Department of Neuroscience and Biomedical Engineering
Aalto NeuroImaging

Ultra-High Field MRI: Transition to Human 7 T in Finland

Workshop Memorandum

Toni Auranen, Synnöve Carlson, Matti Hämäläinen, Veikko Jousmäki, Ville Renvall, Riitta Salmelin

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A!7T **Ultra-High Field MRI: Transition to Human 7 T in Finland**
Aalto University, Espoo, Finland, October 8–9, 2015

Workshop Memorandum

April 12, 2016

Edited by:

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Background and Objective

The Finnish Infrastructures for Functional Imaging (FIFI, functionalimaging.fi) brings together strong Finnish knowledge on magnetoencephalography (MEG), magnetic resonance imaging (MRI), positron emission tomography (PET), and navigated transcranial magnetic stimulation (nTMS), ranging from animal to human studies. FIFI belongs to the Roadmap of Research Infrastructures of the Academy of Finland. The internal roadmap of FIFI includes an ultra-high field (UHF) 7 T MRI scanner placed in the Aalto University and operating as part of the Aalto NeuroImaging (ANI, ani.aalto.fi) research infrastructure which currently houses state-of-the-art MEG, 3 T MRI, and nTMS systems. The target year of the acquisition of the 7 T MRI scanner was originally set to 2017, but in recent considerations 2018 is a more feasible goal for making the purchase.

As a part of the preparation process for acquisition of the scanner, a workshop on "Ultra-High Field MRI: Transition to Human 7 T in Finland" was organized at Aalto University on October 8–9, 2015. The organizers included the Aalto University School of Science, FIFI, ANI, Aalto Brain Centre (ABC, abc.aalto.fi), and Department of Neuroscience and Biomedical Engineering (NBE, nbe.aalto.fi). ABC is a strategic initiative in the fields of neuroscience and neurotechnology at the Aalto University and NBE the administrative host of the ANI research infrastructure. The purpose of the workshop was to demonstrate scientific achievements and possibilities enabled by UHF MRI, as well as the challenges. This meeting brought together a group of top-level scientists for two days to give presentations and immerse in discussions both in a panel debate and also more informally.

After the discovery and characterization of proton nuclear magnetic resonance (NMR) in the 1940s and 1950s, medical applications of NMR started to emerge. The first MR imaging systems in the 1970s were electromagnets of up to 0.15 T whereas the first superconducting systems (0.35 T) appeared in the 1980s after successful commercialization of MRI. Since then, the field strength has steadily increased, with 1.5 T whole-body systems introduced in the mid-1980s and the first 4 T scanners becoming operational by the early 1990s. The development of the mainstream commercially available MRI systems focused on the 1.5 T and, later, 3 T systems. The first 7 T magnets were introduced in the academia already before the year 2000. Since then, 9.4 T and even 11.7 T human imaging systems have emerged, and the quest for higher field strengths and the new research they enable continues. Currently, 7 T is becoming the standard in top-level academic and clinical research (with over 50 installations worldwide), whereas 1.5 T and 3 T serve the everyday diagnostic clinical use. In the Nordic countries, Denmark (Copenhagen) and Sweden (Lund) have operated a 7 T device since 2015.

In this memorandum, we summarize the answers offered by the invited experts to topics and questions proposed by the audience both upon registration and during the workshop. The report represents the current knowledge in the field and consensus achieved in the workshop. The purpose of this record is not only to document the meeting, but also to pave the way for making the first human 7 T scanner operational in Finland in the near future, as an important means of continuing to produce top-level scientific and clinical research in the field of human fMRI/MRI. With this aim, in addition to the scientific and clinical topics, we include preliminary information on the procurement and practical operation of a 7 T scanner. The plan is for an open-access service that will provide efficient and economical use of the device to all interested institutions and other users in Finland.

Participants

The invited speakers were:

- **Marta Bianciardi**, Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA
- **Stuart Clare**, FMRIB Centre, University of Oxford, UK
- **Elia Formisano**, Maastricht Brain Imaging Center, Maastricht University, The Netherlands
- **Risto Kauppinen**, School of Experimental Psychology and Clinical Research and Imaging Centre, University of Bristol, UK
- **Mikko Kettunen**, A. I. Virtanen Institute for Molecular Sciences, University of Eastern Finland, Kuopio, Finland
- **Jonathan Polimeni**, Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA
- **Siegfried Trattnig**, Department of Biomedical Imaging and Image Guided Therapy, Medical University of Vienna, Austria
- **Robert Turner**, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany
- **Kamil Ugurbil**, Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, MN, USA

In addition to the scientific speakers' sessions, we organized a manufacturers' session, where we heard from three major UHF MRI system vendors. Their representatives were:

- **Mark Symms,** GE Healthcare
- **Karin Markenroth Bloch,** Philips Healthcare
- **Christina Triantafyllou,** Siemens Healthcare

The workshop attracted more than 120 participants (speakers included). Out of the 110 who had pre-registered and answered to the question about their primary interest in the workshop, 75% identified themselves as potential users (basic research, clinical research, diagnostic) of a 7 T facility, fewer than 5% were from research administration and one fifth attended the symposium for other purposes. To the question regarding whether the participant or his/her group would be willing to use a 7 T scanner installed in Otaniemi, Espoo, we received 44 replies, out of which the vast majority (more than 90%) was either 'yes' or 'maybe' (see, Figure 1).

Participants, excluding the invited speakers, arrived from 13 different national institutions/hospitals and 2 institutions from abroad (Marmara University,

Turkey; Nencki Institute of Experimental Biology, Poland). The Finnish institutions and hospitals and corresponding percentages are shown in Table 1.

Table 1 Participant distribution (percentages) from different institutions. *Others include the following national institutions: Folkhälsan, Laurea University of Applied Sciences, North Karelia Central Hospital, Oulu University Hospital, Tampere University of Technology, University of Jyväskylä, University of Oulu, University of Turku, Validia Rehabilitation Helsinki, and Åbo Akademi University.

