IMAGING METHODOLOGY – Workshop Summary

Magnetic Resonance in Medicine 67:317–321 (2012)

Ultrahigh Field Systems and Applications at 7 T and Beyond: Progress, Pitfalls, and Potential

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About 150 researchers around the world convened at the Chateau Lake Louise on February 20–23, 2011 to present and discuss the latest research in human and animal imaging and spectroscopy at field strengths of 7 T or above (termed ultrahigh field) at the third ISMRM-sponsored high field workshop. The clear overall message from the workshop presentations and discussion is that ultrahigh field imaging is gaining momentum with regard to new clinically relevant findings, anatomic and functional MRI results, susceptibility contrast advancements, solutions to high field-related image quality challenges, and to generally push the limits of resolution and speed of high field imaging. This meeting report is organized in a manner reflecting the meeting organization itself, covering the seven sessions that were approximately titled: (1) high field overview from head to body to spectroscopy; (2) susceptibility imaging; (3) proffered session on susceptibility, ultrafast imaging, unique contrast at 7 T, and angiography; (4) neuroscience applications; (5) proffered session on coils, shimming, parallel imaging, diffusion tensor imaging, and MRI-PET fusion; (6) high field animal imaging and spectroscopy, as well as a vendor overview, and (7) Cutting edge technology at 7 T. Magn Reson Med 67:317–321, 2012.

Key words: high field; fMRI; MRI; DTI; susceptibility

With well over 30 7 T human scanners now being used or installed worldwide, and many more on the way, the need for the international community to meet to exchange information on recent technical advancements as well as novel findings is more pressing than ever. Research at ultrahigh field, a term used to describe a scanner field strength of 7 T and above, has resulted in new imaging technology and methodology, new findings, and new applications. Many of these applications are clinically applicable already. These advancements have also been used to catalyze methodology improvement across all field strengths.

This meeting, the third International Society for Magnetic Resonance in Medicine (ISMRM)-sponsored high field workshop, was held at the Chateau Lake Louise in Alberta, Canada from February 20 to 23. The first was at Asilomar Conference Center in Pacific Grove, CA, in March of 2007 and the second was in Santa Lucia Hospital in Rome, Italy in October of 2008. Many other high field workshops unaffiliated to ISMRM have also taken place, including those in South Korea and Denmark, as well as the biennial Minnesota high field workshop that has been running for over a decade. The 2011 ISMRM workshop mixed in several kinds of presentations: general keynote lectures sets of lectures on focused themes, such as susceptibility imaging, functional MRI (fMRI), and spectroscopy; a vendor overview session; evening or post-dinner lectures; and proffered lectures. In addition, the meeting had two poster sessions. Posters were nevertheless on display for the entire meeting.Thematically, the intent of this meeting was to have more of an in-depth discussion about applications rather than an emphasis on the technological developments. Overall, the balance between applications, technological development, and new findings regarding contrast mechanisms was a reflection of the maturing state of the field today. Regarding attendance and speakers, those in attendance were: 93 ISMRM members, 26 nonmembers, 25 student members, and four student nonmembers—in total 148 people. There were 51 posters. Out of the meeting's 49 speakers, 37 speakers were invited and 12 speakers presented proffered talks.This meeting summary is not comprehensive but describes the scientific highlights of the meeting—organized by session—as viewed by the authors of this report. Please note that the meeting summary is based on the presentations from the meeting. These presentations were accompanied by a syllabus contribution for the meeting itself. As this syllabus is not a citable document, we believe it not useful to include references to these here so therefore are omitting reference to these syllabi contributions but simply discussing the talks themselves.

SESSION 1: HIGH FIELD OVERVIEW FROM HEAD TO BODY TO SPECTROSCOPY

This session introduced the meeting and consisted of a mix of neuroanatomical, neurofunctional, body imaging, cardiac imaging, spectroscopy, and an overview of the high field potential of imaging myelin.

