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OBSERVATION

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Ultra-high-field magnetic resonance: Why and when?

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Abstract

This paper briefly summarizes the development of magnetic resonance imaging and spectroscopy in medicine. Aspects of magnetic resonancephysics and -technology relevant at ultra-high magnetic fields as well as current limitations are highlighted. Based on the first promising studies, potential clinical applications at 7 Tesla are suggested. Other aims are to stimulate awareness of the potential of ultra-high field magnetic resonance and to stimulate active participation in much needed basic or clinical research at 7 Tesla or higher.

Key words: Alzheimer's disease; Brain tumors; Cartilage; Functional magnetic resonance imaging; Magnetic resonance; Magnetic resonance spectroscopy; Multiple sclerosis; Ultra-high field magnetic resonance methods

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From the very beginning, optimum field strength was a topic of debate in clinical proton magnetic resonance imaging (MRI)[1]. Earlier on it was even suggested that whole-body MRI would not be possible above 10 MHz or 0.24 Tesla[2]. Furthermore, based on *ex vivo* studies it was expected that T_1-contrast between various tissues and pathologies in the human body would strongly diminish above 100 MHz, leading to reduced image contrast[3]. Diagnostic contrast based on relaxation times, in general, was shown to be strongest at very low fields. As we all know, however, the brilliance of high-field MRI ($\geqslant$ 1.5 T) won the race and also benefited magnetic resonance spectroscopy (MRS)[4]. After a decade of high-end clinical 1.5 T MRI, and based on initial experience at 4 T in a few laboratories, research at 3 T started and translated very well into clinical imaging[5,6]. Despite the fact that 3 T clinical MR-systems started selling spectacularly, physicists and engineers continued to work on 7 T and higher fields in human MR-research (following the leading chemical and biochemical NMR work as well as animal research, now operating at up to 20 T for small animals). Note, however, that the first 7 T/90 cm magnet was already installed in 1999 demonstrating increasing signal-to-noise ratio (SNR) and more artifacts as compared to 4 T[7].

Still, it seems to be appropriate to ask whether or not patients will ever actually benefit from higher magnetic field strengths in clinical MRI and MRS, or will this field stay an academic playground? This paper will briefly review some MR-physics and -technology at around 7 T, and touch on current and future applications in clinical diagnostics.

Basically, the application of MR is not simple but the technique is rather versatile[8] in stark contrast to computed tomography or positron-emission tomography (PET) where endogenous contrast manipulation is rather

limited [i.e. image contrast is often achieved *via* exogenous contrast agents (CAs) or tracers]. In MR, three different magnetic fields (i.e. static, circular polarized, (linear) orthogonal gradients) have to interact properly and several data acquisition parameters need to be adjusted in a sensible way in order to obtain reliable diagnostic information. Furthermore, it is not so much the field strength (and corresponding resonance frequency) but the wavelength within the human body, which dictates interaction and, thus, information content. The lower the field strength the longer the length of RF-waves in the tissue will be, changing from about 1 m for protons at 1.5 T to several centimeters at ≥ 7 T. It seems obvious that the much shorter wavelength in proton MRI - now in the range of body organ dimensions - will lead to changing interactions and artifacts. This leads to standing and traveling wave phenomena[9-11] depending on the dielectric properties of the sample causing, at least, B1-inhomogeneities and inhomogeneous sensitivity profiles (e.g. "center bright" in the brain). In addition, spin-lattice and spin-spin interactions, i.e. relaxation times, change with field strength and quite possibly, the various relaxation mechanisms for different nuclei may be weighted differently. Therefore, we cannot expect to simply copy-and-paste techniques developed at lower fields and just linearly adjust certain sequence parameters (e.g. flip angle, echo time, repetition time).

Proton imaging at ≤ 3 T, the workhorse in clinical MRI, is currently rather advanced yet endures sensitivity limits for several applications. On the other hand, specific absorption rate (SAR) represents a legal limit, which is independent of the magnetic field strength and, thus, is more often met at higher fields as SAR increases with the square of the magnetic field strength. Therefore, and due to the lack of efficient whole body coils at 7 T or higher, local SAR replaces global SAR (Note: local SAR limit is about 5 times higher). As a rule of thumb, every application or pulse sequence hitting the SAR limit at 3 T cannot be used the same way at 7 T. On the other hand, any application lacking SNR should definitely be carried over to 7 T as long as SAR is not prohibitive. Alternatively, one could always try to change excitation pulse length (may cause offsets, increasing chemical shift artifacts) or type (e.g. adiabatic pulses), and/or repetition time, to reduce SAR in a particular patient group.

