ERWIN L. HAHN INSTITUTE FOR MAGNETIC RESONANCE IMAGING

ANNUAL REPORT

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Preface

As is true for the wider world, 2020 was a year like no other for the Erwin L. Hahn Institute. From March onwards the COVID-19 pandemic prevented or significantly hindered all active research. It also led to the cancellation of the Erwin L. Hahn Lecture to the deep regret of all concerned. Despite the negative consequences of COVID-19 the scientists of the Erwin L. Hahn Institute have not been inactive: a great deal has been achieved, and in this report we both look back on the achievements of the past year and present an optimistic view of the future.

Without doubt the major event of 2020 was the installation of the completely new 7 T Terra system at the Erwin L. Hahn Institute. Our old Magnetom system that had served us so well since 2006 was decommissioned in June, and the new system handed over in September. This whole procedure is documented graphically in our first report. Other activities such as the DFG-funded research group on fMRI of cortical layers and the German Ultrahigh-Field Imaging Network could continue to some degree, and these are described in our second and third reports respectively. We can also report on a set of new initiatives that will use the new scanner to investigate: Emotional Control; Internet Use Disorder; Treatment Expectation; and Metabolic Imaging for Robotic MR-Guided Interventions (reports 4-7). The Donders Institute will continue to use the system for laminar fMRI studies; interleaved proton spectroscopy and fMRI to better understand Autism Spectrum Disorder; and novel contrast mechanisms for brain activation studies. We were sorry to see our Administrative Director Judith Kösters leave the Institute after three years of dedicated service to the Institute, and we warmly welcome Franziska Günther as her replacement.

We have earmarked the 3rd November 2021 for the next Erwin L. Hahn Lecture when Prof. Oliver Speck from Magdeburg will be our distinguished speaker. We hope you are faring as well as possible given the current difficult circumstances, and hope to welcome you to our Institute and to the Erwin L. Hahn Lecture in the near future.

David Norris,
Nijmegen, May 2021

A new 7-Tesla MRI System for the ELH

Introduction

The year 2020 marks a very special year for the Erwin L. Hahn Institute (ELH). Not just for the obvious reasons. In 2020 the meanwhile 14-year-old 7-Tesla (7T) MRI system was sent into its well-deserved retirement. In the summer of 2020, the ELH with its partners was busy to remove the old 7T MRI system and to prepare the scanner rooms, RF cabin, and institute building to host a new state-of-the-art MAGNETOM Terra 7T from Siemens.

Old 7T MRI system

Since 2006, the Erwin L. Hahn Institute for MR Imaging operated a 7-Tesla ultrahigh-field (UHF) MRI system for human use. Altogether eight principal investigators and their research groups from different faculties of the two founding Universities of Duisburg-Essen and Nijmegen pursued 7-Tesla research in various areas of neurosciences and in radiological diagnostics up to body imaging applications. The development and application spectrum ranged from fundamental research to sequence and methods development, to hardware development and finally to the evaluation of new clinical and diagnostic applications of UHF MRI. At installation in 2006, the 7T MRI system at the ELH was the 6th installation worldwide and second in Europe. Numerous pioneering projects and publications in methods and hardware development and first diagnostic applications of human UHF MRI imaging result from this early phase of research at the ELH. Due to the unique partnership with clinical research partners, about 5500 volunteers and patients have been included into numerous studies and successfully examined in the 14 years of operation.

Under construction

The old 7T MRI system in June 2020 was brought to a halt - and for the first time in 14 years there was no noteworthy magnetic field available in the ELH. Magnet removal and subsequent delivery of the new magnet in early August were scheduled only three weeks apart. The following weeks the system was brought to its final destination, ramped up from 0 to 7 Tesla and was finally handed over to the ELH in September 2020 (Fig. 1)

The new 7T MRI system

The new 7T system comprises an actively shielded magnet with reduced helium consumption, a strong and fast gradient system (80 mT/m, 200 T/m/s), 8-channel parallel radiofrequency transmit system technology, a 64-channel radiofrequency receive system as welll as fast host and image reconstruction computers. Furthermore, the most current operating system is installed allowing for compatibility and interchangeability of sequences and methods between the 7T UHF MRI system and the clinical MRI systems operating at 1.5 and 3.0 Tesla. The new 7-Tesla UHF MRI is, therefore, an essential

Fig. 1: Delivery of the new 7T MR system in August 2020. The new magnet is considerable shorter than the previous magnet but, due to active magnet shielding, is slightly larger in diameter. Just small enough to enter the ELH.

precondition for the successful continuation and extension of the research activities of all research groups at the Erwin L. Hahn Institute and their partners.

Acknowledgements

This major endeavour was only possible with substantial funding by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – Project number 432657511. The ELH is very grateful for the support by the two founding universities, the University of Duisburg-Essen (UDE) and the Radboud University, Nijmegen (RUN) and also likes to acknowledge the support of the new partner university, the Ruhr University Bochum (RUB). The fast and successful realization of the 7T MRI system exchange in a summer with pandemic constraints would not have been possible without the very engaged support by the UDE construction department, Siemens Healthcare, Stiftung Zollverein, ELH staff, and numerous other partners and supporters.

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Quick HH: 7-Tesla Ultrahochfeld Magnetresonanztomographie-System. Deutsche Forschungsgemeinschaft (DFG) - Projektnummer 432657511.