The first speaker, Bruce Rosen (MGH), gave a broad overview of what high field offers, showing several recently obtained examples of findings from anatomical imaging, angiography, and fMRI carried out at 7 T and above (1) that could not have been made at lower field strengths. The key gain with high field is signal-to-noise ratio, which is then traded for exquisite resolution. The

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Received 23 May 2011; revised 13 July 2011; accepted 22 July 2011.

DOI 10.1002/mrm.23151

Published online 14 November 2011 in Wiley Online Library (wileyonlinelibrary.com).

clear message from this talk is that this capability has substantial practical potential, truly novel contrast, and receding technical challenges that are being overcome.

One of the major areas covered was the potential role of ultrahigh-field MRI in neuroscience. In the second keynote lecture, Robert Turner (Max Planck Institute [MPI], Leipzig) introduced this topic, describing recent technical progress from his laboratory and others and some unique applications. According to Turner, the basic challenge for neuroanatomical MRI at 7 T is to make productive use of the high spin magnetization before the free induction decay quickly disappears, due to short T_2 and T_2*, while at the same time keeping radiofrequency (RF) power deposition within tolerable levels. Good brain coverage with spin-echo contrast can be obtained using the gradient and spin echo sequence (2), which uses few 180° pulses. The present state of the art is that whole-brain structural images with sufficient contrast-to-noise ratio can be obtained in a single measurement, typically taking under 20 min, with voxel volume of 0.4 mm isotropic resolution (3). Of course, any typical motion during this scan time can result in an actual resolution that is slightly reduced. The precise amount of physiologically related resolution reduction that can result has not been fully determined. This is normally achieved using a gradient-echo acquisition. Higher in-plane resolution can be achieved at the expense of larger slice thickness, but in long organelles such as the hippocampus this sacrifice can be worthwhile, allowing in-plane resolution of less than 200 μm (4).

Turner also mentioned that parallel acquisition methods have shown remarkable success with echo-planar imaging (EPI) at 7 T. Acceleration by sensitivity encoding or generalized autocalibrating partially parallel acquisition techniques provides improved image quality. Further acceleration, effectively up to a factor of 6, can be achieved by restricting the field of view with outer-volume suppression pulses. For example, readout-segmented EPI, with navigator-driven reacquisition, has been combined with generalized autocalibrating partially parallel acquisition to provide nine-segment multishot images which can be diffusion weighted, with 0.7 mm in-plane resolution and no trace of motion artifact (5). Use of multiband RF pulses combined with parallel acquisition can also yield acceleration factors as high as 16 (6). The comparative shortness of T_2* and T_2 at high field poses a particular challenge for diffusion-weighted MRI—it is difficult to have a high enough b factor in the sequence before the signal disappears. However, it has recently been shown that zoomed EPI with generalized autocalibrating partially parallel acquisition acceleration allows diffusion-weighted images with submillimeter resolution to be acquired with unprecedented clarity at 7 T (7).

Both Rosen's and Turner's lectures served as introductions to subsequent sessions in body and neuroimaging.

Siegfried Trattnig (Vienna) and Mark Ladd (Essen) provided overviews of body, musculoskeletal, and cardiac imaging. Ladd showed high-quality spoiled gradient-echo cardiac images. He also showed examples of entire body 7 T images. After outlining the three major problems/challenges in high field imaging (B_0 inhomogeneity, B_1 inhomogeneity, and RF power deposition), Robin De Graaf (Yale) focused his talk on methods for improving B_0 inhomogeneity covering novel techniques that include dynamic, spherical-harmonic-based shimming, as well as nonspherical harmonic approaches. In the final talk of this session, Alex MacKay (Vancouver) described the rapid recent advances that have been made in myelin imaging at 1.5 and 3 T through imaging of short T_2 components corresponding to "myelin water." He also characterized the potential that high field offers in this area along with the challenges that must be overcome in implementing quantitative mapping of myelin water at 7 T (8).

