11th Annual Scientific Symposium

Ultrahigh Field Magnetic Resonance:
Clinical Needs, Research Promises and Technical Solutions

September 03rd - 04th 2020
Virtual Meeting at the Max Delbrück Center,
Berlin, Germany

Local organizers: Thoralf Niendorf (MDC & Charité, Berlin), Lucio Frydman (Weizmann Institute of Science, Rehovot, Israel), Jeanette Schulz-Menger (Charité, Berlin), Michal Neeman (Weizmann Institute of Science, Rehovot, Israel), Min Chi Ku (MDC, Berlin), Sebastian Schmitter (PTB, Berlin), Sonia Waiczies (MDC, Berlin)

www.uhf-mr.de
Dear colleagues and friends,

Very warm welcome to Berlin.

We are mostly excited by the larger audience that has joined us for the 11th Scientific Symposium on Clinical Needs, Research Promises and Technical Solutions in Ultrahigh Field Magnetic Resonance, due the “convenience” of having a virtual meeting. The silver lining of the corona pandemic is that we are quickly learning how to become more digitally connected. Limitations that have kept scientists from linking with others at the other end of the world are connected to travel (jetlag, time), environmental concerns (carbon footprint) and expenses (flights, outrages conference fees) that have been prohibitive for many of us; these have been narrowed down to the triviality of time-zone differences. For scientists this is of little consequence, most of us are anyway renowned night owls.

Imaging bridges a crucial gap in space and time in life science and medicine: from atomic to anatomic objects to whole body imaging, from picoseconds to years in population studies. New molecular and cellular insights are obtained from imaging. These findings should be integrated with data science into a coherent picture of tissues, organs and organisms for early interception of disease. These fundamental developments call for hitherto unavailable research frameworks, international partnership and collaborative culture to promote strong ties across multiple research domains and imaging modalities; connecting nanoscopic views, length scales, time scales and mesoscopic pictures with mechanistic insights and macroscopic function of biological and clinical importance.

To meet this goal the Max Delbrück Center for Molecular Medicine; the Weizmann Institute of Science in Rehovot, Israel; the Humboldt University of Berlin and the Charité-University Medicine, Berlin have joined forces to establish a Helmholtz International Research School (HIRS) on imaging from the NANo to the MESo (iNAMES, https://www.mdc-berlin.de/inames). The this year’s symposium marks the official start of iNAMES. These efforts are complemented by the Helmholtz Imaging Platform (HIP), with the Max Delbrück Center being a HIP core in collaboration with the DESY Hamburg and DKFZ Heidelberg. iNAMES and HIP are acting as springboards to intensify scientific interactions in imaging, data sciences, information technologies and digital engineering research fields.
The field of Magnetic Resonance (MR) has evolved rapidly over the past quarter of a century, allowing for an ever growing number of applications across a broad spectrum of basic, translational and clinical research. One important development which is in the spotlight of MR research is Ultrahigh Field Magnetic Resonance (UHF-MR). The pace of discovery is heartening and a powerful motivator to transfer the lessons learned at ultrahigh fields from basic research into the clinical scenario. These efforts are fueled by the unmet clinical needs and the quest for advancing the capabilities of diagnostic MR imaging – today.

The development of UHF-MR is moving forward at an amazing speed that is breaking through technical barriers almost as fast as they appear. UHF-MR has become an engine for innovation in experimental and clinical research. With more than 60,000,000 MR examinations already performed at 7.0 Tesla, the reasons for moving UHF-MR into clinical applications are more compelling than ever. Images from these instruments have revealed new aspects of the anatomy, functions and physio-metabolic characteristics of the brain, heart, joints, kidneys, liver, eye, and other organs/tissues, at an unparalleled quality. UHF-MR has a staggering number of potential uses in neuroscience, neurology, radiology, neuroradiology, cardiology, internal medicine, oncology, nephrology, ophthalmology and other related clinical fields. As they are developed, we will push the boundaries of MR physics, biomedical engineering and biomedical sciences in many other ways.

Realizing these opportunities, we are very much delighted to very warm welcome you at the 11th Annual Scientific Symposium on Clinical Needs, Research Promises and Technical Solutions in Ultrahigh Field MR. The symposium is a collaboration between the Max Delbrück Center for Molecular Medicine, the Charité, the German Metrology Institute (PTB) and the Weizmann Institute of Science, Rehovot, Israel. The symposium is designed to provide an overview of state-of-the-art (pre)clinical UHF-MR, to discuss the clinical relevance of UHF-MR, to explore future directions of UHF-MR, to foster explorations into UHF-MR and to initiate local, regional, national and international collaboration and last but not least to provide plenty of opportunities to engage into fruitful exchange with peers and colleagues.

For the scientific program we are very much honored to present extraordinary speakers including MR technology leaders, distinguished clinical experts and emerging scientists – all bridging disciplinary boundaries and stimulating the im-
aging community to throw further weight behind the solution of unsolved problems and unmet clinical needs. The scientific program is tailored to survey current trends in UHF-MR technology, to provide an overview of state-of-the-art (pre)clinical UHF-MR, to discuss MR safety topics, to demonstrate the clinical relevance of UHF-MR, to explore future directions of UHF-MR and to brainstorm about physiometabolic imaging technologies. We wish to acknowledge the passion and dedication of the many imaging students who put their heads together to brainstorm on the topics covered in the scientific program.

We would like to draw your attention to the electronic posters, all being made readily available for viewing and download. We wish to thank those of you who walked the extra milage and submitted poster contributions. We really appreciate your efforts. Thanks to your valuable feedback we have also included several slots of 2 min enlightening poster power presentations into the program. This will give a large number of poster presenters the opportunity to be in the spotlight of the audience. Please support the poster presenters and do not miss to vote for the best poster.

We cordially invite to the advertisements included in the digital program booklet ready for viewing and download. It also behooves us to emphasize that this is the right moment to acknowledge our generous sponsors who provided marvelous support to the symposiums scientific and educational activities. Thank you very much to our sponsors and supporters.
# Table of Contents

- **Organization** ................................................................. 3
- **Program** ........................................................................ 4
- **Poster Abstracts** ......................................................... 13
- **Sponsors** ....................................................................... 90
RF Coils & Accessories for Animal and Human Imaging

We provide successfully tested products as well as custom solutions that exactly meet your needs and specifications.

Our portfolio encompasses clinical and preclinical RF coils for field strength from 1.5 T to 11.5 T and for the nuclei of your choice.

