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# General discussion

The development of magnetic resonance imaging (MRI) systems with increasing field strengths is driven by the promise of higher signal-to-noise ratios (SNR) resulting in imaging structures that could not be visualized before. However it is not trivial to obtain the improvements that can be theoretically expected. The transition from a conventional 3 Tesla MRI scanner to a research 7 Tesla system creates intrinsic challenges, such as radiofrequency (RF) inhomogeneity, $B_0$ inhomogeneity and increased tissue heating that can negate the expected improvements. In this thesis several new techniques have been developed and applied to 7 Tesla MRI to optimally benefit from the expected improvements in SNR, and contrast.

## INTRINSIC CHALLENGES OF 7 TESLA MRI

### *RF field inhomogeneities*

Creating a highly homogeneous RF field ($B_1$) is of great importance for many MR applications. In addition to the homogeneity it needs to be created with high efficiency to reduce the tissue induced heating. However this is not easily achieved. The short wavelength (approximately 11 cm in human tissue) and as a result deconstructive interference of the RF field (1) prohibits, or at least seriously limits the application of conventional RF coils (2, 3) used at lower field strengths. Almost all recently developed pulse sequences and system calibration sequences for 1.5 Tesla and 3 Tesla systems assume a homogeneous $B_1$ field, therefore a simple translation of protocols will not work at 7 Tesla. There are two ways to mitigate these issues, the first is to develop different coils which are sufficiently homogeneous within a certain region-of-interest (ROI), and the second approach is to develop sequences which are robust to variations in the $B_1$-field. Since the introduction of 7 Tesla MRI systems a range of different coils has been developed. When the ROI is sufficiently small, such as for imaging leg muscles, the eye lens, or even the heart or spine, a relatively simple local transmit-receive (Tx/Rx) coils can provide adequate coverage and homogeneity (4–7). This thesis has shown the development of a local Tx/Rx coil for cardiac imaging, which was used to visualize the lumen of the right coronary artery (8). For larger anatomies, or for improved homogeneity more sophisticated design is required using multiple independently driven RF coils simultaneously ($B_1$-shimming) to create constructive addition of $B_1$-fields (9–11), or using “traveling wave” antennas (12, 13). Concurrently pulse sequences can be adapted to provide robustness for variations in the $B_1$-field while staying within the specific absorption rate (SAR) limits for tissue heating. SAR intensive protocols involving turbo spin echo and fluid attenuated inversion recovery sequences have been adapted to cope with these issues (14). For small targeted areas, such as in single voxel MRS the $B_1$ field can be considered homogeneous, relatively independent from the used coil configuration. This thesis has shown that a volume specific RF calibration can accurately establish the relation between RF amplifier power and generated $B_1$ field in a small localized region, resulting in an increased SNR of single voxel spectra obtained in the calf muscle (6).

Although the RF field inhomogeneities of 7 Tesla MRI will likely continue to be a challenge, several techniques, both in hardware and pulse sequences have been developed to overcome some of the issues.

### *Static magnetic field inhomogeneities*

Inhomogeneities in the main magnetic field ($B_0$) become increasingly larger for higher magnetic field strengths. These inhomogeneities can be separated into static distortions and dynamically fluctuating distortions. The former are created by transitions in magnetic susceptibility between different types of tissue and particularly by air cavities and produces on MR imaging local areas of deformation or signal drop out. The latter can create an overall degradation of image quality, especially for sensitive protocols, such as $T_2^*$-weighted gradient echo sequences. Higher order shimming is used to counteract the static $B_0$ inhomogeneities and is available on most 7 Tesla systems. Additional improvements in compensating for static inhomogeneities have been shown using slice specific shim settings, however this requires dedicated hardware (15). Correcting for dynamically fluctuating magnetic fields, which can substantially degrade image quality becomes increasingly important for long scan durations. These fluctuations can be introduced by breathing, coughing or involuntary body movements (16, 17). Solutions have been proposed that prospectively change the shim settings depending on the respiratory cycle (18), by the additional placement of field probes (19, 20) or that retrospectively correct the images using an additionally acquired navigator echo (17, 21). Ultimately when the magnetic field distortions are known in real time it is possible to pro-, or retrospectively correct for the image artifacts, resulting in robust imaging. This thesis has shown that correcting for these artifacts is important for patient studies, which typically are more restless than healthy young volunteers. Similarly the frequent use of high resolution scans with a long scan duration lead to an increased chance of motion induced artifacts.