SESSION 2: SUSCEPTIBILITY IMAGING

The second session of the meeting focused on the "hot topic" of quantitative susceptibility mapping at ultrahigh field, with six speakers each giving a short presentation followed by lively discussion. Jürgen Reichenbach (Jena), Richard Bowtell (Nottingham), and Yi Wang (Cornell) described a range of techniques (9–11) that can be used to calculate susceptibility maps from phase images acquired using gradient echo techniques. Reichenbach also introduced the sophisticated harmonic artifact reduction in phase data method (10) for rapidly removing the effect of field variation generated by sources outside the region of interest, offering significant speed-up of the preprocessing needed in susceptibility mapping. All three speakers showed relatively high resolution and high signal-to-noise susceptibility maps of the brain generated from a set of phase images acquired with the head at different orientations to the magnetic field and also demonstrated that with appropriate regularization, quantitative whole brain susceptibility maps can be calculated from phase images acquired at a single orientation.

Craig Jones (John Hopkins) introduced a new saturation-based method for measuring small susceptibility-induced field offsets. This method, which involves acquiring a series of images with varying saturation frequency, eliminates the need for phase unwrapping. Jeff Duyn (National Institutes of Health [NIH]) described the opportunities and challenges currently faced in exploiting susceptibility contrast. In particular, he presented his work on post-mortem brain tissue which has shown that exchange (12) makes a significant contribution to the small differences in resonant frequency between different brain tissues and that the susceptibility of white matter (WM) is anisotropic (13). Chunlei Lei (Duke) described how characterization of this anisotropy can provide information about the orientation of nerve fibres and showed that phase images acquired at multiple orientations can be used for susceptibility tensor mapping (14).

The overall impression from the session was of a field of research that is moving forward very quickly, particularly with mapping approaches, but that further work is needed to understand the tissue characteristics underlying measured susceptibility. This area is a example of what occurs quite often in MRI: revisiting a phenomenon (in this case, susceptibility) that was previously thought to be fully understood and exploited, just to realize that there are entire new vistas of research to be explored and applied.

SESSION 3: PROFFERED SESSION ON SUSCEPTIBILITY, ULTRAFAST IMAGING, UNIQUE CONTRAST AT 7 T, AND ANGIOGRAPHY

Magnetic susceptibility effects also formed a common theme in several of the proffered papers that were presented in the first open oral session. Jongho Lee (NIH) described a detailed investigation of the orientational dependence of R_2* in post-mortem brain tissue at 7T (15). The results confirmed the previous observation of a significant variation ($\sim 6\ s^{-1}$) of WM R_2* with fiber orientation to the magnetic field (characterized by angle, θ). Analysis of the angular dependence revealed both sin 2θ and sin 4θ variation, the latter possibly being a signature of the effect of anisotropic magnetic susceptibility. Karin Shmueli (NIH) presented an in vitro study that tested whether exchange effects due to cerebrosides might in part explain the small difference in the resonance frequency of water in grey matter and WM. She measured a frequency offset of 0.18 parts per billion (ppb) per mM of cerebroside, which suggested that the 31.5 mM WM/grey matter difference in cerebroside concentration would produce a ~ 6 ppb WM-grey matter frequency difference—a value which is similar to that previously measured in fixed tissue samples. Signal phase changes on brain activation formed the focus of a talk by Marta Bianciardi (NIH). Using careful preprocessing, including elimination of phase fluctuations due to respiration spatial polynomial fitting, she was reliably able to identify phase changes linked to brain activation. The measured phase variation was consistent with that expected from changes in venous blood oxygenation. Also in this session, Cern Deniz (New York University (NYU)) showed that RF shimming with a four-channel array improved the quality of hip images at 7 T, while Sebastian Schmitter (Minnesota) described a useful optimization of contrast in 7 T time-of-flight angiography where specific absorption rate constrains performance.