Institution	
Aalto University	53%
Hospital District of Helsinki and Uusimaa	15%
University of Helsinki	14%
Others*	18%

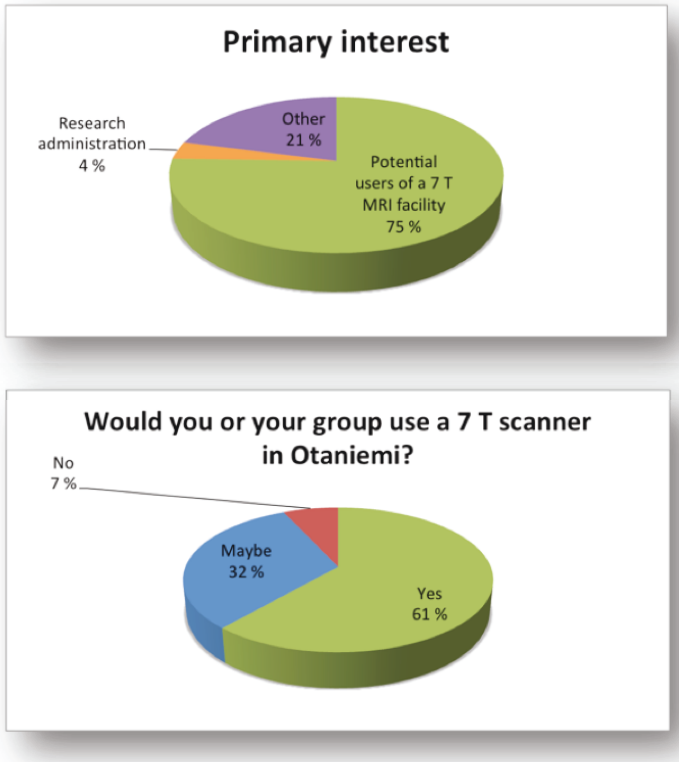


Figure 1. Primary interest of symposium participants and their willingness to use a 7 T human fMRI/MRI scanner based in Otaniemi.

Scientific and Clinical Relevance and Value

Benefits of 7 T in comparison to conventional field strengths (1.5 T and 3 T)?
The first and foremost benefit of an UHF MRI is the markedly higher signal-to-noise ratio (SNR). Raw SNR increases linearly with the field strength and even more owing to the nature of relevant contrast mechanisms [*e.g.*, blood oxygenation level dependent (BOLD) contrast typically measured in fMRI], and other technical advances, such as development of multi-channel coil arrays, that can be used to a greater benefit in the high-SNR regime. This will lead to a major signal enhancement in fMRI studies as well as improvements in other cerebral hemodynamics-based measures, such as cerebral blood flow and volume (CBF/CBV). These signals can be exploited in neuroscience research to study the physiology of cerebral hemodynamics, cognitive neuroscience, functional organization of the brain, structure-function relationship in the brain as well as brain pathologies.

> *"Going to submillimeter spatial resolution in vivo makes a big difference."* — **Robert Turner**

A 7 T device enables as small as 0.35 mm isotropic voxels in structural imaging, 0.65 mm isotropic voxels in functional imaging and 0.8 mm isotropic voxels in connectivity measures (diffusion weighted imaging/diffusion tensor imaging, DWI/DTI). In structural scans, this offers superior distinction between the gray and white matter, which is of great value for many applications, and also facilitates the identification of substructures of the gray matter, such as the stria of Gennari in the primary visual cortex. In practice, ~1 mm isotropic whole-head coverage can be routinely performed in functional studies with 7 T in comparison to the 3–5 mm isotropic voxels obtained with a 3 T scanner. If a coarser resolution suffices, a 7 T scanner provides the required functional SNR in a markedly reduced time as compared with the conventional field strengths, thus also reducing subject motion related issues.

> *"This kind of neuroscience work is possible only at 7 tesla."* — **Kamil Ugurbil**

With the improved spatial accuracy and the voxel size approaching vessel sizes, one can examine the spread of activation across cortical depths as well as observe the local vascular anatomy with improved sensitivity. The exquisite spatial resolution facilitates estimation

of connectivity and information flow also between cortical regions and the deep structures in the midbrain and brainstem, thus improving the characterization of, *e.g.*, resting-state and task-related networks. With 7 T scanners, layer specificity of brain activations has been shown, *e.g.*, in visual and auditory cortices, enabling imaging of input and output activity in the cortex. This is crucial for fully understanding the neural functions of the human brain and, in practice, impossible to achieve at lower field strengths.

Imaging microstructure of brain tissue?

A 7 T MRI system facilitates joint studies of function, structure and connectivity in submillimeter resolution. This enables *in vivo* neuroanatomy and very detailed examination of the functional gradients of, *e.g.*, hippocampus, insula, striatum, thalamus, locus coeruleus, and nucleus accumbens. New possibilities emerge in imaging variation of myelin and iron content of the brain tissue. This may also have applications in clinical diagnostics.

Undesired properties of 7 T for neuroscience? Is 3 T better in some cases or can we replace 3 T with 7 T in human imaging? Should we aim even higher?

7 T technology has now reached the level of maturity where its potential can be safely exploited in many neuroscience applications. The resolution benefits generally favor using a 7 T scanner. In some cases, if the study focuses on brain regions of reduced transmit efficiency, such as the temporal lobes, or where the magnetic susceptibility gradient is very steep one might consider using 3 T. However, the higher SNR of 7 T enables higher parallel imaging acceleration (depending on the receive coil), which can be used to counteract the signal reduction and distortion caused by magnetic susceptibility. Even higher field strengths are pursued in dedicated research centers. However, as those techniques (9.4 T and >10 T) are still in an experimental phase, their use requires a large, highly trained technical team in order to enjoy the benefits and not fall prey to problems associated with extremely high fields, such as challenges in the radiofrequency (RF) penetration.