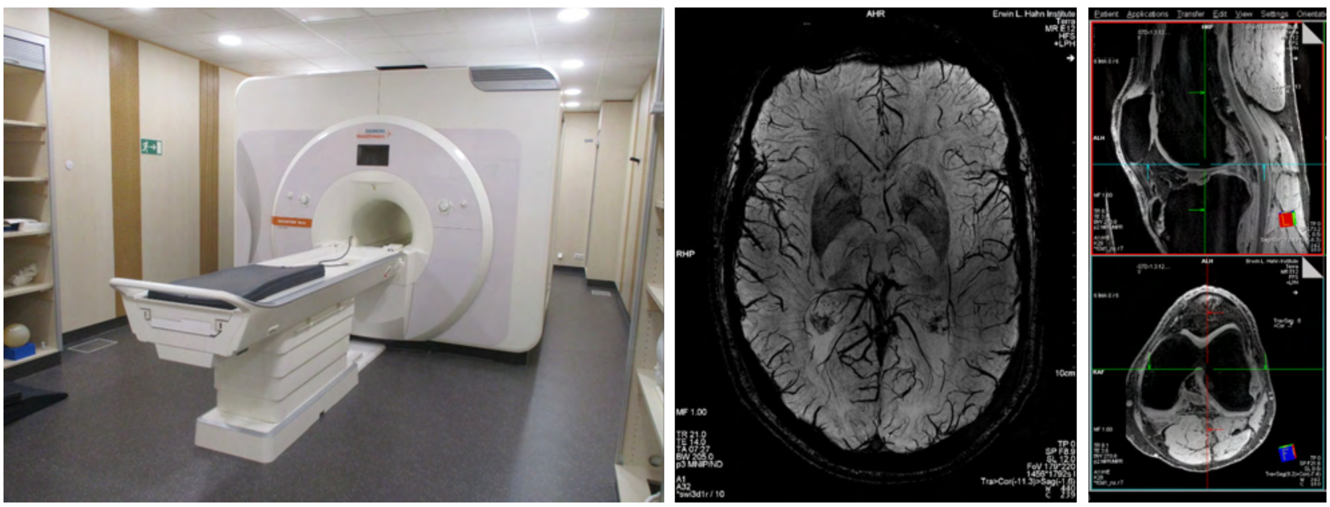

Fig. 2: The ready-to-use Siemens MAGNETOM Terra 7T MRI system in September 2020 and first images of the head and knee of a volunteer.

New Research Unit – FOR2974 "Affective and cognitive mechanisms of specific Internet-use disorders"

Matthias Brand

The Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) supports the transregional Research Unit FOR2974 with 3.3 Million Euros for the first funding period of three years (Project number: 411232260). The Spokesperson is ELH Director Matthias Brand (University of Duisburg-Essen). Further PIs are Martin Diers (Bochum), Tim Klucken (Siegen), Christian Montag (Ulm), Astrid Müller (Hannover), Hans-Jürgen Rumpf (Lübeck), Rudolf Stark (Gießen), Sabine Steins-Löber (Bamberg), Elisa Wegmann (Duisburg-Essen), Oliver T. Wolf (Bochum) and Klaus Wölfling (Mainz). Seven scientific projects (plus coordination project) will address the involvement of affective and cognitive mechanisms in specific Internet-use disorders and will contribute to a better scientific understanding of the underlying psychological and neurobiological processes of these phenomena, but will also contribute to the (further) development of therapeutic applications.

The inclusion of gaming disorder in the eleventh version of the International classification of Diseases (ICD) by the World Health Organization in 2018 emphasizes the clinical relevance of this specific Internet-use disorder. Additional potential further Internet-use disorders are currently discussed. In particular, problematic buying-shopping, problematic use of pornography and problematic use of social-networks have been suggested as potentially belonging to the ICD-11 category "other specified disorders due to addictive behaviors" (Brand et al., 2020). A better understanding of the psychological and neurobiological processes involved in these types of specific Internet-use disorders is important in order to optimize treatment and prevention. Based on the Interaction of Person-Affect-Cognition-Execution (I-PACE) model (Brand et al., 2019), the Research Unit FOR2974 aims to investigate the potential involvement of the theoretically argued (bio)psychological mechanisms underlying the development and maintenance of the aforementioned predominantly online addictive behaviors.

One of the research projects that involves an fMRI experiment (PIs Brand, Wolf, Diers) will look at the behavioral and neural correlates of cue reactivity and craving in gaming disorder compared to pornography use disorder. The fMRI experiment with 170 individuals will be carried out at the ELH institute. The project will address the potential contrast between processing pornography-related stimuli, which may be considered as triggering the anticipation of natural rewards, and gaming-related stimuli, which may be considered as secondary reinforcers. The project will therefore contribute not only to the understanding of specific addictive behaviors, but also to a better understanding of the neural mechanisms involved in reward processing in a broader sense (i.e., natural and secondary reinforcers). The data will be compared with fMRI data of another research project within the FOR2974 that will be performed at the Bender Institute of Neuroimaging at the University of Gießen (Klucken and Stark).

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Transregional Collaborative Research Center: "Treatment Expectation"

Ulrike Bingel

In June 2021 the DFG funded the transregional collaborative research centre (CRC/Transregio 289) entitled "Treatment Expectation", led by ELH PI Ulrike Bingel (Department of Neurology, University Medicine Essen, University of Duisburg-Essen) and contributions of other UDE/UME research groups. For details also see (www.treatment-expectation.de).

Background: Patients' expectations about treatment benefits are important modulators of health outcomes. An individual's expectation can substantially shape symptoms and disease progression and influence the efficacy and tolerability of treatments. The ultimate goal of this CRC is to generate the knowledge base for the systematic utilization of patients' expectation in order to optimize therapeutic strategies and thereby improve health outcomes. To achieve this goal, we will characterize the psychological and neurobiological mechanisms underlying positive and negative expectations and their impact on treatment outcomes, and how expectation effects interact with actual (e.g., pharmacological) treatment effects.

We will initially focus on the pain and affective system, as experimental and clinical evidence indicate substantial and clinically relevant effects of expectation on patient-reported treatment outcomes in both normal and pathological forms of pain and affective processing. Using a highly interdisciplinary and translational approach and guided by a unified theoretical framework, we will conduct basic experimental studies in animals, healthy volunteers, as well as clinical proof-of-concept studies in patients to investigate the mechanisms and effects of treatment expectation alone and, importantly, in combination with gold standard treatments. Modern non-invasive neuroimaging techniques including 3T and 7T MRI will play a key role in several of the projects and both structural and functional brain imaging data from the University of Duisburg-Essen, Marburg and Hamburg will be pooled to allow for large scale participant-level meta-analyses and to identify brain signatures that may predict interindividual differences in the mechanisms and effects of expectation on health outcome. Two recently published studies from our group demonstrate the feasibility of such approach (Spisak et al., 2020). The paper by Dr. Spisak (BingelLab) was awarded with the research award of the German Pain Society (Deutsche Schmerzgesellschaft) in 2020.

Based on novel findings regarding the contribution of the cerebellum (Zunhammer et al., 2021) in placebo analgesia, PIs Timmann-Braun and PI Bingel have initiated first studies to follow-up on the detailed role of the cerebellum and cerebellar circuitry with prefrontal brain areas to placebo analgesia.