With our coils, we provide a certificate issued by a notified body which confirms compliance with IEC 60601-1 and IEC 60601-2-33.

Examples from our portfolio

- 32 channel modular transceiver array for cardiac/body imaging at 7.0 Tesla
- 8 channel transceiver array for carotid imaging at 3.0 Tesla
- 8 channel $^1$H knee RF coil for pTX application at 7.0 Tesla
- 6 channel transceiver array for eye imaging at 3.0 Tesla and 7.0 Tesla
- 4 channel $^{23}$Na and 4 channel $^1$H RF coil for cardiac/liver imaging at 7.0 Tesla
- $^{19}$F/$^1$H transceiver array for lung imaging at 3.0 Tesla and 7.0 Tesla
- Small monkey volume RF coil for brain imaging at 11.7 T
- $^{19}$F/$^1$H volume RF coil for mouse imaging at 9.4 T

... and more

Device Testing and Certification

We offer dedicated consulting and testing services with the focus on in-house-built hardware including custom RF coils.

We prepare all documents and procedures including the certificate issued by a notified body for your IRB or local safety board.

Contact us:

www.mritools.de
info@mritools.de
+49 30 9489 2582
Organizers:
Thoralf Niendorf Berlin, Germany (MDC & Charité)
Lucio Frydman Rehovot, Israel (Weizmann Institute of Science)
Jeanette Schulz-Menger Berlin, Germany (Charité & Helios Klinikum)
Michel Neeman Rehovot, Israel (Weizmann Institute of Science)
Min-Chi Ku Berlin, Germany (MDC)
Sebastian Schmitter Berlin, Germany (PTB)
Sonia Waiczies Berlin, Germany (MDC)

Conference Office:
Lien-Georgina Dettmann, Matthias Runow & Timkehet Teffera
E-Mail: MRSymposium@mdc-berlin.de
Max Delbrück Center for Molecular Medicine in the Helmholtz Association
Robert-Rössle-Straße 10
13125 Berlin
Phone: +49 (0)30 9406/3720/4255/2719

Office Prof. Niendorf:
Carolin Heydrich
E-Mail: Carolin.Heydrich@mdc-berlin.de
Max Delbrück Center for Molecular Medicine in the Helmholtz Association
Robert-Rössle-Straße 10
13125 Berlin
Phone: +49 (0)30 9406 4505
## 11th Annual Scientific Symposium on Ultrahigh Field Magnetic Resonance

### Day 1

<table>
<thead>
<tr>
<th>Time (CEST)</th>
<th>Time (EDT)</th>
<th>Time (CST)</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:00</td>
<td>06:00</td>
<td>18:00</td>
<td>Welcome</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>chair: Thoralf Niendorf, Berlin, Germany</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sonia Waiczies, Berlin, Germany</td>
</tr>
<tr>
<td>12:15</td>
<td>06:15</td>
<td>18:15</td>
<td>KEYNOTE: Why all the Fuss About Ultrahigh Field MRI: New Directions in Optical Imaging from the Nanoscopic to the Mesoscopic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Katrin Heinze, University of Würzburg</td>
</tr>
</tbody>
</table>

### Scientific Session I

**Getting to the Matter of the Heart: Clinical Needs and Research Promises of Cardiovascular UHF-MR**

Chair: Lucio Frydman, Rehovot, Israel

Thoralf Niendorf, Berlin, Germany

<table>
<thead>
<tr>
<th>Time (CEST)</th>
<th>Time (EDT)</th>
<th>Time (CST)</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:35</td>
<td>06:35</td>
<td>18:35</td>
<td>Ten Reasons for Doing Cardiac MRI at 7.0 T: Dreams versus Reality</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ibrahim El-Sayed, Medical College of Wisconsin, Milwaukee, USA</td>
</tr>
<tr>
<td>12:55</td>
<td>06:55</td>
<td>18:55</td>
<td>Physiometabolic Probing of the Heart with Multinuclear MR at 7.0T</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tanja Platt, DKFZ Heidelberg, Germany</td>
</tr>
<tr>
<td>13:15</td>
<td>07:15</td>
<td>19:15</td>
<td>LUNCH BREAK / BREAKFAST BREAK</td>
</tr>
<tr>
<td>14:00</td>
<td>08:00</td>
<td>20:00</td>
<td>Size Matters: High Density RF Array for Cardiac MR at 7.0 T</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thomas Eigentler, Max Delbrück Center for Molecular Medicine, Berlin, Germany</td>
</tr>
<tr>
<td>14:20</td>
<td>08:20</td>
<td>20:20</td>
<td>Rich Opportunities for Discovery: Vascular and Body MRI at 7.0 T Revisited</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Natalie Schön, PTB-Physikalisch-Technische Bundesanstalt, Berlin, Germany</td>
</tr>
<tr>
<td>Time</td>
<td>Session Details</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>---------------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14:40</td>
<td>POSTER POWER SESSION (5 x 2 min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Identifying Radiation Therapy Effect on Cardiac Function Using Ultrahigh Field 9.4 T MRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>El-Sayed Ibrahim, Medical College of Wisconsin, Milwaukee, USA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Towards Carotid Arteries Characterization: Time-Resolved 3D Flow-MR Fingerprinting Implementation at 7.0 T</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lisa Leroi, PTB-Physikalisch-Technische Bundesanstalt, Berlin, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SAR distribution for the Transceiver Array for Human Cardiac MRI at 7.0 T: Variations due to Displacement on Thorax.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Terekhov Maxim, University Hospital Würzburg, Würzburg, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cardiac Functional Imaging Using Ultrahigh Field 7.0 T MRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>El-Sayed Ibrahim, Medical College of Wisconsin, Milwaukee, USA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Whole-Heart 4D Flow MRI at 7.0 T Using Self-Gated Respiratory Motion Correction</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jean Pierre Bassenge, PTB-Physikalisch-Technische Bundesanstalt, Berlin, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14:50</td>
<td>PANEL DISCUSSION: CARDIAC MRI at UHF</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>chair: Min-Chi Ku, Berlin, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sebastian Schmitter, Berlin, Germany</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15:05</td>
<td>COFFEE BREAK / RELAXATION WITH LIVE MUSIC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SCIENTIFIC SESSION II