Figure 2. Robert Turner is one of the pioneers in UHF MR research. Photo by Mikko Raskinen, Aalto University School of Science.

How will 7 T complement electromagnetic brain mapping? Can one have an MEG scan right after a 7 T scan?

Electromagnetic and hemodynamic imaging detect fundamentally different types of signals, thus offering complementary windows to brain function. Above and beyond their differential emphasis on high temporal resolution (electromagnetic recordings) and spatial resolution (hemodynamic recordings), their inherent characteristics may also highlight different types of neural processing (*e.g.*, bottom-up vs. top-down processing). These are fundamental research questions that can open up important future possibilities for neuroscience. The high spatial resolution of 7 T fMRI that allows to far more reliably focus on actual neural activity (and less on the veins) is pivotal to a deeply informative combined use of electromagnetic and hemodynamic brain imaging.

MEG recordings immediately after an MRI scan (whether 1.5 T, 3 T or 7 T) can be problematic if the individual has magnetic material on his/her body (*e.g.*, in hair color, permanent eye liner etc.). Such magnetization may not interfere noticeably with the MRI scan but may appear as intolerable magnetic artifacts in the extremely sensitive MEG recordings. The magnetization dissolves over time.

Status of clinical scans at 7 T?

Currently 3 T is the gold standard in clinical imaging and diagnostics. The achievements and progress made with 7 T are thus compared with the results obtained using a 3 T device. Many clinical applications, such as fMRI, susceptibility weighted imaging (SWI), multinuclear MRI and magnetic resonance spectroscopy (MRS), are being used at 3 T but they suffer from limited sensitivity. 7 T will greatly expedite their usefulness for diagnostic purposes. Higher spatial resolution of UHF also opens the door for *in vivo* microscopy.

However, in some cases 7 T already plays a role in the clinical environment and there is indication that, in the future, 7 T will be used more routinely in specific cases. For example, detection of gray matter pathologies in multiple sclerosis with 7 T may improve the diagnostic possibilities. Also, subregions of the hippocampus are better accessible with 7 T than 3 T, thus enabling detection of pathologies such as hippocampal sclerosis. High resolution imaging of microadenoma at 7 T might provide a direct criterion of cavernous sinus infiltration. Furthermore, angiograms of lenticulo-striate arteries have shown differences between dementia patients and controls. In preoperative fMRI, spatial accuracy is of utmost importance in order to reach the best possible

outcome. In a comparison study between 7 T and 3 T, it was shown that 7 T fMRI provided more accurate information about the location of the tumor in relation to functionally important brain areas.

It is essential to start using 7 T in basic research and clinical research as soon and as widely as possible to support the development of 7 T into a future valuable tool of clinical diagnostics.

Is it possible to use 7 T for other than neuro applications, such as liver fat and muscle imaging? What about spectroscopy and multinuclear imaging?

UHF has significant potential in imaging also other tissues, *e.g.*, musculoskeletal tissues. With a modern 7 T scanner it is also feasible to image the human body, as many of the early-stage issues with 7 T, such as inhomogeneity of the RF field, have been solved. Preoperative median nerve imaging has been performed, as well as multiparametric MR mammography at 7 T, demonstrating that MR imaging has potential to obviate unnecessary breast biopsies.

In spectroscopy, 7 T compared to 3 T affords better chemical discrimination (larger separation between the spectral peaks representing different metabolites) and higher SNR within a practicable imaging time. With chemical exchange saturation transfer (CEST), it is possible to map glutamate, which has not been possible with traditional methods of spectroscopy.

Studies have shown that non-invasive sodium cartilage imaging could be helpful not only for assessment of the cartilage status, but also predictive for osteoarthritis. Non-invasive phosphorous saturation transfer of the liver at 7 T may replace invasive liver biopsy. Hepatic energy metabolism is of high interest as its alterations are indicative of inflammatory and neoplastic liver diseases, a phenomenon that has been demonstrated in type 2 diabetes patients at 3 T.

Practical Operation and Procurement Issues

Artifacts and possible difficulties in 7 T? Solutions for minimizing the artifacts and distortions?

UHF MRI manifests artifacts and imaging challenges that are more problematic than at lower field strengths. Echo planar imaging (EPI), causes image distortion and signal dropout especially adjacent to frontal sinuses and ear canals. This problem scales with field strength. However, recent advances in imaging technology and signal processing, especially multi-channel array coils and parallel transmit/receive methods, can reduce the susceptibility artifacts to a manageable level. Thinner slices reduce artifacts, but at the same time increase scan time. There are new methods, such as simultaneous multislice (SMS) EPI, which enables significantly decreased scan times: the whole brain can be imaged with 1 mm isotropic voxels in less than 3 seconds. Fast sampling also somewhat reduces physiological noise artefacts. Elimination of physiological noise is, however, particularly critical at 7 T. Many important advances have been recently made in alleviating the noise contributing to EPI signal fluctuations.

At 7 T, the wavelength of the RF field required in measurements is about 12 cm. As the size of the head is ~20 cm and the torso ~40 cm, the RF field within the imaging volume is uneven when using a single transmit channel. In particular, the RF field varies within the volume due to constructive and destructive interferences as well as dielectric shielding, resulting in fluctuating tissue contrast in images. However, parallel transmit strategies and new pulse sequences (such as MP2RAGE) have been implemented to solve these problems.

SAR and other safety considerations when using 7 T?

By default, specific absorption rate (SAR) is retained within safety limits in all scanning sequences approved by the manufacturer. SAR is also monitored by the scanner software and hardware at run-time. In case advanced techniques are used that are not directly provided by the scanner vendor and that might cause increased SAR, the safety considerations are carefully evaluated. This is standard procedure for all sites operating an MRI scanner at any field strengths, not only at UHF.