Another highly valuable asset for the ELH research strategy and infrastructure is the University Essen Medicine Advanced Clinician Scientist Programm UMEA2 that will be funded by the BMBF, as announced on March 29th by the BMBF. This program will allow 12 high achieving advanced clinician scientists to found their independent research groups along with 50% strictly protected research time for up to 6 years. This program represents an excellent addition of the existing clinician scientist programs at the UME and will allow clinician scientists to conduct cutting-edge research at the UDEs research sites including the ELH and thereby complements the long tradition of clinician scientists performing research at the ELH funded by our intramural IFORES and other programs.

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DFG Emmy Noether research group: fMRI of Cortical Layers

Our research group focuses on the development of measurement and analysis methods for functional MRI of cortical layers. The human cortex consists of multiple histological laminae, and these layers play different roles in information processing in a cortical area. Some receive input from areas earlier in the processing stream for example, whilst others receive feedback information from areas higher up in the hierarchy. This is an extremely useful bit of information as it may allow us to infer a much sought after aspect in connectivity neuroimaging: causality of connections. Most connectivity imaging to date has been limited to non-directional measures. Put simply: we can see that areas A and B are communicating, but we cannot determine which area does the talking and which one the listening. With layer-specific fMRI we hope to address this issue. Our research group focuses on two important topics in this field: improving the functional specificity of the fMRI contrast and the subsequent analysis of the layer data, and we'll start with the former.

The discussion of functional specificity of different fMRI contrast mechanisms predates the advent of sub-millimetre 7 Tesla fMRI capabilities by a comfortable margin of at least a decade. By far the most used method for fMRI is gradient-echo BOLD contrast measured with EPI. GRE-EPI is extremely sensitive to the effect neuronal activity has on the local blood oxygen concentration. It is also known however that this is mostly thanks to the sensitivity to large draining veins. These veins are located downstream of the area of the original neuronal activity and therefore GRE-EPI is deemed not very specific. Many attempts have been made to develop other methods to measure neuronal activity using MRI that are less sensitive to these draining veins. These include Arterial Spin-Labeling (ASL), Vascular Space Occupancy (VASO), and spin-echo BOLD, all typically employing an EPI readout for its high efficiency. Our group is working on a method closely related to spin-echo BOLD, namely T2-prepared imaging with a FLASH readout. Like aforementioned alternatives, it sacrifices efficiency to (greatly) enhance specificity of the signals, no longer being sensitive to draining veins. The multiecho FLASH readout allows us to calculate a response without any T2-prime weighting. Our data show that even a tiny amount of T2-prime weighting (which is intrinsic to EPI readouts) already has a very large negative effect on the specificity of the sequence (see Figure 1).

A major issue in all high-resolution fMRI is the time it takes to encode all these tiny voxels. To try and accelerate acquisition as much as possible we are working together with the ELH coil-building group of Prof. Quick on a 32-channel transmit-receive coil to be able to do local signal excitation, which in turn allows larger GRAPPA coil acceleration factors without extreme g-noise penalties. In 2020 we also published a new method for partial Fourier imaging for multi-echo or time-series data (Figure 2) which allows larger undersampling factors than was possible previously, resulting in faster imaging. The second main topic in laminar fMRI is developing analysis methods that can exploit the layer-specificity of our signals. This field is rather underdeveloped at present. Only recently the first studies

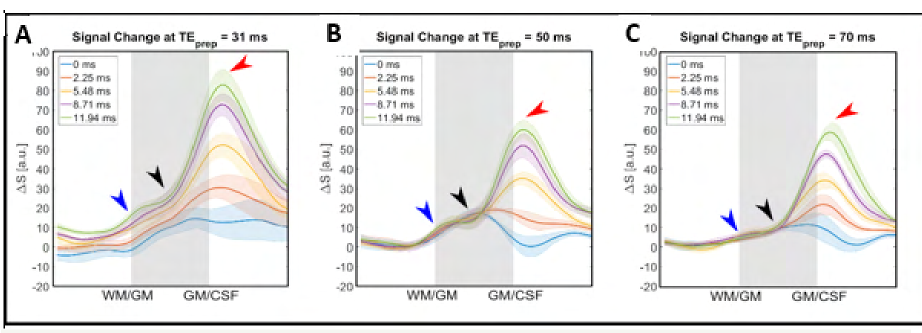


Figure 1. Laminar signal change profiles for different amounts of T2-weighting. We see that for larger amounts of T2-weighting (panels B and C), the lines all fall on top of each other (black & blue arrows). Furthermore, the blue lines go towards zero signal change in the CSF compartment (red arrows). Both are indicative of high functional specificity of the T2-prep method. (Work currently under review at Neuroimage)

have been published that explore how we could embed these laminar possibilities in our analysis frameworks that look at connectivity in conventional fMRI. This Emmy Noether project maintains our continued efforts in this direction (e.g. embedding in DCM together with the ETH in Zürich, and through psychophysiological interactions (PPI)). Our latest work has focused on the attentional modulation of connectivity in visual cortex using layer-fMRI jointly measured with electroencephalography (EEG) shown in Figure 3. Here we find attentional effects in particular frequency bands in the EEG spectrum to correlate with modulations in the fMRI signals at specific depths, which leads to very new insights in terms of how feedback is resembled in functional connectivity imaging using fMRI and/or EEG.