SESSION 4: NEUROSCIENCE APPLICATIONS

Submillimeter functional resolution at 7 T opens up structure–function relationships, laminar specialization, and columnar structure. Jon Polimeni (Massachusetts General Hospital [MGH]) showed in 2010 that a visual pattern is mapped onto V1 most precisely in central layers of the cortex, probably corresponding to Layer IV (1). He described follow-up studies, involving functional connectivity MRI. Studies using lesions, recorded potentials, and tracer injections in animal models reveal distinct, fine-scale spatial patterns of anatomical connections that reflect underlying functional architecture. Polimeni described high-resolution (1 mm) fMRI at 7 T, exploring spatial specificity tangential to and radial to the cortical surface. He showed retinotopically-specific patterns of functional connectivity in human V1 within and across hemispheres and directionally dependent laminar-specific functional connectivity between V1 and the visual motion area V5/MT. This demonstration of laminar-specific correlations provides evidence for highly local hemodynamic control. In a similar vein, in his earlier talk, Turner showed results of a recent blood oxygen level dependant (BOLD) 7 T human fMRI study (0.70 mm isotropic voxels), which investigated cortical laminar-specific BOLD time courses in response to three closely related finger-tapping paradigms: motor ideation, motion without touch, and finger tapping (16). He found that the time course of BOLDsignal in M1 differed significantly between cortical layers.

Emrah Düzel (University College London (UCL)) described a 7 T study of the hippocampal subregions in humans that are involved in processing the novelty signals that activate the substantia nigra and ventral tegmental area. In this study, a novelty-encoding paradigm was used. It was possible to identify, with very high structural and functional precision, encoding and novelty-related activity in hippocampal subfields. High-resolution imaging at 7 T thus appears to be a feasible tool to dissect the functional and structural anatomy of mesolimbic circuitry. This is likely to provide a unique approach for theoretical and clinically motivated cognitive neuroscience studies.

In his talk, Federico de Martino (Minnesota) presented recent 7 T functional studies of the basic (columnar) organization of sensory areas. Using accelerated gradient echo whole-brain fMRI images with 1 mm isotropic voxels, the group has identified conventional resting state networks (e.g., the "default mode network") with high spatial specificity and quantified the partial voluming effect of poorer resolution. A second study, analyzed using multivoxel pattern analysis methods, demonstrated columnar organization in V5/MT related to visual motion direction.

Adam Anderson (Vanderbilt) described segmentation of the substantia nigra and ventral tegmental area using gradient and spin echo and fast field echo scans at 7 T and imaging of the hippocampus at submillimeter (0.7 mm isotropic) resolution. For functional imaging, higher BOLD contrast allows higher spatial resolution and contrast-to-noise ratio (CNR) in functional maps. As an example, Anderson showed that single digit representations in the primary somatosensory cortex (areas 1 and 3b) can be reliably mapped at 7T. The activation to stimulation of the finger pads of digits 1–4 was found to have a somatotopic organization in each area, with the spacing between adjacent digit representations in area 3b about 1.6 times that of area 1.

In closing this session, Elizabeth Hillman (Columbia) provided an overview of the neurophysiology underlying the BOLD response, drawing from her own extensive optical and other experimental studies in animals (17). Surprisingly, little is known about how, or even why neurovascular coupling occurs. Using optical techniques, it is possible to measure local changes in the concentration of oxyhemoglobin and deoxyhemoglobin. Some of her findings suggest that the hemodynamic response might have several phases, a reflex response to neuronal input, followed by later phases corresponding to changes in local demand.

SESSION 5: PROFFERED SESSION ON COILS, SHIMMING, PARALLEL IMAGING, DIFFUSION TENSOR IMAGING, AND MRI-PET FUSION

This second proffered session offered a potpourri of technical development topics that included how to deal with RF power deposition, B_0 and B_1 inhomogeneities, as well as recent developments in parallel imaging, diffusion tensor imaging, and MRI-PET fusion.

