Syllabus

Advanced Neuroimaging 1st Course
Ultrahigh field MR (7 Tesla): Specific clinical applications in neuroimaging

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Background

Presently, at least three major MR vendors provide commercial 7T units for clinical research under adequate ethical permission. During the last years, the number of installations finalized or under preparation has increased to about 40. This rapid increase indicates the growing interest in ultra-high field MRI brought forward by improved results regarding morphological detail as well as functional and metabolic imaging capability.

High resolution morphological neuroimaging

Since the SNR scales linearly with the field strength (Bo) the most obvious application of increased sensitivity at 7 Tesla is obtaining higher spatial resolution in the brain.

Of specific clinical interest for neuro-applications is that different layers of the cerebral cortex can be seen at 7T (in general not possible at lower field strengths) due to the improved image SNR, contrast-to-noise ratio (CNR) and spatial resolution. At 7T a spatial resolution of 100-200 micrometers can be obtained in vivo and this improvement may be used, for example, for the detection of changes in cortical structure as a first sign of early dementia, as well as for visualisation of small lesions, vascularisation and myelin pathology in early multiple sclerosis.

Another structure of interest is the hippocampus, a challenging structure to depict at low fields due to its small size and heterogeneous structure. The high-resolution depiction of the hippocampi is possible at 7 T without significant artefacts with proton density, T2, and T2* sequences, but also with the T1 MPRAGE with an isotropic 0.5 mm resolution. Even subfields of the internal hippocampal anatomy can be visualised with excellent resolution, which motivates the search for clinical applications. Cryptogenic epilepsy, for instance, remains an unresolved problem; in these patients, no structural abnormality can be diagnosed at MRI up to 3 T. The higher resolution of 7 T MRI would appear to be beneficial and is currently being evaluated; initial investigations have been conducted in patients with known mesial sclerosis. Of course, also of interest are hippocampal changes associated with dementia of Alzheimer type.

Malignant brain tumors

The significantly enhanced sensitivity of 7 T may prove to be a decisive advantage for the diagnosis of tumourous entities. The increased sensitivity to susceptibility artefacts can for example be used to make haemosiderin visible in a SWI sequence; such haemosiderin deposits may be associated with bleeding within tumours or metastases. The appearance of venous vessels is also markedly increased by the enhanced artefact used as static BOLD effect in susceptibility-weighted imaging (SWI). This can be helpful to reveal the vascular distribution and possible neovascularisation in primary brain tumours. Gliomas can already...
be well depicted with conventional field strengths. The improved representation of vessel-rich areas, however, could be of relevance: These areas should be indicative of higher malignancy. A more accurate target determination might thus be conducted before a stereotactic biopsy. In addition to other techniques such as MR spectroscopy, the visualisation of augmented vascular presence could be a further component in the assessment of primary brain tumour malignancy. Additionally, using SWI with high resolution the efficacy of new antiangiogenetic drugs, which should suppress the development of new tumor vessel formation in malignant tumors, can now be monitored if the patients respond to the therapy or not.

Microangiopathic Changes

Ultra-high field is certainly not necessary for the diagnosis of microangiopathic changes in the brain. In the case of such microangiopathic white matter changes, a SWI gradient-echo sequence should certainly be added to the clinical workup. This sequence is particularly sensitive to susceptibility artefacts as may originate from haemosiderin deposits in brain tissue. This allows the identification of small microbleeds that can occur in patients with microangiopathy, even if the microangiopathic changes themselves are not yet very pronounced. Previous investigations have shown a correlation between the number of microbleeds and the extent of cognitive deficits. Furthermore, it has been put forward that in patients with microbleeds, secondary prevention measures with anticoagulants should be reconsidered. With the help of higher field strengths such as 7 T, the detection limit for microbleeding can be significantly improved. If many microbleeds have already been established at 1.5 T or 3 T, the patient does not need to undergo a 7 T MRI, but if an anticoagulant therapy is planned in a patient with known microangiopathy and often co-existing cardiovascular pathologies, one should be as certain as possible that no microbleeding exists, so that the prophylactic therapy can be individually adapted and large intracerebral bleedings prevented. In such cases, the more sensitive detection method, SWI at 7T, might be important and helpful.

Multiple Sclerosis

In the context of the first appearance of clinical symptoms, MRI can often diagnostically confirm MS. Some lesions, however, cannot be depicted or are only very poorly depicted at 1.5 T or 3 T. This is important if, for example, this is the only lesion of the patient. Particularly cortical lesions are often difficult to depict; imaging at 7 T, with increased resolution, can be more successful in this regard. Moreover, it is possible to reveal the anatomical features of the plaques almost microscopically. The typical localization of the plaques around small venules can, for example, be clearly shown on SWI. This ability might provide an additional radiological differentiator between MS lesions and microangiopathic white matter lesions. Recently, it could be demonstrated that MS plaques contain more white matter veins compared to normal appearing white matter and show an increase of vessel density in the follow-up of one year, but only in the recurrent-relapsing type of MS. This may be an indirect sign of hypermetabolism within the plaqued which leads to a higher oxygen demand and therefore higher deoxygenation in small veins which consequently become more visible. In addition also small spots of iron accumulation could be found in MS plaques, which recently are an issue in the discussion on the pathogenesis of MS. Local release of iron is considered as a trigger for formation of free radicals with mitochondrial damage as an important factor for the induction of MS lesions. Moreover, iron induced radical formation may be a possible cause as a secondary enhancement factor for neurodegeneration.
Angiography

With increasing field strength, proton T₁ relaxation times are prolonged, which is anticipated to benefit time-of-flight (TOF) angiography. Combined with the much higher spatial resolution, which can be implemented due to enhanced sensitivity, the depiction of much finer vessel branches is achievable. With this technique it is now possible to depict very small blood vessels such as the lenticulostrate arteries. Even perforating arteries with their origin in the posterior communicating artery can be visualised at 7 T.