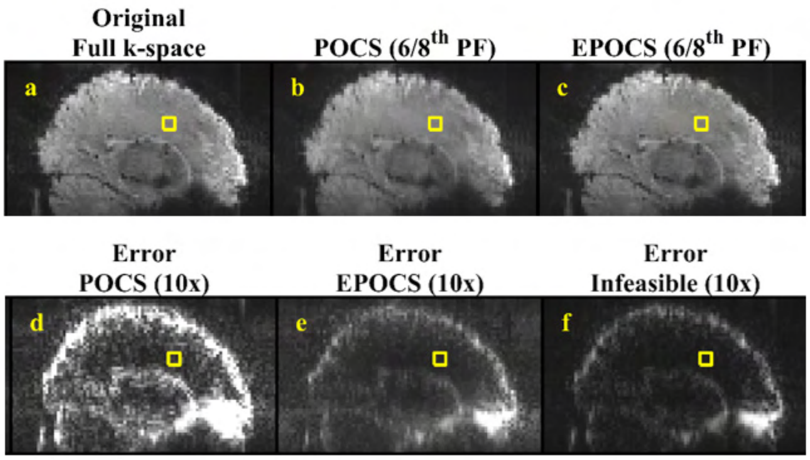


Figure 2. Image quality of the new Enhanced-POCS (EPOCS) method vs. the current best standard (POCS).POCS and EPOCS are used to accelerate imaging, but to be able to show the errors of each method, this figure uses fully sampled MR data that are retrospectively 'accelerated'.(A) The original data. (B) The POCS method with 25% acceleration (note the blurry appearance). (C) The new EPOCS method. (D-E) The errors of (B-C) w.r.t. the full data shown in (A). (F) a control condition where the reconstruction algorithm was allowed to cheat showing the best possible reconstruction one could hope to achieve. There are reasons why you can never hope to recover (A) fully, so (F) gives a 'upper bound' on performance, which the EPOCS method gets very close to. Work published in: Magn Reson Med. 2021 Jan;85(1):140-151. Enhanced POCS reconstruction for partial Fourier imaging in multi-echo and time-series acquisitions. PJ Koopmans & V. Pfaffenrot

In summary: our Emmy Noether research group aims to improve the specificity and efficiency of high-resolution fMRI methods to measure functional signal changes in cortical layers, and to develop the analysis techniques necessary to optimally use this laminar information in brain connectivity imaging. Future work includes collaborations with the pain research group of Prof. Bingel as modulating feedback pathways play a crucial role in the perception of pain.

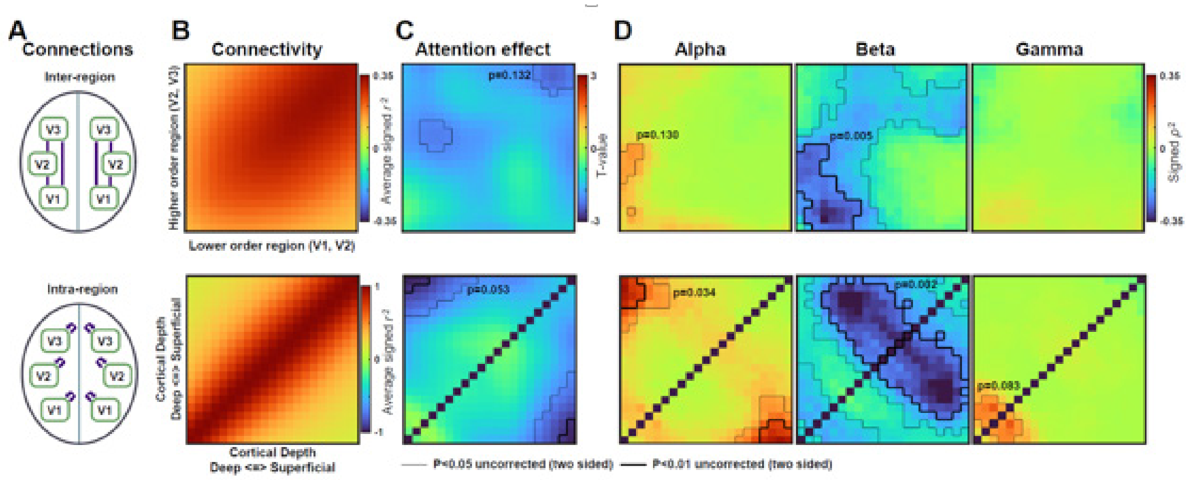


Figure 3. Laminar signal change profiles for different amounts of T2-weighting. Figure 3. Visual attention in laminar fMRI together with simultaneous EEG. Column A shows which connectivity is depicted in each row, inter-regional following the information stream through early visual areas V1-V3 (top) or intra-regional in each of these areas (bottom). Column B shows the fMRI connectivity (correlation values) which as expected is highest in the intraregional case, particularly near the diagonal (note that scales for bottom and top row are different). Column C shows the attention effect in the laminar fMRI data, showing an overall decrease, with a very prominent significant effect in for deep-superficial connections in the intra-regional case (the dark-blue corners in the bottom panel of C). Section D shows the relation of the attention effects in the EEG signal per frequency band (alpha, beta, gamma) with the attention effect in the layer fMRI data. Both alpha and beta show strong effects in the intra-regional case, but very notably they differ in sign, despite them both correlating negatively with main BOLD task effects, and attention effects in the BOLD data decreasing everywhere (panel C). (Work currently under review at eLife)

The DFG-Funded German Ultrahigh Field Imaging (GUFI) Network – a Retrospective on Achieved Goals and Contributions to the Scientific Community.

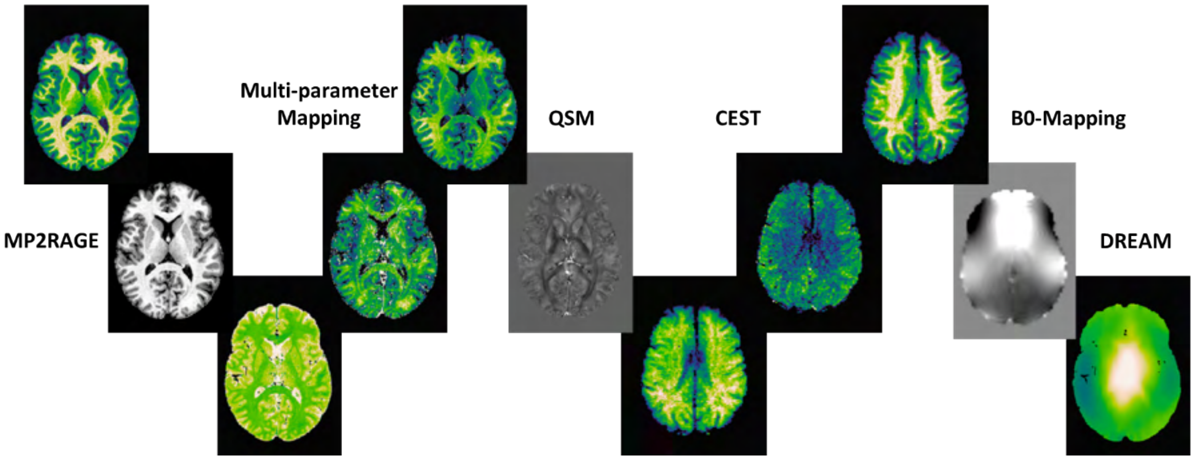
The German Ultrahigh Field Imaging (GUFI) network was founded at the end of 2013 with the aid of DFG funding provided by the call to establish Core Facilities including distributed national networks. The initial project duration of three years (2013-2016) [1] was prolonged for a second DFG-funded 36-month period (2016-2019) [2], with an additional prolongation until the end of 2021 due to current restrictions with respect to the COVID-19 pandemic. Over the years of project duration, a total of all 11 German and two neighboring (Vienna, AT, and Maastricht, NL) sites that all operate UHF MRI systems (7T or 9.4T) actively contributed to the world-wide highly acknowledged network, whose overall goal is to facilitate and harmonize the work of UHF MRI sites.