Ultra-high magnetic fields and the associated techniques may cause short-term side-effects. These include dizziness and nausea, nystagmus (eye drifts) and possibly phosphenes. Most participants do not report anything out of the ordinary when undergoing a 7 T study. In some follow-ups, one third has reported short-term vertigo when the patient table was moving in and/or out of

the scanner. Thus, in the research environment and with healthy and young volunteers, subject recruitment should not pose a problem.

Most implants, clips, pins etc. have not yet been tested for 7 T. As only very few sites are currently performing clinical research or clinical diagnostic imaging, there may yet appear safety unknowns that could limit clinical scans on patients or specific groups of patients. Apparently, approximately 25% of the population over 50 years of age may not be well suited for scanning with 7 T.

What kind of a technical team is needed for operating a 7 T scanner?

7 T operation is becoming much more routine. One may already foresee that, in the near future, 7 T is going to be the main MRI system in a research laboratory. In many 7 T sites, students and non-technical personnel can operate the scanner independently, indicating that the basic operation of a 7 T scanner is not much more challenging than operating a 3 T scanner. However, the precision measurements enabled by 7 T may warrant additional steps in adjustments and calibration as compared with the standard procedure on a 3 T scanner.

In basic upkeep, a 7 T site requires 1–2 relatively senior MR physicists who constantly follow the development in the field and implement new innovations rapidly. Specifically, both MR hardware and MR software oriented individuals are needed. A lot of methods sharing goes on in the UHF community, thus not every site has to develop everything by themselves (*e.g.*, non-standard sequences, such as simultaneous multislice/multiband EPI). However, in case the 7 T site wants to push the limits by designing and using advanced techniques, the number of required physicists increases; the scientific potential of the instrument may remain untapped if a strong physics and signal processing team is absent. In any case, for clinical research a

Figure 3. One of the highlights of the workshop was the panel discussion. Photo by Tuomas Tolvanen and Mikko Nyrhinen, Aalto NeuroImaging.

The panel was unanimous — *Finland needs to have a 7 T scanner in order not to drop out of advanced neuroscience.*

tight collaboration with research technicians is a must.

Challenges in data analysis in comparison to 3 T?

The amount of data produced by a 7 T scanner is often underestimated. A 7 T site needs highly qualified experts for dealing with the data and analyses. Advanced techniques in the acquisition also require sophisticated processing and analysis methods. One detail of major practical importance is that data smoothing should no longer be used (as opposed to the common approach at 3 T). Localization information is lost in smoothing and, because the increase in SNR is considerable, unsmoothed data is adequate to reveal significant cortical activity. Smoothing introduces false positives and makes it difficult to distinguish activations on different sides of sulci, thus leading to vague and misleading associations of functional activity and neural substrates.

Single-subject analysis before averaging is an essential step in data analysis. For the subsequent group-level analysis, improved methods of normalization should be used as the spatial resolution is dramatically enhanced in 7 T imaging. The exquisite spatial resolution also allows linkage to the myeloarchitecture based atlases.

How will patient flow and imaging time be organized if 7 T is to be installed in Aalto University, Otaniemi campus?

The premises will be suitable for clinical research (at least for outpatients). Given the interest and prospective users and applications, specific arrangements can be implemented to also secure a patient flow. In the first stages of UHF imaging in Finland, most studies will likely be done on healthy volunteers and patients who do not require hospital environment. The technologically oriented domain at Aalto University will strongly support the development of the 7 T scanner and its use also for precision measurements in both basic and clinical research.

The 7 T will be an open-access facility, with imaging time distributed among the user groups via a web-based reservation system, taking care of equal scanning opportunities and ensuring efficient use of the device. In specific cases (visitors from abroad, urgent patient/subject groups, nature of the study) a group can be given privilege to reservations for a limited time. This policy has been successfully in use in the ANI infrastructure for several years. In case the demand would surpass the supply, a joint expert board between the user institutions will prioritize the use.

Status of vendors?

Previously, the UHF MRI scanners have been research instruments more or less custom-built to the order. We have started inquiries with all major vendors (Siemens Healthcare, GE Healthcare, and Philips Healthcare), in order to further explore their current UHF systems and solutions. Siemens Healthcare has recently launched a 7 T product, MAGNETOM Terra[1]), and is pursuing the FDA and CE approvals for future clinical use. To our knowledge, GE Healthcare and Philips Healthcare are also committed to their 7 T programs.

Research agreements with vendors (*e.g.*, sequence development) if other than Aalto or FIFI-affiliated users need to do some development?

The owner organization (Aalto University) will make a research agreement with the winner of the procurement process among vendors (this will be a condition in the competitive bidding). If possible and agreed by the vendor, an option will be included for other users to take part in, *e.g.*, sequence development. This is likely the case, but if not, ANI will offer research collaboration and its knowhow in sharing the advanced methods with the larger community as well.

Procurement process and cost

The owner organization (Aalto University) will handle the procurement process and competitive bidding of the future 7 T system provided that funding can be secured. Our current estimate for the price of a 7 T system is 7 000 000 €. The required stimulus systems, physiological measurement devices and related computer systems needed in basic and clinical research sum up to approximately 500 000 €. With additional costs in, *e.g.*, implementing a possibility for handling a patient flow, the total cost of the project is expected to be **close to 8 000 000 €**. This estimate is made by the institute and is not committed to by any of the vendors. The final cost depends on the particular configuration of the system and may be subject to changes.