## THE (CLINICAL) VALUE OF 7 TESLA MRI: CURRENT STATUS

Following the technical advancements and solutions to many of the initial problems, 7 Tesla MRI is gradually being used in a clinical setting. To date the number of pure patient studies is still very limited. By far, the majority of studies have been performed in patients with neurological diseases, likely because the techniques for brain imaging are most developed. Patients with a variety of neurological disorders have been studied. To name a few, in patients with Multiple Sclerosis (MS) enhanced lesion detection and location of lesions was obtained (22–24). In patients suffering from Huntington's disease (HD) single voxel MRS could be obtained from small brain structures, such as the caudate nucleus and putamen known to be affected by the disease. Due to the increased chemical shift and SNR accurate metabolite concentrations were obtained showing a decrease of NAA, creatine and glutamate levels in patients (25). The visualization of small arteries using time-of-flight (TOF) angiography benefits both from the higher SNR and from the increased background suppression of static tissue due to prolonged $T_1$ relaxation times. This technique has been applied to visualize the small perforating lenticulostriate arteries in stroke, vascular dementia and in cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) patients (26–28). Studies from this thesis have shown the applicability of 7 Tesla MRI in patients with AD (chapters 5 and 8). Based on the phase images from a high resolution $T_2^*$-weighted sequence, which is very sensitive to changes in the magnetic field homogeneity differences were found between patients and controls. This difference is ascribed to local increases in iron concentration co-localized with Amyloid-β, one of the hallmarks of the disease. This technique benefits from an increased contrast caused by the increased sensitivity to magnetic field inhomogeneities in addition to the higher SNR.

Overall, more clinical studies are expected to be performed in the future, especially because subject tolerance for 7 Tesla examinations is high, as was shown in this thesis (chapter 10) and by others (29). Currently, 7 Tesla brain imaging is the most widely applied, for other anatomies of the human body it is still mainly an experimental system requiring more technical development for use in a clinical environment. Some initial studies using $^{31}$P MRS in breast cancer or $^{23}$Na imaging in patients after cartilage repair surgery (30, 31) have been performed, but numbers are very limited so far.

## FUTURE DIRECTIONS AND OUTLOOK

In the near future, 7 Tesla MRI is not likely going to replace lower field strength MRI for a broad range of applications. The number of problems arising from the transition from 3 Tesla to 7 Tesla is more complicated than the previous transition from 1.5 Tesla. For many applications merely an increase in

SNR does not make up for much increased inhomogeneity, complexity and increased number of contra-indications (e.g. implants). Therefore research efforts need to focus on types of contrast that benefit from the higher magnetic field strength *in addition* to the higher SNR. The most promising applications, such as the detection of microbleeds, measuring disease related changes of iron in AD, single voxel MRS in small structures and native contrast angiography of small vessels all benefit from increased contrast in addition to SNR. In a more research setting is the potential for arterial spin labeling, or blood oxygen level dependent (BOLD) functional MRI.

Combining increased contrast with high resolution scans, often results in long scan durations making scans susceptible to subject induced artifacts. For the robust introduction of 7 Tesla MRI in clinical routine it is important to be able to correct for these artifacts. Proper subject fixation can be used to limit involuntary motion, however fluctuations of the magnetic field due to breathing, coughing or movement of other body parts is more difficult to avoid. A further complicating factor is that the amplitude of the magnetic field fluctuations scales with field strength. Navigator echo based measurement and correction of these fluctuations has already shown to substantially improve image quality (this thesis). Some very promising approaches measure real time field changes using magnetic field probes placed around the body or use multiple receive coil elements to sample the spatial distribution of the magnetic field (this thesis). In conjunction with the ability to prospectively switch higher order gradient shim terms in real time, this would allow for highly robust imaging even for scans with long scan duration. On the longer term with adequate hardware to individually drive multiple RF coils and modified sequences, other anatomies are likely to benefit from similar improvements in contrast and resolution, ultimately leading to improved and earlier diagnosis.

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