Sites of the GUFI network. All sites are operating UHF (10x 7T, 2x 9.4T) MRI systems provided by the same vendor (Siemens Healthcare).

In its first years, GUFI has made important contributions to address challenges for all German UHF sites and identify several new areas of common interest. To harmonize access procedures between sites and thereby to facilitate access to UHF systems for external researchers, a consensus guideline document has been formulated that gives basic recommendations regarding access procedures and rules [3]. Furthermore, the GUFI partners defined and signed a consensus recommendation for dealing with subjects with passive implants [4] to standardize decision-making regarding whether a measurement at UHF MRI can be performed safely. Latter has attracted world-wide recognition and has been referenced numerous times.

Quality assurance (QA) has also emerged as a critical issue for UHF systems and a topic of common interest to all GUFI members. GUFI has implemented a QA protocol to assess radiofrequency (RF) coil and system performance based on SNR, B1+, noise, and stability measures [5]. In addition, all sites were equipped with a dedicated phantom to compare QA parameters between all GUFI sites as well as across three generations of 7T MR technology, i.e. passively and actively shielded magnets of the first generations, including different gradient coils, and the new MAGNETOM Terra 7T MRI systems that emerged in 2017. Very good agreement was found between the sites and across system generations, but the protocol also revealed hardware and calibration deviations at some sites over the years. The underlying issues could be identified and rectified by the

Oliver Kraff, Maximilian Völker, Mark E. Ladd and Harald H.Quick



The Traveling Heads experiment evaluates the multi-site reproducibility of quantitative imaging methods at 7T. In conjunction with the system calibration, MP2RAGE, QSM, CEST and multi-parametric mapping/relaxometry were examined. The results show very high inter-site reproducibility across 10 different sites, with some caveat highlighted.

vendor based on the problem description delivered by the data, and repeat measurements verified conformance of the systems with desired specifications.

Furthermore, the standardized QA was the basis for two successful multi-center brain imaging studies performed across the network. The first "traveling heads" experiment started in 2014 with the focus on qualitative and structural measurements at 7T [6]. In a follow-up study in 2019, inter-site reproducibility was again tested in the same two male subjects from the first study, but now with a focus more on state-of-the-art quantitative imaging methods [7]. In addition, two sites of the network had already been equipped with new Terra 7T MRI systems at that time, allowing also a performance and reproducibility assessment in vivo across the different generations of 7T MRI systems. The GUFI "traveling heads" data showed that even across nearly 15 years of operation not only harmonized state-of-the-art qualitative, but also quantitative imaging methods between different UHF sites and scanner architectures yield comparable results of very high quality and reproducibility. This is a milestone of paramount importance, particularly for those sites that have upgraded their old MAGNETOM 7T MRI systems with a new Terra system like us at the Erwin L. Hahn Institute.

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MI-Robot: Metablic Imaging for Robotic MR guided interventions

Prostate cancer is a very common cancer among men, and its prognosis, treatment and survival largely depends on the aggressiveness and stage of the disease. Localized disease, confined to the prostate, can be actively surveilled or treated with curative intent. More aggressive disease, with (high risk for) the presence of metastases, needs a different treatment plan. Accurate staging of the presence of metastases is therefore crucial for the determination of the treatment plan, but remains challenging. The newly granted EFRO project "Metablic Imaging for Robotic MR guided interventions (MI-Robot)" is focusing on this research question by combining the expertise from industry and scientific research.

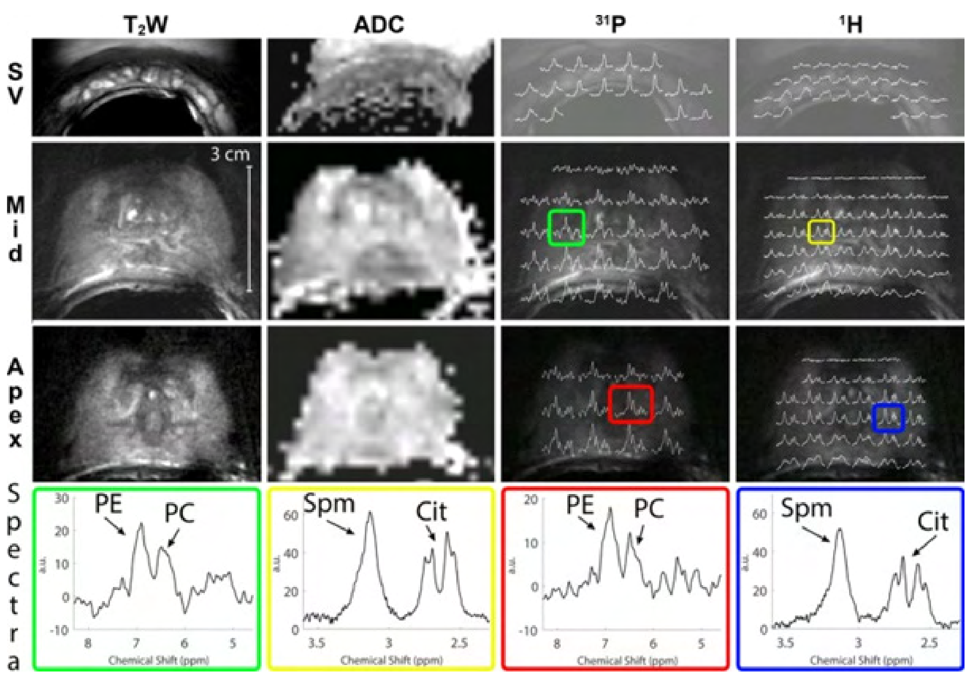

Figure 1: T2W imaging, DWI ADC maps, 31P MRSI spectral maps (31P), and 1H MRSI spectral maps (1H) of three different regions of the prostate of a healthy volunteer (40 yr, 83 kg): the apex, mid-prostate, and the seminal vesicles (SV).

