimensions are now a substantial fraction of the wavelength of the RF irradiation and, particularly for body imaging; this requires a fundamental redesign of data acquisition and hardware.

In our view, it is important to define specific types of examinations that will benefit from the higher magnetic field. For example, standard imaging protocols such as T1, T2 and proton density weighting can all be run with excellent results at 7T, but essentially produce images with no greater diagnostic value (and often considerably lower value) than those at 3T.
Although higher spatial resolution is often touted as a reason for moving to higher fields, the S/N increases approximately in proportion to the field strength [7]. That means that the best that can be achieved under ideal conditions is an isotropic increase in resolution by a factor of about 30% in each dimension or, alternatively, a reduction in slice thickness by a factor of between two and two-and-a-half.

Our research approach is therefore is to use 3T scanning for standard morphological imaging, and the 7T for supplemental scans including high-resolution angiography, susceptibility-weighted scanning and/or localized proton spectroscopy. In the future, we plan to investigate the clinical potential for heteronuclear imaging and spectroscopy, a general area in which 3T simply does not have the sensitivity. Potential targets include $^{13}$C spectroscopy for studying metabolism in Alzheimer patients, $^{23}$Na for studies of migraine, and $^{31}$P for Huntington's disease.

References