GETTING TO THE MATTER OF THE BRAIN: CLINICAL NEEDS AND RESEARCH PROMISES FOR NEUROVASCULAR UHF-MR AND RELATED FIELDS

chair: Michal Neeman, Rehovot, Israel
Paula Ramos Delgado, Berlin, Germany

<table>
<thead>
<tr>
<th>Time</th>
<th>Session Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>15:30</td>
<td>Diffusion and Functional Measurements at High and Ultrahigh Fields. A Preclinical Perspective</td>
</tr>
<tr>
<td></td>
<td>Lucio Frydman, Weizmann Institute of Science, Rehovot, Israel</td>
</tr>
<tr>
<td>Time</td>
<td>Session</td>
</tr>
<tr>
<td>-------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| 15:50 | Speed Saves: Simultaneous Parametric T2 and T2* Mapping in Healthy Subjects and in Patients with Multiple Sclerosis  
Carl Herrmann, Max Delbrück Center for Molecular Medicine, Berlin, Germany |
| 16:10 | Are We Brain Washed During Sleep? Keeping Neuropsychiatric Disorders Away  
Laura Lewis, Boston University, USA |
| 16:30 | Metabolic Profiling of the Human Brain: Clinical High Resolution 3D-MR Spectroscopic Imaging at 7.0 T  
Eva Heckova, Medical University Vienna, Austria |
| 16:50 | POSTER POWER SESSION (5 x 2 min)  
Kinetic Oscillatory Stimulation in the Nasal Cavity Elicits Functional Brain Activation in the Limbic System of the Brain  
Xia Li, China Jiliang University, Hangzhou, China  
Postmortem Human Brain 9.4 T Ultrahigh Field MRI: the UTAP Study  
Stijn Michielse, Maastricht University Medical Center, The Netherlands  
MRI Reveals Brain Ventricle Expansion in Pediatric Patients with Acute Disseminated Encephalomyelitis  
Jason Millward, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany  
In-vivo Repeatability of SPECIAL Based Single-voxel Spectroscopy Using Different Adiabatic Inversion Pulses  
Layla Tabea Riemann, PTB-Physikalisch-Technische Bundesanstalt, Berlin, Germany  
1H NMR Based Serum and Urine Bio-Fluids Metabolic Profile Correlates with the Neurological Recovery in Treated Acute Spinal Cord Injury (ASCI) Subjects: A Prospective Case Control Study  
Alka Singh, King George's Medical University, Daliganj, Lucknow, India |
| 17:00 | PANEL DISCUSSION: BRAIN MRI at UHF  
chair: Ariane Fillmer, Berlin, Germany  
Henning Reimann, Berlin, Germany |
<p>| 17:15 | ADJOURN – End of Day 1 |</p>
<table>
<thead>
<tr>
<th>Time (CEST)</th>
<th>Time (EDT)</th>
<th>Time (CST)</th>
<th>DAY 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:00</td>
<td>06:00</td>
<td>18:00</td>
<td>Welcome</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>chair: Thoralf Niendorf, Berlin, Germany</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sonia Waiczies, Berlin, Germany</td>
</tr>
<tr>
<td>12:15</td>
<td>06:15</td>
<td>18:15</td>
<td>KEYNOTE: 17.6 T MRI of the Perivascular Network: Imaging Brain Waste Clearance Paths</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Malisa Sarntinoranont, University of Florida, Gainesville, USA</td>
</tr>
</tbody>
</table>

**SCIENTIFIC SESSION III**

**TRANSLATIONAL RESEARCH: FROM BLUE SKY EXPLORATIONS EN ROUTE TO CLINICAL APPLICATIONS**

chair: Min-Chi Ku, Berlin, Germany
Philipp Selenko, Rehovot, Israel

<table>
<thead>
<tr>
<th>Time (CEST)</th>
<th>Time (EDT)</th>
<th>Time (CST)</th>
<th>DAY 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:35</td>
<td>06:35</td>
<td>18:35</td>
<td>Using the Visible to Observe the Unvisible: En Route to Deep Tissue MR Imaging</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Paula Ramos Delgado, Max Delbrück Center for Molecular Medicine, Berlin, Germany</td>
</tr>
<tr>
<td>12:55</td>
<td>06:55</td>
<td>18:55</td>
<td>Fluoride Nanocrystals: Tracers for In Vivo Hot Spot 19F MRI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Amnon Bar-Shir, Weizmann Institute of Science, Rehovot, Israel</td>
</tr>
<tr>
<td>13:15</td>
<td>07:15</td>
<td>19:15</td>
<td>LUNCH BREAK / BREAKFAST BREAK</td>
</tr>
<tr>
<td>14:00</td>
<td>08:00</td>
<td>20:00</td>
<td>Pushing the Boundaries of Chemical Exchange Saturation Transfer (CEST) Imaging at Ultrahigh Magnetic Fields</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dario Longo, Italian National Research Council (CNR), Torino, Italy</td>
</tr>
<tr>
<td>14:20</td>
<td>08:20</td>
<td>20:20</td>
<td>MR-Synchronized Optogenetic, Visual and Auditory Stimulation to Probe Sensory Processing in Rats Using Functional MRI at 7.0 T</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ed Wu, The University of Hong Kong, China</td>
</tr>
<tr>
<td>14:40</td>
<td>08:40</td>
<td>20:40</td>
<td>Sea to Summit: Progress in Preclinical MR at Ultrahigh and Extreme Magnetic Fields</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wulf-Ingo Jung, Bruker Biospin MRI GmbH, Ettlingen, Germany</td>
</tr>
</tbody>
</table>
**POSTER POWER SESSION** (5 x 2 min)

Deep CEST MR Fingerprinting at 7.0 T Reveals Tumor Apoptotic Response to Oncolytic Virotherapy In Vivo
Or Perlman, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA, USA

Characterization of Fluorinated Pesticides using Fluorine (19F) MR Methods
Salina Skenderi, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

Towards Non-Invasive Imaging of MS Disease-Modifying 19F Drugs
Fatima Sherazi, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

Performance of Compressed Sensing for Detecting Low SNR 19F MRI in Experimental Autoimmune Encephalomyelitis using Prospective Undersampling
Ludger Starke, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

Point Spread Function Mapping Eliminates Image Distortion From Renal Echo-Planar Imaging: Preliminary Results from a 9.4T Animal MR System
Kaixuan Zhao, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