Alessandro Sbrizzi (Utrecht) focused on rapid estimation of electric fields for a transmit array from B_1

measurements to address the issue of minimizing specific absorption rate while maximizing homogeneity. Hoby Hetherington (Yale) gave a talk on methods for improving shimming. He showed that third- and fourth-order shims can provide significant improvements and dramatically demonstrated the effectiveness of a fourth-order shim head insert system, which is placed inside the gradient sets and outside the RF coils. Christoph Juchem (Yale) demonstrated for the first time, dynamic multicoil whole-brain shimming at 7T, as well as a novel nonspherical-harmonic-based shimming approach based on the use of 24 nonorthogonal coils (18).

With regard to parallel imaging, Mehdi Khalighi (GE Medical Systems), filling in for William Grissom, gave a presentation on three-dimensional parallel excitation pulse design using small-tip "spokes" pulses.

In a completely different vein, Zang-Hee Cho (Gachon University, Korea) gave a presentation describing imaging of the Raphe Nuclei in the brainstem by Fusion MRI and PET. He first showed brainstem images acquired at 7 T with submillimeter precision. Using 18F-fluorodeoxyglucose (FDG) (glucose) and 3-amino-4-[2-[(di(methyl)amino)-methyl]phenyl]sulfanylbenzonitrile (DASB) (Serotonin) positron emission tomography (PET) fusion with 7 T imaging, he was able to demonstrate precise metabolic/anatomic correlations. He also presented subcortical tractography (200 μm resolution) results, analyzed by using the high-resolution anatomic images to provide landmarks.

Finally, Ha-Kyu Jong (Vanderbilt) gave a presentation, showing that while multishot approaches likely will improve high resolution diffusion weighted imaging at 7 T (due to prohibitively fast signal decay), this can be performed with minimal sensitivity to motion through high-acquisition bandwidth (multishot EPI and parallel imaging), motion correction using two-dimensional navigators, and full image-space sensitivity encoding reconstruction with phase correction. The final results (b = 700 DTI, 0.57 mm in plane resolution, eight shots, 12 direction, imaging time of 19 min) showed great detail. The authors of this report feel that this appears to be a promising approach for generating DTI results at 7 T that exceed in quality those available at lower field strengths.

SESSION 6: HIGH FIELD ANIMAL IMAGING AND SPECTROSCOPY AND VENDOR OVERVIEW

A series of talks in this session addressed the special opportunities afforded by high field for animal studies. Considerably higher field strengths than are generally feasible for human work are available for the smaller bore sizes used study rodents and other small animals. Such studies also allow rigorous direct comparison and validation with other more invasive methods, including histology. Alfonso Silva (NIH) described his work at 7 T in marmosets (19), which provide a valuable new-world monkey model whose genome has recently been fully sequenced. Ultrahigh resolution imaging in anaesthetized marmosets allows functionally specific brain regions to be identified by their myelin content, as myelin affects T_1 and T_2* contrast. His group has used this approach to demarcate visual areas visual area 1 (V1), visual area 5 (V5)/medial temporal (MT), and visual area 6 (V6)/ dorsal medial (DM), as well as primary auditory area A1 and primary somatosensory cortex (20). The marmoset model may also prove valuable in probing the link between T_2* and WM fiber orientation relative to B_0, as Silva sees strong correlations between these measures. Rolf Gruetter (Lausanne) then described similar work conducted in his laboratory at 14.1 T, in which layer contrast can be observed in rat grey matter from subtle phase differences between the different layers in gradient echo images (21). He went on to describe the potential in disease models for 1 h magnetic resonance spectroscopy at such high field strengths. His laboratory has developed a mouse occlusive stroke model that creates highly reproducible lesions in the striatum. He observes reliable cluster separation between ischamic tissue that successfully reperfuses, equivalent regions from sham experiments, and irreversibly damaged tissue, by plotting the concentration of glutamine versus the concentration of *N*-acetyl aspartate + glutamate + taurine (22). This offers the possibility of better identifying salvageable versus irreversibly damaged tissue. In the final talk in this session, Jun Shen (NIH) showed how ^{13}C NMR can reveal metabolic and glutamatergic neurotransmission.