Previous work has shown that a coil setup with a phosphorous transmit/receive – proton receive only endorectal coil (31P Tx/Rx - 1H Rx ERC) in combination with an 8-channel external multitransmit 1H array enables multiparametric imaging and 1H and 31P spectroscopic imaging of the prostate at 7T (see figure 1). This coil setup allows anatomical and functional imaging in combination with acquiring metabolic information from both 1H and 31P MR spectroscopic imaging. It can be used to safely examine patients and volunteers obtaining the highest local 1H SNR in the prostate compared to an 1H external body array. [1]

The MI-robot project will follow up on this previous work by combining an 8Tx/32Rx 1H body array with an external dual-channel 31P coil developing an ultra-high field Meta-array for non-invasive metabolic imaging. In combination with the development of MRI and MRS pulse sequences for the new 7T Terra system, this will allow a detailed assessment of localized tumor aggressiveness and a prediction of the metastatic

Figure 2: The 8Tx/32Rx 1H body array coil designed by Tesla Dynamic Coils installed at the TERRA in Essen.

potential of the tumor focus. A first version of an 8Tx/32Rx 1H (only) body array has already been installed and tested on phantoms to determine proper functioning and ensure safety on site (Fig. 2). In a next step, examination of healthy volunteers are anticipated.

In parallel, a next generation MRI-compatible robot (current type see figure 3) developed by Soteria Medical for guided movement of a needlewire inside the human body will be developed to enable MR-guided robotic biopsies of the local prostate together with regional lymph nodes. The wire guidance will be live supervised by continuous imaging methods.

The new meta-array coil will provide anatomic, functional and metabolic imaging information in an initial extensive 7T MRI/MRS examination. Based on clinical data and the quantitative information of this first scan, a target for biopsy is identified. In a second examination the MR compatible robot will guide a needle guide-wire towards the target to obtain a biopsy. The result is an innovative technique with hardware and software components which can be transferred to other 7T systems. As the meta-array coil and the next generation robot can be used separately from each other, both systems can be transferred to other applications apart from this oncological focus.

Figure 3: Prototype of the MRI-compatible robot as developed by Soteria Medical.

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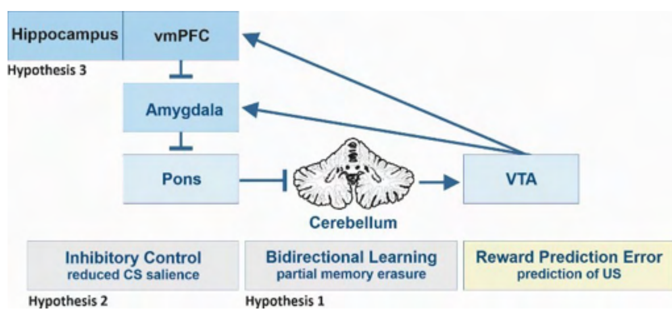
High-Field fMRI studies to unravel the involvement of the cerebellum in the control of emotions

The cerebellum (Latin for little brain), contains more nerve cells than all other brain regions put together. It developed very early in the course of evolution and takes on important control functions in humans and animals, such as controlling fine limb movements. Damage to the cerebellum leads to serious clinical symptoms in humans, which in addition to movement disorders can also include cognitive and emotional impairments. The clinical entity of a "Cerebellar Cognitive Affective Syndrome" has been introduced by Jeremy Schmahmann as early as 1998 (Schmahmann et al., Brain. 1998;121:561-79. doi: 10.1093/brain/121.4.561). Two network grants will likely allow Dagmar Timmann and Harald Quick to study the involvement of the cerebellum in the control of emotions in the next four years in further detail. Dagmar Timmann and Harald Quick are PIs in the collaborative research centre 1280 "Extinction learning" which started in 2017. Dagmar Timmann also serves as the deputy spokesperson of the SFB1280. Decision about granting a possible second funding period will be made by the Deutsche Forschungsgemeinschaft (DFG) in May 2021. In addition, studies will be performed as part of a Marie Skłodowska-Curie Innovative Training Network (ITN) newly funded by the European Research Council. Dagmar Timmann is one of the PIs, and deputy network coordinator of the ITN. The new consortium, called CEN (Cerebellum & Emotional Networks), brings together researchers from across Europe and will address the contribution of the cerebellum in the control of emotions, and in particular fear



Proposed interactions between the cerebellum and the brain extinction network of learned fear.

and anxiety. CEN will start in June 2021, conditional upon successful completion of the grant preparation data and signature of the grant agreement. One important emotion for survival is fear. Being able to learn to predict potentially harmful or threatening events is essential for survival, and can be assessed in the laboratory using fear conditioning paradigms. Animal and human studies have shown that the cerebellum is involved in the acquisition and retention of conditioned fear responses. It is important for survival to learn to predict potentially harmful events, but it is equally important to extinguish previously learned associations if no longer needed. Lack of extinction of learned fear contributes to the pathophysiology of many types of anxiety disorders. As yet, the contribution of the cerebellum to extinction of learned fear responses has not been studied in detail. One important aim of our 7T fMRI studies will be to show that the cerebellum has to be included in the network underlying extinction of learned fear responses. In a recent 7T fMRI study we found cerebellar cortical activation related to the predicted occurrence of an aversive stimulus. This finding was expected and agrees well with the literature. Most prominent cerebellar activations, however, were observed during the unexpected omission of the unpleasant event in unreinforced trials in the acquisition learning phase (Ernst et al., Elife. 2019;8:e46831. doi: 10.7554/eLife.46831). One focus in upcoming studies will be on the initial extinction trials when the omission of the US is equally unexpected. The unexpected omission of the aversive stimulus is thought to be rewarding, and is associated with an increase of dopamine in the ventral tegmental area (VTA). There is new evidence that the cerebellum receives reward signals, and is connected with the VTA. We will perform a series of 7T fMRI experiments to test the hypothesis that the cerebellum is involved in processing of reward prediction error that drives extinction learning. We expect cerebellar activation to be high during initial omission of the US in early extinction and accompanying VTA activation in healthy participants. We expect that this activation is altered in patients with cerebellar degeneration, and by the application of dopaminergic drugs. Finally, we want to show that cerebellar activation is equally present during the unexpected presentation of reward in appetitive conditioning. An MRI safe experimental fear conditioning set-up is available. This includes equipment to perform pupillometry using an eye tracker and to record skin conductance and ECG in the 7T scanner. Key to unlocking new treatments and therapies for emotional disorders is to gain a comprehensive understanding of the nature and function of the neural networks that underpin such behaviours in both health and disease. A central aim of our studies is to share and combine knowledge in the field of cerebellar research and in the field of anxiety disorders studied by other members of the SFB1280 and CEN. The knowledge gained will inform the development of new therapeutic strategies for individuals suffering from emotional disorders.