**PANEL DISCUSSION: TRANSLATIONAL MRI at UHF**

chair: Sonia Waiczies, Berlin, Germany
Jason Millward, Berlin, Germany

**COFFEE BREAK / RELAXATION WITH LIVE MUSIC**

**SCIENTIFIC SESSION IV**

**LOOKING AT THE HORIZON**

chair: Amnon Bar-Shir, Rehovot, Israel
Sebastian Schmitter, Berlin, Germany

**Body MR Imaging at 10.5 Tesla – Toys for Boys?**
Kamil Ugurbil, University of Minnesota, Minneapolis, USA
<table>
<thead>
<tr>
<th>Time</th>
<th>Session Title</th>
<th>Speaker(s)</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:10</td>
<td>Following the Footsteps of Neurological Disease with UHF MRI</td>
<td>Priti Balchandani, BioMedical Engineering and Imaging Institute at Mount Sinai, New York, USA</td>
<td></td>
</tr>
<tr>
<td>16:30</td>
<td>(UHF-)MR Image Reconstruction: How Deep Learning Will Shape the Future of MRI</td>
<td>Chen Qin, University of Edinburgh, Edinburgh, UK</td>
<td></td>
</tr>
<tr>
<td>16:50</td>
<td>Thermal MR: Generalization of the Time- and Frequency Multiplexed Problem of Radiofrequency Induced Heating Intervention</td>
<td>Andre Kühne, MRI.TOOLS GmbH, Berlin, Germany</td>
<td></td>
</tr>
<tr>
<td>17:10</td>
<td>Sea to Summit: Progress in Clinical Ultrahigh Field MRI</td>
<td>Robin Heidemann, Siemens, Erlangen, Germany</td>
<td></td>
</tr>
<tr>
<td>17:30</td>
<td>POSTER POWER SESSION (5 x 2 min)</td>
<td>Rapid Mapping of Radiofrequency Coil Fields with Computer Vision</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Egor Kretov, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Respiration-Resolved 3D Multi-Channel Absolute B1+ Mapping of the Body at 7.0 T</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sebastian Dietrich, PTB-Physikalisch-Technische Bundesanstalt, Berlin, Germany</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Evaluation of Static 2D and 3D Parallel Transmission of the Human Heart at 7.0 T</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Christoph Stefan Aigner, PTB-Physikalisch-Technische Bundesanstalt, Berlin, Germany</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$B_0$ Robust Adiabatic Multi-Band Inversion Pulses</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Christoph Stefan Aigner, PTB-Physikalisch-Technische Bundesanstalt, Berlin, Germany</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multi-Channel RF Power and Phase Supervision Systems Technology for Thermal Magnetic Resonance: Development, Evaluation and Application</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Haopeng Han, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany</td>
<td></td>
</tr>
<tr>
<td>17:40</td>
<td>PANEL DISCUSSION: FUTURE of UHF MRI</td>
<td>chair: Christoph Aigner, Berlin, Germany</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ludger Starke, Berlin, Germany</td>
<td></td>
</tr>
<tr>
<td>17:55</td>
<td>END OF SYMPOSIUM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MAKING THE LEAP IN IMAGING PERFORMANCE

- High resolution T₂*-imaging
- Optimal diffusion MRI
- Fast fMRI readouts
- Robust non-Cartesian imaging
Go further than ever before with Bruker Ultra-high Field MRI

The Bruker BioSpec series offers multi-purpose high field MRI/MRS research systems, designed for the emerging market of preclinical veterinary imaging and molecular MRI.

Superconducting Magnet System

- Actively-shielded superconducting wide-bore magnet
- Nitrogen free (no cryogenic maintenance by customer)
- Cryo-refrigerator (Minimal helium consumption, long hold-times, long maintenance intervals)
- Reduced stray field

BioSpec 152/11 USR/R
Field strength: 15.2 Tesla
Diameter of clear bore: 110 mm

BioSpec 117/16 USR
Field strength: 11.7 Tesla
Diameter of clear bore: 160 mm

BioSpec 117/11 USR
Field strength: 11.7 Tesla
Diameter of clear bore: 110 mm

Innovation with Integrity
Evaluation of static 2D and 3D parallel transmission of the human heart at 7T

Christoph Stefan Aigner¹, Sebastian Dietrich¹, Sebastian Schmitter¹
¹Physikalisch-Technische Bundesanstalt (PTB), Braunschweig and Berlin, Germany

Introduction

Three-dimensional human heart imaging at ultra-high fields is highly challenging due to respiratory and cardiac motion-induced artefacts as well as spatially heterogeneous $B_1^+$ profiles. Various methods have been proposed to address the problem of spatial heterogeneities of the $B_1^+$ fields, including parallel transmission (pTx). So far, however, the lack of 3D human abdominal $B_1^+$ maps at 7 T hindered the development of 3D imaging methods in the body. In this study, we investigate the feasibility of static pTx for 2D/3D heart flip angle homogenization at 7 T based on relative 3D $B_1^+$ maps. In addition, in vivo data of 6 subjects of different body sizes were acquired with 3D GRE radial phase encoding (RPE) using subject specific static phase-only pTx.

Methods

MRI was performed on a 7T scanner (Siemens, Erlangen, Germany) with a commercial 8Tx/32Rx thorax coil (MRI.TOOLS, Berlin, Germany) certified by a notified body to comply with the local SAR limits in first level controlled mode of 20 W/kg (IEC 60601-2-33). Six healthy volunteers (2f/4m, 21-35 years) with a wide range of BMI (20-34 kg/m²) were scanned in the supine position according to an approved IRB protocol.

Relative, 3D channel-wise $B_1^+$ estimates were computed from a 3D free breathing GRE RPE scan following references. The channel-wise superposition of the resulting $B_1^+$ maps were then used to manually draw the region-of-interest (ROI) of the heart on a slice-by-slice basis (9-16 slices). The ROI was used as a binary mask for static shimming solving a cost function that optimized the homogeneity measured by the coefficient of variation (CV). Two different shim solutions (phase-only, magnitude and phase) were computed for 1 slice (ROI), 3 slices (ROI₃) and the whole heart (ROI₃) with a slice gap of 8 mm.

The subjects were scanned in the same MRI session additionally with a high-resolution 3D RPE-GRE free-breathing sequence using the optimized ROI₃ static phase-only shim. The 3D dataset was reconstructed for an isotropic voxel size of 1.4 mm with a respiratory motion surrogate retrieved from a 1D projection in the head-feet direction in the k-space center. The underlying motion field was estimated via
image registration based on the respiratory resolved reconstructions and used to correct the respiratory motion\(^5\).