Imaging techniques originally developed at 1.5 T and already applicable at 7 T include high-resolution anatomical MRI[12,13], BOLD-based functional MRI[13,14], functional MR-Angiography[13,15], and susceptibility weighted imaging (SWI)[16,17]. In addition to standard magnitude images, phase images reveal new and additional information at 7 T[13,17,18]. Basically, these techniques do not use 180°-pulses, which are critical in terms of SAR and B_1-homogeneity, and gain from increased image SNR or time series SNR. The latter, relevant for functional MRI (fMRI), is limited by physiological noise[19]. On the other hand, high spatial resolution is not only possible but a must at 7 T in order to fully exploit the advantages at high field strength[13,20-23]. As a consequence, 1 mm^3 isotropic resolution is not only achievable for anatomical but also for functional MRI and this information may be mapped onto each other easily[13]. This enables brain research and pre-clinical tumor diagnosis to be performed at a new level, greatly helping neurosurgeons. As of today, there are first results available[13,24] and several applications are already close to clinical use. Of course, they still require confirmation by larger, multi-center studies: musculo-skeletal applications, in particular cartilage[13,25-27], multiple sclerosis[12,28], and whole body imaging[13]. Based on these promising studies, I would expect preoperative brain tumor surgery planning, using high resolution fMRI, multiple sclerosis and Alzheimer's disease, using high resolution MRI and SWI, and early diagnosis of defects in cartilage and vertebral discs to represent the first useful clinical applications of 7 T proton MRI.

Imaging methods not gaining as much at 7 T include diffusion weighted imaging (DWI), which gains in SNR but not from the basic physical mechanism which is field independent, and contrast-enhanced MRI, when standard, gadolinium-based CAs are used. Of note, iron-based CAs like USPIO are now approved for human use and will do a much better job at 7 T. In addition to MRI, MRS is gaining substantially from the high field, which was known for a long time in *ex vivo* NMR and animal studies[4,13,29,30]. Non-proton techniques, employing, e.g. ^{23}Na and ^{31}P nuclei, gain even more as they are lacking sensitivity at lower fields due to the lower gyromagnetic ratio and resonance frequency. Sodium imaging, which was developed at 1.5 T many years ago[31,32], despite its general importance in many diseases like stroke or brain tumors, might become a useful clinical tool only at 7 T or higher[13,33]. This may improve clinical diagnosis in stroke patients and help to better differentiate brain tumors and surrounding edema. I believe that ^{31}P-MRS will gain the most from higher fields. Why? Because for many applications ^{31}P-MRS and MRSI need better SNR than available at 3 T today and will profit also from the increased spectral dispersion (line splitting), enabling improved quantification of metabolites like phosphocreatine, adenosine triphosphate, inorganic phosphate, phosphomonoesters and phosphodiesters, relevant for energy metabolism. Furthermore, there is no nuisance background to be suppressed, like water and fat in proton-MRS. Finally, in a recent study, we demonstrated that metabolites' T_1-relaxation times in human skeletal muscle actually decreased with field strength[34], as compared to 1.5 T and 3 T[35], enabling faster scanning without loss in SNR (or saturation). This will enable fast, dynamic and localized ^{31}P-MRS[36,37] to study energy metabolism in patients and also higher resolution ^{31}P-MRSI (i.e. spectroscopic imaging), thus increasing specificity. In my opinion, ^{31}P relaxation times are also decreasing in human brain tissue if interpreted correctly[38]. Potential clinical applications are all kinds of metabolic disturbances of skeletal muscles based on

genetic or functional defects like muscle dystrophies or diabetes.

What has been discussed so far, can be achieved on a "standard", first generation 7 T system, i.e. with single channel transmit and local multi-array-receive coils (i.e. in the brain, skeletal muscle, joints, cartilage, *etc.*). When attempting to scan the body trunk, e.g. heart, liver, kidneys, multi-channel transmit techniques are inevitable and they also may improve brain and joint imaging to name a few. However, this technology is still under development and problems with inhomogeneous and inefficient body excitation, causing not only degraded image quality but also SAR problems, have to be solved within the next few years[9-11,13]. Furthermore, multi-array receive coils are far from mature today. Together with improved coil designs, dedicated artifact reduction techniques have to be developed to achieve robust and reliable imaging quality within legal SAR limits[13]. At the end, it will be the best possible combination of organ size and location, tissue structure and composition, Tx/Rx coil, imaging protocol and contrast mechanism that will provide the best data quality available in a given time. Much improved MRI and MRS at UHF may also help foster multi-modal imaging, e.g. MR-PET[8,13]. This novel hybrid technique may help to gain more relevant information to better characterize the complexity of normal organ functions and, subsequently, characterize their breakdown, e.g. in brain tumors. This should pave the way towards novel and validated individualized therapies.

To summarize, novel contrast mechanisms, applicable through advanced technology and a sound understanding of MR-physics and -technology, pave the way to novel clinical applications. However, there are not only technical challenges, clinicians will also have to rethink and expand their current knowledge used to interpret diagnostic images at 1.5 T and 3 T. In some areas, such as standard contrast agent applications or DWI, nothing may change dramatically and one could argue to stay with the current 3 T systems. In other areas, however, only 7 T or even higher fields will enable scientists and clinicians to fully explore the potential of magnetic resonance techniques towards evidence based clinical diagnostics. Nevertheless, I would like to end this preliminary account on UHF-MR with a word of caution. We are only at the very beginning of UHF-MR applications and both hardware and measurement techniques are immature and need to be improved substantially before any sound conclusions on the clinical use of UHF-systems in general can be made. In particular, several safety issues have to be clarified, including the potential hazard of body implants, in order to minimize any risk to patients and operators.

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