Participating universities of CEN (Cerebellum & Emotional Networks):

University of Bristol, United Kingdom (Richard Apps, network coordinator and Charlotte Lawrenson)
University Hospital Essen, Germany (Dagmar Timmann, deputy network coordinator)
École Normale Supérieure Paris, France (Daniela Popa and Clement Lena)
University Hospital Würzburg, Germany (Philip Tovote)
University of Edinburgh, United Kingdom (Peter Kind, Thomas Watson and Sally Till)
Università Pavia, Italy (Egidio D'Angelo and Lisa Mapelli)
Universitet Uppsala, Sweden (Tomas Furmark)

Members of SFB 1280 „Extinction Learning":
Spokesperson: Onur Güntürkün, Biopsychology, RUB
Information on the PIs of the 20 projects participating in the SFB1280 can be found here: https://sfb1280.ruhr-uni-bochum.de/en/team/members/

Current Grants

T. W. Scheenen, J. J. Fütterer, F. Witjes, M. Sedelaar, M. Maas, J. O. Barentsz, D. W. J. Klomp, H. H. Quick: Radboudumc: **A personalized image-based assessment of metastatic potential of prostate cancer** (2018-2021)

In this grant the assessment of the aggressiveness of localized prostate cancer is correlated and validated with early detection of the first metastases of the disease.

N. Axmacher, D. Timmann-Braun, H. H. Quick: DFG: **Focus group Neuroimaging: Extinction network connectivity across learning paradigms** (2017-2021)

In this joined project between PIs of the RUB and UKE, metaanalyses will be performed of fMRI data acquired in SFB1280. The main aim is to systematically investigate structural and functional extinction network connectivity across different learning paradigms and subject populations.

D. Timmann-Braun, H. H. Quick: DFG: **The contribution of the cerebellum to extinction: intrinsic mechanisms and cerebello-cerebral-interactions** (2017-2021)

The main aim of the project is to provide experimental evidence that the cerebellum has to be included as part of the neural circuitry underlying extinction of conditioned fear responses.

P. Koopmans: DFG Emmy Noether Programme – Independent Junior Research Group: **Functional Magnetic Resonance Imaging of cortical layers to measure directionality of information flow in brain networks for pain** (2016-2021)

Dr. Koopmans proposal focuses on the development of a high-resolution fMRI technique to improve understanding of how the brain processes pain.

M. E. Ladd, H. H. Quick, O. Speck: DFG: **German ultra-high field imaging (GUFI)**, Core Facility (2016-2021)

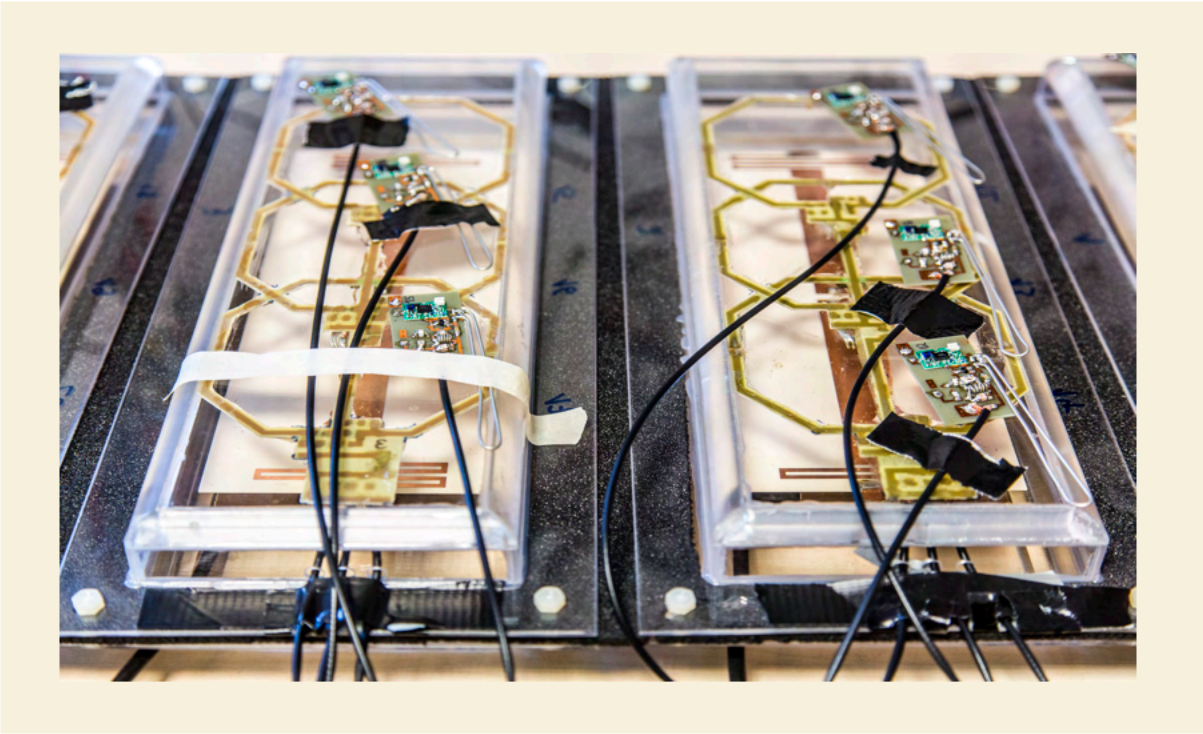
Aim of this project is to maintain and expand a nationwide network of UHF-MRI sites.

T. W. Scheenen, H. H. Quick, J. O. Barentsz: Radboudumc: **Nanotechnology at ultra-high magnetic field: towards in vivo detection of small lymph node metastases with MRI** (2016–2020)

In this project the highest sensitivity of 7T to detect in vivo small lymph node metastases will be validated with histopathology of resected tissues in patients with rectal cancer.