**Results and Discussion**

Figure 1 shows the 4 mm isotropic 3D relative \(B_1^+\) maps of subject 1 for all 8 transmit channels. Both, the magnitude and the phase are free of breathing artefacts, despite acquiring the underlying 3D GRE data under free breathing. The same observation has been made for all 6 subjects. Figure 2 shows the \(B_1^+\) predictions of the optimized static phase-only phase shims for ROI\(_1\) and ROI\(_3\) and ROI\(_H\). Whereas the central slice has comparable \(B_1^+\) homogeneity, the shim of ROI\(_3\) and ROI\(_H\) shows more pronounced \(B_1^+\) variations. Figure 3 summarizes and compares the coefficient of variation (CV) of the nominal FA for each ROI and subject. Across all subjects, the phase-only shims resulted in a CV of 21.9% (ROI\(_H\)), 18.8% (ROI\(_3\)) and 17.2% (ROI\(_1\)) which could be reduced by approximately 2.5% for the magnitude and phase shims. Figure 4 qualitatively validates the 3D \(B_1^+\) prediction of the optimized phase-only ROI\(_3\) shim setting using the reconstructed 3D GRE RPE measurements. The experimental GRE measurements reproduce well the nominal flip-angle patterns of the \(B_1^+\) predictions. The remaining signal drop in AP-direction results from receive-profile, which has not been corrected in the plots.

**Conclusion**

This study demonstrates in 6 subjects that 3D relative \(B_1^+\) mapping can be used to investigate and reduce FA heterogeneities via pTx across the entire 3D heart volume at 7 T. However, it also shows that the degree of freedom of static shims is not enough to compensate FA heterogeneities below an acceptable CV level of about 15% with the used coil, which is likely achievable with dynamic pTX such as 2D slice selective spokes or 3D non-selective kT-points pulses.

![Figure 1: 3D relative estimated \(B_1^+\) maps (left: magnitude, right: phase-angle) of subject 1 at 7 T. Four channels are located on the chest and four channels are positioned under the subject’s back. The phase angle of channels 2 to 8 are computed relative to channel 1.](image-url)
Figure 2: 3D view of the complex sum of estimated $B_1^+$ maps with optimized ROI$_1$, ROI$_3$, and ROI$_H$ static phase setting of subject 1.

Figure 3: Coefficient of variation (CV) for optimized static shim settings of all subjects (left: phase-only, right: magnitude and phase). Three different settings have been optimized and evaluated for an ROI of 1 slice (ROI$_1$), 3 slices (ROI$_3$) and the entire heart volume (ROI$_H$).

Figure 4: $B_1^+$ predictions and reconstructed respiration corrected 3D GRE images for subjects 1 with optimized subject-specific ROI$_3$ static phase-only pTx. The 3D images are free of breathing artifacts and demonstrate, despite some differences close to the coil elements, the validity of the $B_1^+$ maps and the resulting $B_1^+$ predictions with the optimized phase-only shim. The remaining signal changes in AP direction in the measured views are a result of receive ($B_1^-$) variations.
B₀ robust adiabatic multi-band inversion pulses

Christoph Stefan Aigner¹, Sebastian Schmitter¹

¹Physikalisch-Technische Bundesanstalt (PTB), Braunschweig and Berlin, Germany

Introduction
Adiabatic RF pulses generate homogeneous flip angles (FA) despite inhomogeneities of the transmit magnetic radio frequency (RF) field (B₁⁺) at the cost of high RF peak amplitudes and RF power¹. To tackle this problem, multiple methods exist to reduce RF peak amplitudes² or a combined reduction of RF peak amplitudes and RF power³,⁴. In this work, we extend the design of adiabatic multi-band (MB) inversion pulses⁵, where RF power becomes an even stronger problem, for variable slice selective gradient shapes and combine it with low power gradient offset independent adiabatic (GOIA⁴) pulses. The proposed GOIA MB pulses result in smooth slice selective gradients with highly increased bandwidth and matched multi-band RF waveforms. Phantom and in vivo experiments at 7T validate the simulations and demonstrate the B₁⁺ and B₀ robust inversion of multiple slices.

Theory and Methods
Adiabatic MB pulses can be designed with a superposition of frequency offset shifted adiabatic single-band (SB) pulses. The frequency offset is computed as a function of the slice selective gradient, to correct for the time-variable slice selective gradient shapes, and phase scrambling is used to reduce RF peak amplitudes⁶,⁷,⁸. Two different adiabatic inversion pulses, hyperbolic secant (HS)¹ with a constant slice selective gradient and GOIA⁴,⁵ with a time varying slice selective gradient were designed for a pulse duration of 12 ms and a spectral bandwidth of 1.25 kHz (HS) and 20 kHz (GOIA). Gradients were designed for a slice thickness of 20 mm. Three SB pulses, inverting at positions -50, 0, +50 mm measured from isocenter were superposed to form an MB pulse with an optimized phase scrambling scheme⁷ (MB3ps). The MB3ps inversion pulses were implemented in a pulse sequence followed by an orthogonal slice selective excitation and cartesian phase encoding and read-out. High-resolution scans (TR/TE = 2000/4.8 ms, FOV = 256x128 mm, matrix = 384x192) have been acquired on a 7T system (Siemens, Erlangen, Germany) with a 1Tx32Rx Nova Medical head coil. Each scan was performed twice (without and with the adiabatic inversion pulse) and the inversion profiles were calculated by the complex difference of the two images.
Results and Discussion

Figure 1 compares HS-MB3ps and the proposed GOIA-MB3ps pulse which results in a 16 times higher bandwidth with only a 2-fold RF power increase. As expected, phase scrambling of adiabatic MB pulses resulted in a sub-linear scaling of the peak $B_1$ amplitude and as expected from theory a linear scaling of RF power demand with the number of bands. While there are strong RF magnitude and phase variations, the GOIA Gs waveform is smooth and does not require correction of gradient imperfections$^{8,9}$. Figure 2 shows simulated inversion profiles (scaled from 0 to 1) of the adiabatic multiband pulses for a $B_1$ variation of 0-150% and a $B_0$ offset range of 0-500Hz shows a similar transition to the adiabatic threshold and a different impact of $B_0$ variations. For instance, a 500Hz $B_0$ offset shifts the inversion profiles by 12 mm for HS and only by 1.2 mm for the GOIA pulse with a maximal error of 2.5% at 500Hz. Figure 3 shows inversion slice profile measurements in a phantom bottle and a healthy volunteer at a 7T system. The reconstructed inversion slices were computed from two measurements without and with the inversion pulse and the resulting difference of both complex images has been normalized by a reference scan. The reconstructed data clearly shows a precise inversion of the proposed GOIA MB3ps example despite $B_1^+$ and $B_0$ variations.