The annual expenses after purchase include rental cost of approximately 100 000 €/year (400 m^2), service contract for the scanner 200 000 €/year (our best estimate at this point), and a minimum of two MR physicists, together about 200 000 €/year depending on their seniority. Thus, the basic operation and upkeep will cost approximately **500 000 €/year**, which would be covered by user fees. During and right after the startup phase (2 years after installation), when most groups are still learning to use a 7 T scanner, the total use will likely not yet fully cover the running costs. However, 2–3 years after installation, the 7 T system is

[1] www.healthcare.siemens.com/magnetic-resonance-imaging/7t-mri-scanner/magnetom-terra

anticipated to have a well-established user base in Finland, and the upkeep will be covered mainly by user fees.

The high cost of the 7 T project necessitates a broad support from all universities and institutions in Finland that are interested in using UHF human devices. Such support may include sharing of some of the initial costs. Most importantly, strong financial and scientific support from the top officials of Aalto University is an absolute prerequisite for a successful outcome of this project.

Delivery time and installation requirements

The delivery times vary by vendor due to undisclosed reasons. The latest estimate for an approximate delivery time is 12 to 18 months from placing the order. The installation should take about 2 months and testing phase an additional month. If full or a major part of the funding can be secured in the Academy of Finland's Research Infrastructure (FIRI) call in 2016 (there is no call in 2017) and any necessary complementary funding in 2017, the purchase should be feasible in the early 2018. In this case, the operations would start in 2019.

As such, the current site of the 3 T scanner at the Advanced Magnetic Imaging (AMI) Centre, Aalto NeuroImaging (Otakaari 5 I, Magnet house), meets the installation requirements for a 7 T scanner. However, as the 3 T scanner will be kept operational, the plans for the location of the new 7 T scanner need to be finalized in 2017. Ideally, the two scanners would be placed close to each other, either in (or next to) the current Magnet house or in another, better suited location in the Otaniemi campus.

Next Steps

As the next step of the Aalto 7 T project, we are preparing an application for the Academy of Finland FIRI 2016 call, contacting vendors for latest information about their products, as well as continuing discussions with the workshop participants and universities/institutions throughout Finland about their interest in taking part in this major national-level project. We will provide information about the progress of the project on the website of the 7 T symposium (tinyurl.com/aalto7t). Please contact the editors for further information (toni.auranen@aalto.fi).

Message from the Dean of Aalto University School of Science

"Let's push together for this 7 tesla magnet! I think the time is right for Finland to take the next step."

—

Risto Nieminen

Figure 4. Risto Nieminen, Dean of Aalto University School of Science. Photo by Mikko Raskinen, Aalto University School of Science.

Acknowledgements

The editors wish to thank all the speakers for excellent presentations and, individually, Kamil Ugurbil, Risto Kauppinen and Christina Triantafyllou for minor corrections and recommendations to the text. Cover photo by Mikko Raskinen, Aalto University School of Science.

Workshop Organizers

Aalto University School of Science

- Aalto Brain Centre (ABC, abc.aalto.fi)
- Aalto NeuroImaging (ANI, ani.aalto.fi)
- Department of Neuroscience and Biomedical Engineering (NBE, nbe.aalto.fi)

Finnish Infrastructures for Functional Imaging (FIFI, functionalimaging.fi)

Organizing committee:

- **Toni Auranen**
- **Annika Hultén**
- **Matti Hämäläinen**
- **Veikko Jousmäki**
- **Harri Piitulainen**
- **Ville Renvall**
- **Riitta Salmelin**

Appendices

As appendices to this memorandum, we publish the program of the symposium and abstracts of the invited presentations.

Those presentations to which we received a written consent from the speaker were recorded for internal use at Aalto University. As this 7 T project is fundamentally a joined national effort, we are happy to share those recordings, to be used by individuals in the Finnish neuroscience and neuroimaging community. Unfortunately, we cannot release them publicly. However, we have created a short summary video[2] of the workshop and published it on YouTube.

[2] www.youtube.com/watch?v=6F9_Izz_Gnw

A!7T Ultra-High Field MRI: Transition to Human 7 T in Finland

Aalto University, Espoo, Finland, October 8–9, 2015

Venue: Aalto Design Factory, The Stage
Betonimiehenkuja 5C, Espoo (Otaniemi)

Lunches: Restaurant Antell Calori (code: "7T")

Thursday, October 8

11:30 – 12:00	On-site registration
12:00 – 12:30	Opening ceremony
12:30 – 14:10	Scientific session Turner: **How 7T MRI can transform neuroscience** Formisano: **High-resolution investigations of the human auditory system with functional MRI at 7 Tesla (and more)**
14:10 – 14:40	Coffee break
14:40 – 16:20	Scientific session Polimeni: **High spatial and temporal resolution fMRI at Ultra-high fields: prospects for new neuroscience** Kettunen: **When ultra-high magnetic field is not enough: Hyperpolarised 13C MRI and its applications**
16:20 – 16:30	Break
16:30 – 18:10	Scientific session Kauppinen: **Haemodynamic MRI of the brain at 7T** Bianciardi: **Echo-planar-imaging of human brain function, physiology, and structure at 7 Tesla: challenges and opportunities**
18:10 – onwards	Cocktail reception

Friday, October 9

08:30 – 10:10	Scientific session Trattnig: **The Forefront of Clinical MRI Studies at Ultra High Fields** Clare: **Translational and clinical research with ultra-high field MRI**
10:10 – 10:40	Coffee break
10:40 – 11:30	Scientific session Ugurbil: **Imaging Function and Connectivity in the Human Brain with High Magnetic Fields: spanning scales from cortical columns to whole brain**
11:30 – 12:20	Panel discussion
12:20 – 13:20	Lunch
13:20 – 14:50	Manufacturer's session GE Healthcare, Symms: **7T MRI with the General Electric MR950 - the Pisa experience** Philips Healthcare, Markenroth Bloch: **Scandinavian Neuroscience with Philips 7T MRI** Siemens Healthcare, Triantafyllou: **Translating 7T power into clinical care**
14:50 – 15:00	Adjournment

Abstracts

Robert Turner
Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany
How 7T MRI can transform neuroscience

Like any other science, systems neuroscience seeks mechanistic explanations that can lead to predictive law-like generalizations. For this reason MRI, and its specializations fMRI and diffusion-weighted MRI, have come to play a major role in cognitive neuroscience research.