H. H. Quick, DFG: **7-Tesla Ultrahochfeld Magnetresonanztomographie-System** (2020)

With the help of this grant the Erwin L. Hahn Institute was able to replace the old 7 Tesla scanner with a newer model.



Personnel and Organisational Structure at ELH

Directorate / Principal Investigators

Managing Director/PI
Prof. Dr. David G. Norris

Directors/PIs
Prof. Dr. Matthias Brand
Prof. Dr. Harald H. Quick

PIs
Prof. Dr. Ulrike Bingel
Prof. Dr. Dr. h.c. Onur Güntürkün
Dr. Tom W. J. Scheenen

Associated PIs
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Prof. Dr. Mark E. Ladd
Prof. Dr. Dagmar Timmann-Braun

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Administrative Director
Judith Kösters

Staff Scientist
Dr. Oliver Kraff
Dr. Stefan Maderwald

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Stefanie Zurek

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MSc. Mahmoud Bagheri
Dr. Giorgi Batsikadze
Dr. med. Cornelius Deuschl
Dipl.-Phys. Thomas Ernst
Dr. rer. nat. Marcel Gratz
Dr. med. Tijmen Koëter
Dr. Bernhard Müller
Dr. Silke M. Müller
Dr. Stephan Orzada
MSc. Viktor Pfaffenrot
Dr. René Scheeringa
Dr. Jennifer Schulz
MSc. Daniel Sharoh
MSc. Tobias Spronk
Dr. Emma Sprooten
Dr. Katrin Starcke
MSc. Carlijn Tenbergen
Prof. Dr. med. Indira Tendolkar
Dr. med. Andreas Thieme
MSc. Jan-Willem Thielen
Dr. Patrick Trotzke
Dipl.-Ing. Maximilian Völker

Students

Dennis Haupt
Michael Klein
Anna Lauth
Philip Zeidan

New in 2020

Dennis Haupt
Anna Lauth

Left in 2020

Judith Kösters
Stephan Orzada
Patrick Trotzke
Maximilian Völker

Participation at ISMRM 2020 (online)

Chen, Bixia; Sato, Taku; Gembruch, Oliver; Forsting, Michael; Radbruch, Alexander; Rodemerk, Jan; He, Shiqing; Maderwald, Stefan; Quick, Harald H.; Ladd, Mark, E.; Sure, Ulrich; Wrede, Karsten: Relationship between thrombus and aneurysm wall in partially thrombosed intracranial aneurysms visualized with 7T MPRAGE (Digital Poster)

Heerschap, Arend; Peeters, Tom; Veltien, Andor; Scheenen, Tom: 31P MRSI of the human brain: do we need 7T to detect two Pi pools, UDPG signals and determine the NAD+/NADH ratio? (Abstract)

Koëter, Tijmen; Stijns, Rutger; Philips, Bart; Futterer, Jurgen; Zamecnik, Patrick; van Asten, Sjaak; Maas, Marnix; Scheenen, Tom: R2* relaxation rates of pelvic lymph nodes in USPIO-enhanced MRI of rectal cancer at 3T and 7T (Abstract)

Orzada, Stephan; Ladd, Mark. E.; Quick, Harald H.: A 2kW RF power amplifier for 7T proton imaging with digital pre-distortion (Digital Poster)

Schulz, Jennifer: Arterial Blood Contrast (ABC) enabled by Magnetization Transfer (MT) (Talk)

Stelter, Jonathan; Bitz, Andreas K.; Ladd, Mark E.; Fiedler, Thomas: Body imaging at 7T: Comparison of the transmit/receive performance of microstrip antennas and fractionated dipoles (Digital Poster)

Wollrab, Astrid; Kraff, Oliver; Speck, Oliver; Quick, Harald H.; Ladd, Mark E.: On the successful implementation of a first homogenized multicenter online safety training for ultrahigh field MRI (Digital Poster)

Publications on 7T MRI

Antons, S. & Brand, M. Inhibitory control and problematic Internet-pornography use – The important balancing role of the insula. (2020) *Journal of Behavioral Addictions,* 9, 58-70.

Börnert, P.; Norris. D.G. A half-century of innovation in technology - preparing MRI for the 21st century. (2020) *The British Journal of Radiology*

Fortuin, A.S.; Philips, B.W.J.; van der Leest, M.M.G.; Ladd, M.E.; Orzada, S.; Maas, M.C.; Scheenen, T.W.J. Magnetic resonance imaging at ultra-high magnetic field strength: An in vivo assessment of number, size and distribution of pelvic lymph nodes. (2020) *PLOS One* 15(7)

Hütter, B.; Altmeppen, J.; Kraff, O.; Maderwald, S.; Theysohn, J. M.; Ringelstein, A.; Wrede, K.H.; Dammann, P.; Quick, H.H.; Schlamann, M.; Moenninghoff C. Higher sensitivity for traumatic cerebral microbleeds at 7 T ultra-high field MRI: is it clinically significant for the acute state of the patients and later quality of life? (2020) *Therapeutic Advances in Neurological Disorders* 13

Koopmans, P.J.; Pfaffenrot, V. Enhanced POCS reconstruction for partial Fourier imaging in multi-echo and time-series acquisitions. (2020) *Magnetic Resonance in Medicine*

Lazik-Palm, A.; Kraff, O.; Rietsch, S.H.G.; Ladd, M.E.; Kamminga, M.; Beck, S.; Quick, H.H.; Theysohn, J.M. 7-T clinical MRI of the shoulder in patients with suspected lesions of the rotator cuff. (2020) *European Radiology Experimental* 4(1)

Öz, G.; Deelchand, D.K.; Wijnen, J.P.; Mlynárik, V.; Xin, L.; Mekle, R.; Noeske, R.; Scheenen, T.W.J.; Tkáč, I. Experts' Working Group on Advanced Single Voxel 1H MRS (2020) *NMR in Biomedicine*

Orzada, S.; Fiedler, T.M.; Bitz, A.K.; Ladd, M.E.; Quick, H.H. Local SAR compression with overestimation control to reduce maximum relative SAR overestimation and improve multi-channel RF array performance. (2020) *MAGMA*

Scheenen, T.W.J.; Zamecnik, P. The Role of Magnetic Resonance Imaging in (Future) Cancer Staging: Note the Nodes. (2020) *Investigative Radiology*

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