Conclusion

The Bloch simulations and measurements on a 7T system showed the potential of using phase scrambled adiabatic GOIA-MB pulses for simultaneous inversion of multiple slices and will serve as a basis to reduce chemical shift artefacts and voxel bleeding in multi-voxel spectroscopy.

Figure 1: Magnitude and slice selective gradient of phase scrambled adiabatic Hyperbolic Secant (first row) and GIOA (second row) based multi-band pulses and simulated inversion profiles for the central slice and the entire spatial domain.
Figure 2: Simulated impact of $B_1$ and $B_0$ off-resonance scaling on the adiabatic multi-band pulses. The simulations in the first row were performed assuming an ideal $B_0$ field with a fixed $B_0$ off-resonance of 0 Hz. The simulations in the second row are performed with a fixed $B_1$ scaling of 1.5. The cross sections indicate the excellent $B_1$ and $B_0$ robustness of the proposed GOIA MB3ps example.

Figure 3: Inversion slice profile measurements in a phantom bottle and a healthy volunteer using the adiabatic HS- and GOIA-MB3ps pulses from Figure 1 at a 7T system. The reconstructed inversion slices were computed from two measurements without and with the inversion pulse and have been normalized by a reference scan.

7) Wong EC, ISMRM 20, 2209, 2012
Whole-heart 4D flow MRI at 7T using self-gated respiratory motion correction

Jean Pierre Bassenge1,2, Sebastian Dietrich2, Christoph Aigner2, Christoph Kolbitsch2, Sebastian Schmitter2

1Working Group on Cardiovascular Magnetic Resonance, Experimental and Clinical Research Center, a joint cooperation between the Charité Medical Faculty and the Max-Delbrück Center for Molecular Medicine, Berlin, Germany, 2Physikalisch-Technische Bundesanstalt (PTB), Braunschweig and Berlin, Germany

Introduction

4D flow MRI, the three-dimensional and ECG-gated acquisition of blood velocity vector fields, is of interest in a multitude of cardiovascular conditions. [1] Acquisitions at ultra-high field strengths such as 7T offer large potential for 4D flow due to increased signal-to-noise ratio and more localized coil sensitivity profiles, which improve parallel imaging. [2,3] Nevertheless, thoracic 4D flow MRI is more challenging at 7T compared to lower field strengths due to highly inhomogeneous B1+ fields. In the worst cases, B1+ inhomogeneities yield signal dropouts that can impair both acquisitions at the target region and of navigators for respiratory motion compensation. In previous publications, thoracic 4D flow MRI at 7T was limited to the aorta, and prospective respiratory-gating was performed using cross-hair navigator pairs at the intersection of liver and lung, which requires dynamic switching between separate B1+ shim sets for target region and navigator [2,3]. Here, we investigate the feasibility of 4D flow MRI at 7T in a large FOV covering aorta, heart and pulmonary vessels, using a single B1+ shim set in combination with self-gated retrospective motion correction.

Methods

After IRB approval and giving informed consent, a healthy volunteer (m35, BMI 27.8) was scanned at 7T (Magnetom 7T, Siemens, Erlangen, Germany) in pTx mode using a commercial 32Rx/8Tx thorax coil (MRI.Tools, Berlin, Germany). Relative B1+ estimates were acquired for each Tx channel following [5] (3D acq., 3.9mm isotr. res., TA=3:25). A 3D region of interest was manually selected to calculate a magnitude and phase B1+ shim set that optimizes flip angle homogeneity across the heart and the aorta. 4D flow data was obtained with this shim set using a GRE sequence with symmetric referenced velocity encoding (VENC=1.5m/s) in a sagittal slab (width 200mm). The sequence employs radial phase encoding [6], i.e. one cartesian read-out dimension (kx: head-feet, FOV=400mm) and two non-
cartesian phase-encode dimensions (ky: ant.-post. and kz: right-left). For respiratory self-gating, the k-space center (ky=kz=0) was updated every 400ms. Further parameters: 2.5mm isotr. res., TR=5.0ms, TE=2.9ms, nom. FA=24°, BW=640Hz/px, TA=13:37.

A surrogate respiratory signal was calculated from coil PCA of the k-space center projections, and was used to bin the acquired data into 8 respiratory phases. Non-rigid motion-transformation-fields were calculated to co-register all respiratory phases to the end-expiration phase. Subsequently, all data was binned into 24 cardiac phases using the recorded ECG-signal, and the motion-fields were used in an iterative kt-SENSE reconstruction to obtain a motion-compensated 4D flow data set. [4]

For reference, a 2D cartesian flow sequence was acquired in a breathhold (6mm slice thickness, 2.5mm in-plane res., prosp. ECG-trig., temp. res. 34.8ms, VENC=1.5m/s through-plane), using the same B$_1^+$ shim set as for the 4D flow sequence. In addition, a validation scan for the respiratory self-gating was conducted, in which the 4D flow sequence was acquired for 52s during which the volunteer followed a respiration paradigm (Fig. 2).

Results

Fig.1 shows the impact of the applied B$_1^+$ shim for the compensation of signal dropouts in this subject. Fig.2 demonstrates that the self-gating signal reflects the subject’s respiration. A pathline visualization of the obtained whole-heart 4D flow vector field at peak systole is presented in Fig.3 along with derived wall-shear-stress values. While the time-resolved blood flow curves match those of the 2D reference (Fig.4), peak flow was slightly underestimated by 4.2% in the ascending and by 5.5% in the descending aorta.

Discussion

Our preliminary results indicate that whole-heart 4D flow MRI with 100% respiratory navigator efficiency and predictable scan time at 7T is feasible. While a single shim set was sufficient in this subject, further studies with more subjects and a range of BMI are needed to investigate the robustness of the method.
Fig. 1: Acquired field-of-view (FOV) without and with subject specific B$_1^+$ shimming. In the non-optimized default mode, dropouts can be observed across the heart and the left-ventricular outflow tract (red arrows). The default mode was set by the manufacturer to provide sufficient B$_1^+$ throughout the entire ascending and descending aorta. Using a subject specific whole-heart B$_1^+$ shim, signal dropouts were minimized in the target region.

Fig. 2: Respiratory self-navigator (red curve) obtained from a 4D flow scan using the whole-heart B$_1^+$ shim as shown above. In order to validate the self-gating procedure, the subject was following a 52 seconds respiration paradigm, starting in exhale breathhold. After 15 seconds, the subject received directions via headphones to breath in and breath out for 4 and 6 seconds respectively.