Experiments using proton beam microscopy have enabled a quantitative relationship to be established between measured brain tissue iron and myelin content on the one hand, and quantitative values of T1, T2* and quantitative magnetic susceptibility, on the other. This has allowed an increasingly empirical and individual-subject approach to systems neuroscience, in which the image intensity is interpretable in terms of the neurally significant microstructure of the human brain.

At 7T, MRI can now provide human brain images of structure, function and connectivity with isotropic voxels smaller than one millimeter, and thus much smaller than the cortical thickness. This resolution, achievable in scan times of less than one hour, allows visualization of myeloarchitectural layer structure, intracortical variations in functional activity – recorded in changes in BOLD signal or cerebral blood volume CBV – and intracortical axonal orientational structure via dMRI.

While recent improvements in radiofrequency receiver coils now enable excellent image data to be obtained at 3T, scanning at the ultra-high field of 7T offers further gains in signal-to-noise and speed of image acquisition, with structural image resolution up to about 300 micrometers. These improvements throw into sharp question the strategies that have become conventional for the analysis of functional imaging data, especially the practice of spatial smoothing of raw functional data prior to further analysis. Creation of a native cortical map for each human subject that provides a reliable individual parcellation into cortical areas related to Brodmann Areas enables a strikingly different approach to functional image analysis. The proposed parcellation approach involves surface registration of the cortices of groups of subjects using maps of the longitudinal relaxation time T1 as an index of myelination, and methods for inferring statistical significance that do not entail spatial smoothing. The outcome is a far more precise comparison of like-with-like cortical areas across subjects, which can greatly increase experimental power, discriminate activity in neighboring cortical areas, and allow correlation of functional activity and connectivity with specific cytoarchitecture.

Furthermore, the high spatial resolution at 7T of fMRI, using BOLD contrast and cerebral blood volume measurement with a method called VASO, now allows cortical layer-dependent analyses to be performed, which may offer far more powerful methods of assessing neuronal causality. VASO, in particular, can provide excellent localization of brain function, which will be described in some detail. Such techniques may lead to more convincing modelling of brain mechanisms, at the scale of 1 mm or better, than current graph-based methods that require gross over-simplification of brain activity patterns in order to be computationally tractable.

Elia Formisano
Maastricht Brain Imaging Center, Maastricht University, The Netherlands

High-resolution investigations of the human auditory system with functional MRI at 7 tesla (and more)

Magnetic Resonance Imaging (fMRI) at ultra-high magnetic fields holds considerable promises for studying the anatomy and function of the human brain. In this talk - using the auditory system as a model - I will illustrate a number of experiments where functional MRI at 7T is combined with advanced analyses and modeling (fMRI decoding and encoding) to reveal the representation and processing of (natural) sounds in the human auditory cortex. Furthermore, I will show how the high spatial resolution and specificity achievable at high fields opens up the possibility to explore "unknown" territories, such as the fine-grained functional organization of relevant subcortical nuclei (e.g. MGB, IC) along the auditory pathway and the columnar and laminar architecture in the primary auditory areas.

Jonathan Polimeni
Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA

High spatial and temporal resolution fMRI at ultra-high fields: prospects for new neuroscience

Accelerated image encoding and the increased sensitivity afforded by highly-parallel receive arrays and ultra high-field (7T) systems have recently enabled sub-second, sub-millimeter isotropic resolution studies of the functional architecture of the human brain with fMRI, the spatial and temporal accuracy of which is increasingly limited by the biological point-spread of the BOLD signal. In this presentation, I will review recent work investigating the limits of spatial and temporal accuracy of fMRI. I will present studies designed to characterize the specificity of the BOLD signal by combining subsecond or submillimeter isotropic voxels and a surface-based analysis approach that together allow the BOLD signal to be measured over large extents of the folded cortical surface. With such small voxels and rapid sampling times, the characteristics of the BOLD signal become increasingly influenced by the details of the vascular anatomy and physiology. I will also review several recent studies into neurovascular coupling mechanisms which together suggest that the hemodynamic responses to neuronal activity are more tightly coupled in space and in time than what was previously believed. I will also survey recent methodological work aimed at increasing the imaging resolution and the time-series signal-to-noise ratio for future high-resolution 7T fMRI studies.

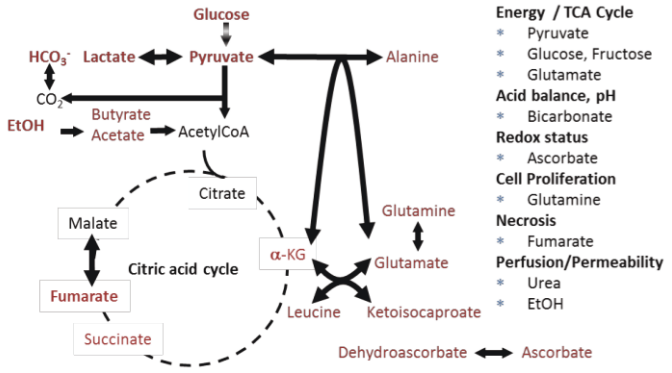
Mikko Kettunen
A.I.Virtanen Institute for Molecular Sciences, University of Eastern Finland, Kuopio, Finland

When ultra-high magnetic field is not enough: hyperpolarized ^{13}C MRI and its applications

Among the common pre-clinical and clinical imaging modalities, MR-based methods are unique in that they allow high spatial resolution and non-invasive separation of a range of metabolites. Furthermore, dynamic studies of metabolism of the marker molecule can be performed using ^{13}C-labelled molecules although this method has traditionally suffered from low sensitivity, even

at high external magnetic fields available. Dissolution dynamic nuclear polarisation (dDNP) technique, which increases ^{13}C sensitivity >10,000-fold (1), largely removes this obstacle making real-time metabolic imaging viable both in pre-clinical and clinical settings.