Thus far it has been shown that a reliable depiction of all diagnostically relevant intracranial vessels is possible. Various gradient-echo sequences can be used (TOF; interpolated 3D Fast Low-Angle Shot (3D FLASH), and Magnetization-Prepared Rapid Gradient-Echo (MPRAGE) can be used. The use of MPRAGE to depict the intracranial vessels only becomes feasible at ultra-high field strength, since at lower field strengths the vasculature contrast is not sufficient. This option opens up new possibilities in the diagnosis of intracranial vascular changes: In addition to the vessels themselves, which appear hyperintense without contrast medium as in TOF MR angiography (MRA), the perivascular structures are well depicted and can be assessed in the source images.

Clinical functional MRI (fMRI)

With the increasing field strength of available magnets, fMRI continues to gain importance in cognitive neuroimaging. The blood oxygenation level dependent (BOLD) signal rises appreciably with increasing field strength, as it benefits doubly from both the higher SNR and the increased susceptibility sensitivity. This makes it possible, among other prospects, to use fMRI to examine individual events without the necessity for repetitions of the active stimuli in contrast to the rest condition, enabling new paradigms. Furthermore, a significantly improved spatial resolution is possible, so that activations can be represented in millimetre resolution. Due to the increased BOLD-sensitivity, standard smoothing is no longer required, enabling single patient activation maps and more specific functional diagnostics.

The most common clinical application of fMRI is usually the representation of eloquent areas before tumour removal. Typically, this involves motor or linguistic paradigms, which can be well applied at 7 T similar to lower field strengths. The success of fMRI can be significantly higher at 7 T, particularly in cancer patients, as here the increased signal facilitates good activations even with limited subject compliance. A very recent study in 17 tumor patients performed presurgical localization of the primary motor hand area, a rather benign area in terms of magnetic field homogeneity, compared 3 T and 7 T results based on identical investigational procedures and comparable system specific sequence optimizations. Significantly higher functional sensitivity was obtained at 7 T, as shown via percent signal change, mean t-values, number of suprathreshold voxels and contrast-to-noise ratio. On the other hand, 7 T data suffered from significantly increased ghosting and head motion artefacts. To what extent this advantage is relevant to clinical practice, i.e., treatment options and survival rate, and whether this gain is achievable in more difficult brain areas will have to be examined in future studies.

Brain metabolism

Although ¹H-MRS at 1.5 T has been approved by the FDA several years ago, it is still not in wide clinical use. 3 T has already helped to improve sensitivity and specificity in ¹H-MRS. The 3 major metabolites, i.e., NAA (N-Acetyl-Aspartate), Cr (total Creatine), Cho (Choline compounds), are reliably accessible whereas other important metabolites like myo-Inositol (mlns) strongly overlap with other metabolites, and the amino acids Glutamine and Glutamate are not well separated and thus summed to Glx, limiting specificity. Furthermore,
GABA and glucose detection and, most importantly, quantification are rather limited. Here, 7 T may provide the extra amount in sensitivity and spectral dispersion to increase specificity in both directions, anatomically (smaller voxel size) and spectrally (distance between peaks on the frequency axis).

Pathologic alterations are more often distributed across larger parts of the brain and, therefore, spectroscopic imaging might be more valuable in clinical diagnosis. Although ultra-high magnetic field ¹H-MRSI is one of the most promising methods for the assessment of brain tissue and pathologic changes, there are several challenges to be met. It has been demonstrated that higher-order shimming of the brain at 7 T results in massive improvements in B₀ homogeneity, helping in particular functional (EPI) and spectroscopic (MRSI) measurements as compared to typical 1ˢᵗ and 2ⁿᵈ-order shims implemented in clinical systems. Some groups improved the suppression of subcutaneous lipid signals, whereas others aimed to optimize the detection of specific amino acids. For example, glutamate and/or glutamine, important in epilepsy, as well as taurine and GABA can be detected directly via ¹H-MRS at 7 T, and even glycine becomes visible. Recently, a method based on free induction decay (FID) acquisition, with optimized outer volume suppression enabled high-resolution (64x64) metabolic (NAA, NAAG, Cr, Cho, mI) and amino acid (Glu, Gln, Tau) mapping of the human brain in reasonable measurement time. High spatial resolution results have been obtained, resulting in excellent separation of grey and white matter voxels in the brain, achieved with high sensitivity due to ultra-short TE* (=1.3 ms). The high spatial resolution significantly reduces contamination (blurring) between voxels located in different tissue types, reduces the linewidth and, therefore, allows for full separation of Glu and Gln, similar to the 10 times larger single voxel spectrum.

Conclusion

Ultrahigh field MR at 7 Tesla due to the increase in SNR can be used to increase spatial resolution in the brain within clinically acceptable scan times. Furthermore, the BOLD effect used as static in SWI as well as dynamic in fMRI is significantly enhanced at 7T and can be combined with high spatial resolution. The higher spectral resolution at 7T can be used to improve ¹H MR spectroscopy as well as metabolic imaging with reduction in voxel size and gain in spectral quality.