Fig. 3: Left: Pathline visualisation of whole-heart 4D flow vector field at peak systole acquired with whole-heart B$_1^+$ shim and motion-compensation. Right: Corresponding wall-shear-stress (WSS) values. Post-processing was done using the 4D flow prototype of Circle CVI42.
Fig. 4: Flow curves of the motion-compensated 4D flow scan in comparison to the 2D flow reference scan.

Respiration-Resolved 3D Multi-Channel Absolute $B_1^+$ Mapping of the Body at 7T

Sebastian Dietrich¹, Christoph Aigner¹, Johannes Mayer¹, Christoph Kolbitsch¹, Tobias Schäffter¹, ², Sebastian Schmitter¹

¹Physikalisch-Technische Bundesanstalt (PTB), Braunschweig and Berlin, Germany, ²Division of Imaging Sciences and Biomedical Engineering, King’s College London, London, United Kingdom

Introduction
A major challenge of ultra-high field body MRI is the spatially inhomogeneous transmit (Tx) radio frequency field ($B_1^+$) that induces spatial contrast variations and in the worst cases areas with no signal. This problem has been addressed by combinations of multi-channel Tx coils, spatial mapping of $B_1^+$ or the flip angle (FA), and by $B_1^+$ shimming or parallel transmission [1,2].

Since channel-wise mapping of the $B_1^+$ fields over a 3D body volume is highly challenging, most applications in the body so far are applied as (fast 2D) slice selective method and performed under a breath-hold [3, 4]. Nevertheless, 3D applications in the human body require the FA to be adjusted over a 3D volume and, thus, the knowledge of the underlying 3D $B_1^+$ maps is essential.

To close this gap we propose a free-breathing method for 3D absolute, channel-wise respiration-resolved $B_1^+$ mapping of the human body at 7T. The method is an extension of a technique proposed initially for the human brain [5] to estimate the $B_1^+$ maps of the individual Tx channels, which has also been applied in 2D as relative $B_1^+$ mapping method to the human body.

Methods
The method requires two different GRE-based free-breathing scans that are obtained using a 3D radial phase-encoded (RPE) trajectory [6, 7] (Fig 1a). The first acquisition, termed RPE-GRE (cf. Fig 1b) acquires channel-wise 3D images for each Tx channel where only a single Tx channel is active that is toggled between scans while all receive channels Rx acquire the signal. The RPE-GRE data is used to compute relative $B_1^+$ maps for each Tx channel and respiratory state following [5] by assuming that the sum of $|B_1^+|$ of all Tx channels equals the sum of $|B_1^-|$ of all Rx channels. Since these scans provide only relative estimates of the individual $B_1^+$ maps, a second, RPE-based actual flip angle (AFI) [8, 9] scan is obtained, termed RPE-AFI that is acquired using an efficient $B_1^+$-shim setting $\phi_{eff}$ that maximizes...
the $B_1^+$ field in the anterior section of the heart ($ROI_{\text{heart}}$). This map was used to derive a calibration factor $\lambda$ in $ROI_{\text{heart}}$ that converts the channel-wise relative $B_1^+$ maps to absolute $B_1^+$ for each respiratory state. Data was reconstructed into 5 respiratory motion states using a NUFFT iterative SENSE reconstruction [10, 11]. The method was tested on 11 volunteers on a 7T (Magnetom 7T, Siemens, Germany) and a 32Rx/8Tx channel body coil (MRI.Tools, Berlin, Germany) according to an approved IRB protocol and after providing informed consent. All subjects were asked to breath regularly except for two subjects that have been asked to deliberately breath deeply to test the method. Acquisition parameters are listed in Table 1.

**Results**

Respiration-resolved in-vivo 3D $B_1^+$ maps of the 8 Tx channels in one of the 11 subjects are illustrated in Fig.2 for 3 different orientations. As can be seen, clean estimated $B_1^+$ maps free from motion artefacts are obtained for the magnitude as well as for the phase for all transmit channels.

Fig.3, displays $B_1^+$ maps for 2 orientations and 3 respiratory motion states for Tx channel 3 and 4 demonstrate $B_1^+$ variations of up to $1.0\pm0.5 \ \mu T/\sqrt{\text{kW}}$ ($28\pm18 \ %$) between inhale and exhale across the heart for Tx channel 3.

A head-feet motion of right hemi-diaphragm of $2.8\pm0.6 \ \text{cm}$ was measured across the two deeply breathing subjects.

**Discussion & Conclusion**

In this work we present a novel technique to retrieve channel-wise, motion-resolved absolute 3D $B_1^+$ maps of the human body at 7T. Although the maps inherently contain a proton density bias, similar non-respiration-resolved maps obtained in 2D have been used successfully for cardiac pTx and other applications at 7T. Ideally, a direct merging of RPE-AFI and RPE-GRE is preferable, which was unfeasible because of insufficient $B_1^+$ amplitudes available in the body center. The present method circumvents this limitation by using AFI data only in regions with high $B_1^+$ amplitude for calibration purposes.
fig.1: RPE trajectory with cartesian data acquisition along read out direction $k_x$ on a radial grid in phase encoding plane $k_y$ - $k_z$. Between successive radial lines the angle is increased by the golden angle, k-space data is retrospectively binned into different respiratory motion states with the help of a motion surrogate. Each bin is reconstructed and RPE-GRE data for different motion states can be acquired (a). (b) Workflow of proposed $B_1^+$ mapping approach which uses acquired AFI data with efficient shim setting $\phi_{\text{eff}}$ (1) and calculated magnitude of the sum of estimated channel-wise $B_1^+$ for efficient shim setting (2,3) to calculate calibration factor $\lambda$ in ROI$_{\text{heart}}$ (4) resulting in channel-wise estimated absolute $B_1^+$ maps (5).

fig.2: $B_1^+$ magnitude and phase distribution of 8 Tx channel in 3 different orientations in exhale motion state for one volunteer performing deep breathing.
fig.3: $B_1^+$ magnitude distribution in 2 orientations, obtained from a breath deeply multi-channel acquisition for 2 of the 8 Tx channels in 3 different respiratory motion states; Line plots show $B_1^+$ values across the heart for motion state exhale (red), half-inhaled (gray) and inhale (black), with maximum difference of 1.0 μT/kW (28%) for Tx channel 3.