A wide range of molecules have already been successfully hyperpolarised and used in vivo (2-5, Figure). The majority of dDNP studies so far have focused on cancer studies, and to a slightly lesser degree cardiac studies, using [1-^{13}C]-pyruvic acid. For example, increased glycolytic activity (Warburg effect) in tumors leads to accumulation of lactate and to an elevated hyperpolarised lactate signal that can be used as a marker for therapy response (3). The first clinical trial of pyruvate imaging in prostate cancer demonstrated that the technique can be translated to the clinic (6). It was also recently demonstrated that hyperpolarised glucose can be used for real-time detection of glycolytic pathway flux in vivo (7). This important development suggests that dDNP technology may allow analysis of more complex metabolic pathways than anticipated previously.



Metabolites with red label have shown in vivo metabolism following hyperpolarization.

In this talk, the basics of the technique and current applications are described. The limitations and future potential of the technique are also discussed.

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Risto Kauppinen
School of Experimental Psychology and Clinical Research and Imaging Centre, University of Bristol, UK

Haemodynamic MRI of the brain at 7T

Haemodynamics of the brain involving cerebral blood flow (CBF) and cerebral blood volume (CBV) can non-invasively be imaged and quantified using T1-based contrast mechanisms of MRI. In addition to CBF and CBV, blood oxygenation level (i.e. BOLD) is revealed by T2(*)-based MRI. Thus, MRI provides a comprehensible repertoire to map cerebral haemodynamics and oxidative metabolism for a wide range of basic and clinical neuroscience applications. While 7T offers immensely greater signal-to-noise ratio for human brain MRI than the clinical field scanners, it also places both MR technical and NMR-related challenges that need to be tackled prior to full

exploitation of the high sensitivity by the ultra-high field (UHF) for haemodynamic MRI. In this presentation haemodynamic MRI techniques, i.e. arterial spin labelling (ASL) for CBF (or cerebral perfusion) and vascular space occupancy (VASO) for CBV, as well as the BOLD MRI for 7T will be covered.

Several ASL MRI variants are increasingly used in clinical scanners (typically 3T) by neuroscientists and clinicians owing to implementations by scanner vendors. In order to take full advantage of prolonged 'label duration' at 7T to map CBF by ASL more accurately from finer anatomical regions than at clinical fields, increased B0 and B1 inhomogeneities and SAR issues have to be dealt with. In addition, standard MR hardware (i.e. labelling coil configuration) in commercial 7T scanners will limit choice of ASL schemes. Regarding VASO or its descendants for CBV MRI, in addition to B0 and B1 issues a change in the tissue-to- blood T1 ratio relative to clinical fields and a strong BOLD signal complicate recall of a pure CBV contrast at UHF placing technical challenges for 7T MRI. Nevertheless, recent developments have demonstrated implementations of both ASL and VASO MRI for high spatial resolution imaging of CBF and CBV in the human brain. In contrast to ASL and VASO MRI, use of conventional T2*-BOLD contrast at 7T meets less technical problems and hence, neuroimagers widely exploit UHF systems for high resolution fMRI. UHF makes spin echo (T2) MRI attractive for fMRI due to its inherently smaller intravascular BOLD contribution for improved spatial specificity. Technical nature of haemodynamic MRI techniques at UHF is discussed in the light of neurovascular coupling in vivo.

Marta Bianciardi
Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA

Echo-planar-imaging of human brain function, physiology, and structure at 7 Tesla: challenges and opportunities

Echo-planar-imaging (EPI) is a fast MRI technique, which is commonly used at 3 Tesla and lower magnetic field strength to investigate brain function during task execution and at rest. At 7 Tesla, the use of EPI is challenged by the higher magnetic field strength and in-homogeneity, which increase EPI artifacts (e.g. spatial distortion, signal drop-out) and crucially the amount of noise contributing to the EPI signal fluctuations.

In this talk, we will present the different sources of instrumental and physiological noise in EPI time- courses, the methods to remove these noise sources, and their contribution evaluated in high spatial resolution EPI, acquired at 7 Tesla during our previous research at the NIH. Our work demonstrates that, after proper noise removal, residual signal changes attributed to spontaneous neuronal activity are among the major contributors to the measured fMRI signal fluctuations, increasing almost twofold relative to earlier experiments under similar conditions at 3 Tesla.

In our recent work at the MGH, we investigated if the increased contribution of physiological noise at 7 Tesla can be turned into an opportunity to endogenously study brain physiology, specifically cerebro- vascular and brain parenchymal compliance in response to cardiac and respiratory pulse waves. To this end, we employed a fast non-gated EPI technique to cover most of the brain, and constrained the EPI sequence parameters to: a) produce an endogenous contrast dependent primarily on changes in total spin concentration (e.g. volume), as opposed to changes in velocity as in previous MRI and Doppler sonography work; b) achieve a 6-fold gain compared to Ernst-angle acquisition, in order to investigate pulsatile signal changes of fast flowing/moving spins without the need of an exogenous contrast agent. We will show the cardiac and respiratory MRI pulse waveform evaluated in arteries, veins, cerebrospinal fluid

compartments and brain parenchyma, as well as a novel indicator of cerebrovascular compliance, the pulsatile Volume Index, characterized and validated by multi-echo and breath-holding experiments.