SESSION 7: CUTTING EDGE TECHNOLOGY AT 7 T

RF inhomogeneity at high field formed a common theme of several talks in the final session. David Hoult (National Research Council, Canada (NRC-C), Winnipeg) gave an educational talk, starting from an analysis of the various fields and potentials generated by a wire loop and ending with an explanation of RF inhomogeneity in conductive and dielectric media (23), with a valuable account of static field inhomogeneity provided en route. Brian Rutt (Stanford) focused on RF shimming (24) and parallel transmit (25) approaches for ameliorating RF inhomogeneity effects during excitation. He stressed the importance of rapid and robust B_1 mapping, describing a combined B_0/B_1 mapping approach using the Bloch-Siegert effect (26) that generates maps for two RF channels (<20 slices; 20 cm field of view; 48 × 48 matrix) in 20 s. Imaging experiments carried out using a two-channel system at 7 T on the head showed a significantly greater improvement in homogeneity of excitation using parallel transmit compared with RF shimming. Pierre Francois Van De Moortele (Minnesota) described his group's experience in implementing parallel transmit for liver imaging at 7 T. David Brunner (Zurich) described the hardware requirements for implementation of parallel transmit at high field. He also drew illuminating comparisons between the intrinsic characteristics of parallel transmission and parallel reception. On a different note, David Feinberg (Advanced MRI Technologies) described a new approach for greatly speeding up multislice echo planar imaging via the combined use of multiband excitation and simultaneous image refocusing with EPI (6). This multiplexed EPI approach, which can allow images to be acquired from 12 or more slices after just a single excitation, has some particular advantages for diffusion imaging, as the diffusion weighting can be efficiently shared over multiple slices without requiring *k*-space segmentation (with its associated sensitivity to phase changes across segments). Feinberg also described how the multiplexed EPI approach can be beneficially used to reduce

the pulse repetition time and thus improve temporal resolution in "resting-state" studies of the whole brain.

In the final talks of the meeting, we heard about recent work focusing on the safety of biological exposure to high magnetic fields. In the first talk, Paul Glover (Nottingham) reviewed the theory of magnetic field interactions with biological tissue and concluded that the only relevant phenomena are the frequently noted effects of peripheral nerve stimulation, magneto phosphenes, metallic taste, and apparent vertigo. He showed that all are now quite well understood as resulting either from forces associated with the product of field and field gradient exceeding threshold limits or from current densities established when the field changes for a long enough duration (e.g., when one moves one's head in the vicinity of the magnet). None of these effects appear to be anything other than briefly unpleasant but harmless sensations. In the final talk of the meeting, Dev Shrivastava (Minnesota) summarized 296 MHz (7 T) and 400 MHz (9.4 T) measurements made in a porcine model of RF heating, indicating that it is possible to predict tissue temperature changes associated with RF power deposition by applying a simple bioheat transfer framework (27). This would better allow realistic specific absorption rate parameters to be determined with predictable upper limits in temperature change, which is the more strictly relevant safety parameter. Importantly, Shrivastava's work shows that even over long periods of RF heating a steady state temperature rise is not achieved.

CONCLUSION

The authors of this report strongly feel that ultrahigh field imaging and spectroscopy is here to stay. The efforts of extremely talented engineers and physicists have produced early dramatic results that have, in return, further catalyzed the field. More solutions to the challenges of B_0, B_1, and RF power deposition as well as motion-insensitive high-resolution anatomic, diffusion-weighted, and functional images are being implemented more widely. The neuronal, anatomical, and clinically relevant information that we are now obtaining from high-resolution imaging, susceptibility weighting, spectroscopy, and DTI at high field is not just better than at low field, but in many ways completely different and perhaps more useful than at lower field strengths.Coming from this meeting with so many informative talks, the authors of this report are highly optimistic about the manner in which ultrahigh field imaging is accelerating in improvements and applications.

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