Finally, considering that our EPIs at 7 Tesla are rich in structural details, we developed a multi-contrast (diffusion/T_2/T_2*/T_1-weighted) and distortion-matched 7 Tesla EPI structural approach that enabled us to image in vivo tiny nuclei of the human brainstem involved in arousal, autonomic, and motor functions. In this talk, we will present a preliminary in vivo neuroimaging atlas and connectogram of these brainstem nuclei derived from our EPIs at 7 Tesla.

Siegfried Trattnig
Department of Biomedical Imaging and Image Guided Therapy, Medical University of Vienna, Austria

The forefront of clinical MRI studies at ultra high fields

Presently, three major MR vendors provide commercial 7Tesla units for clinical research under ethical permission, with the number of operating 7Tesla systems increased to over 50. This rapid increase indicates the growing interest in ultra-high field MRI because of improved clinical results with regard to morphological as well as functional and metabolic capabilities. Since the signal-to-noise ratio (SNR) scales linearly with the field strength (B0) of the scanner, the most obvious application at 7Tesla is to obtain higher spatial resolution in the brain, musculo-skeletal system, and in breast. Of specific clinical interest for neuro-applications is the cerebral cortex at 7Tesla, for the detection of changes in cortical structure as an sign of early dementia, as well as for visualization of cortical microinfarcts and cortical plaques in multiple sclerosis. In the imaging of the hippocampus, even subfields of the internal hippocampal anatomy and pathology can be visualized with excellent resolution. The dynamic and static blood oxygenation level-dependent (BOLD) contrast increases linearly with the field strength, which significantly improves the pre- surgical evaluation of eloquent areas before tumor removal. Using SWI, the plaque-vessel relationship and iron accumulation in MS can be visualized for the first time. Multi-nuclear clinical applications, such as sodium imaging for the evaluation of repair tissue quality after cartilage transplantation, and 31-P spectroscopy for the differentiation between nonalcoholic benign liver disease and potentially progressive steatohepatitis (NASH), are only possible at ultra-high fields (UHF). Although neuro and MSK imaging have already demonstrated the clinical superiority of UHF, whole-body clinical applications at 7Tesla are still limited, mainly due to the lack of suitable coils. However with the development of parallel transmit technology at UHF improvements in whole body applications can be expected.

Stuart Clare
FMRIB Centre, University of Oxford, UK

Translational and clinical research with ultra-high field MRI

It has been long established that scanning at higher and higher magnetic field strengths can lead to many gains for MRI. The increased signal, enhanced contrast - particularly to blood oxygenation - and the improved spectral resolution for spectroscopy have all been well demonstrated. However scanning at 7 Tesla and above is also not without its challenges. Good RF homogeneity is hard to achieve, static field artefacts degrade image quality and tissue heating limits are approached more easily than on clinical scanners.

The real test for the utility of the technique is not just the ability to produce impressive images but whether it enables researchers, and ultimately clinicians, to find out information that is not possible in any other way.
From our experiences in Oxford over the past 3 years I will present some of our early applications of Ultra High Field MRI in clinical neuro-scientific research. These include fMRI of the brainstem, identifying atrophy in the hippocampus, and quantifying neurotransmitter changes during short term brain plasticity. I will also highlight some of the challenges that we have faced in relation to subject recruitment and scan tolerance in clinically relevant populations.

It is our experience that, whilst there is still much development to be done with the technology - particularly in robust and integrated approaches utilising parallel transmit and dynamic shimming methods - the current data we are acquiring is already giving us new insights into the human brain and will quickly find clinical utility as well.

Kamil Ugurbil
Center for Magnetic Resonance Research, University of Minneapolis, Minneapolis, MN, USA

Imaging function and connectivity in the human brain with high magnetic fields: spanning scales from cortical columns to whole brain

This talk will focus on some of the achievements within the Human Connectome Project and the potential for mapping human brain connectivity and function using high magnetic fields. Developments in the last two decades transformed our ability to image neuronal activity in the human brain using magnetic resonance techniques, going from early experiments demonstrating relatively course images of activity in the visual cortex to mapping the activity of neuronal ensembles that represent elementary computational units. This development has been complemented with the ability to generate maps of functional connectivity using spontaneous fluctuations detected in an fMRI time series, and obtain measures of structural connectivity using diffusion imaging techniques. Ever increasing magnetic fields have been indispensible for the achievements based on MR based functional mapping signals, while more recent data demonstrate that ultrahigh fields can also provide superior data for diffusion-imaging based tractography despite being disadvantaged due to shorter T2 relaxation times. In both cases development of new imaging and image reconstruction methods, understanding the behavior of radiofrequency waves in the human body, and a rigorous, albeit as of yet incomplete, understanding of the mechanisms underlying the functional mapping signals that reflect neuronal activity have been critical accompaniments to theintroductionof high static magnetic fields. These functional and structural studies have lead to depictions of the complex brain architecture and function in the human brain within the umbrella of the Human Connectome Project with previously unavailable temporal and spatial resolution

GE Healthcare
Mark Symms
7T MRI with the General Electric MR950 – the Pisa experience

Philips Healthcare
Karin Markenroth Bloch
Scandinavian neuroscience with Philips 7T MRI

Siemens Healthcare
Christina Triantafyllou
Translating 7T power into clinical care

Aalto-ST 6/2016

A workshop “Ultra-High Field MRI: Transition to Human 7 T in Finland” was organized at Aalto University on October 8–9, 2015. The organizers included Aalto University School of Science, Finnish Infrastructures for Functional Imaging (FIFI), Aalto NeuroImaging (ANI), Aalto Brain Centre (ABC), and Department of Neuroscience and Biomedical Engineering (NBE). The purpose of the workshop was to demonstrate scientific achievements and possibilities enabled by ultra-high field (UHF) magnetic resonance imaging (MRI). The meeting brought together a group of top-level scientists for two days to give presentations and immerse in discussions. This memorandum not only documents the meeting but also paves the way for making the first human 7 T scanner operational in Finland in the near future.

A!7T

Aalto Brain Centre

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