<table>
<thead>
<tr>
<th>In-vivo</th>
<th>RPE-AFI</th>
<th>RPE-GRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR1 (TR2) [ms]</td>
<td>10 [50]</td>
<td>5</td>
</tr>
<tr>
<td>TE [ms]</td>
<td>2.02</td>
<td>2.02</td>
</tr>
<tr>
<td>TA [s]</td>
<td>12.00</td>
<td>6.80</td>
</tr>
<tr>
<td>oversampling</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>nominal FA [%]</td>
<td>90</td>
<td>20</td>
</tr>
<tr>
<td>reference voltage [V]</td>
<td>170</td>
<td></td>
</tr>
<tr>
<td>FOV [mm²]</td>
<td>250x312-350x350x312-350</td>
<td></td>
</tr>
<tr>
<td>voxel size [mm³]</td>
<td>4x4x4</td>
<td>4x4x4</td>
</tr>
<tr>
<td>BW [kHz]</td>
<td>25.54</td>
<td>25.54</td>
</tr>
<tr>
<td>TS [ms]</td>
<td>480</td>
<td>80</td>
</tr>
</tbody>
</table>

tab.1: Acquisition parameter for RPE-AFI and RPE-GRE with repetition time (TR), echo time (TE), acquisition time (TA), oversampling as factor of phase encoding points additionally acquired compared to a fully sampled cartesian scan with the same field of view (FOV) and voxel size, nominal flip angle (FA), band width (BW) and sampling time (TS) for k-space center points acquired for self-navigation.

Multi-Channel RF Power and Phase Supervision Systems Technology for Thermal Magnetic Resonance: Development, Evaluation and Application

Haopeng Han1, Thomas Wilhelm Eigentler1, Eckhard Grass2,3, Thoralf Niendorf1,4,5

1Berlin Ultrahigh Field Facility (B.U.F.F.), Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany,
2IHP Leibniz-Institut für innovative Mikroelektronik, Frankfurt (Oder), Germany,
3Institute of Computer Science, Humboldt-Universität zu Berlin, Berlin, Germany,
4Experimental and Clinical Research Center (ECRC), a joint cooperation between the Charité Medical Faculty and the Max Delbrück Center for Molecular Medicine, Berlin, Germany, 5MRI.TOOLS GmbH, Berlin, Germany

Introduction
Thermal Magnetic Resonance integrates radio frequency induced thermal intervention and in vivo temperature mapping using MR thermometry to permit supervised targeted in vivo temperature modulation1. To achieve precise energy focal point formation, accurate thermal dose control and safety management, the transmitted RF signals’ amplitude and phase need to be supervised and regulated in real-time. Supervision modules implemented previously2, 3, 4 only monitor the RF signal power level for SAR supervision. Here we propose a multi-channel power and phase supervision module which provides real-time RF power and phase monitoring and regulation.

Methods
Our hardware implements four RF input channels and a reference signal input channel and supports a frequency range of 10MHz to 2.7GHz. Figure 1 shows the block diagram. The reference signal was split into five length- and impedance-matched routes. Each RF input signal was routed to the input A of an AD8302 (Analog Devices, MA, USA) chip. All voltage outputs from the meter chips were fed to a 16-channel, 16-bit analog-to-digital converter AD7616 (Analog Devices). The whole system is managed by a field programmable gate array chip XC7Z020 (Xilinx, CA, USA) which is the core of a system-on-module unit AES-Z7MB-7Z020-SOM-I-G (Avnet, AZ, USA).

A graphical user interface (Figure 2) was developed to monitor the measured RF power and phase information. The phase meters were calibrated with a 4-channel arbitrary waveform generator (M8190A, Keysight, CA, USA). The power meters
were calibrated using a power signal generator (SMGL, R&S, Munich, Germany). The supervision module was integrated with a home-built 32-channel RF signal generator\(^5\), a home-built power amplifier and a directional coupler to form a feedback control loop. Basic PID controllers were implemented to regulate the power amplifier so that its output maintains a stable power level and phase. Ten minute tests were conducted with the control loop open and closed to examine the ability of the supervision module.

Heating experiments were conducted with the control loop either open or closed. A self-grounded bow-tie antenna\(^6\) was applied to an agarose phantom placed into the isocenter of a 7.0T MR scanner (Magnetom, Siemens Healthineers, Erlangen, Germany). The heating paradigm (Fin=400MHz, Pin=42.5dBm at the port of the antenna) was applied for 10 minutes for each experiment. MR thermometry using the PRFS approach (TR=99ms, TE1=2.7ms, TE2=6.7ms, Voxel size=1x1x5mm\(^3\)) was conducted before and after heating.

**Results**

Figure 3 illustrates the supervision module hardware and its operation in RF heating experiments. After calibration, the supervision module demonstrated a power detecting range of 100dBm and a phase detecting range of 180°. Figure 4 highlights the power and phase monitoring/regulating results from two 10-min tests. When the loop was open, there were spikes (>1.5dBm) and substantial deviations over time from the setting point, both having a major impact on the fidelity of the focal energy point in Thermal MR. For the closed-loop experiment, the power level was stabilized around the setting point, with a maximum deviation of 0.5dBm. The signal phases stayed stable for both open- and closed-loop experiments.

Proof-of-principle was demonstrated in RF heating experiments using a phantom setup. Figure 5 shows the MR thermometry results. The applied RF heating paradigm induced maximum temperature increases of 7.0°C and 8.5°C with the control loop open and closed, respectively, in an area close to the antenna. A temperature rise difference of 1.5°C was observed.

**Discussion and Conclusion**

This work shows that the proposed multi-channel RF power and phase supervision module is suitable for Thermal MR. Early applications using a phantom setup at 7.0T demonstrate the module’s feasibility and efficiency for real-time monitoring and regulation of RF power and phase. This provides the technological basis for a Thermal MR hardware system using an integrated RF applicator for anatomical imaging, temperature mapping and RF heating.
Figure 1: System block diagram. There is no difference on the signal propagation delay between the four RF input signals. Two serial peripheral interface (SPI) buses were routed from the FPGA to the conditioning chips (ADL5330, AD5683, Analog Devices, MA, USA; F1956, IDT, CA, USA) for configuration. Customized FPGA logic utilizing direct memory access (DMA) was developed to interface the ADC chip. Digital low-pass filters were also implemented in the FPGA. The data was transferred through the Ethernet port using user datagram protocol (UDP).

Figure 2: Graphical user interface (GUI). The GUI was developed in Haskell and runs on the host computer for monitoring the measurements, and communicates with the supervision module through an Ethernet connection. There is a UDP sever running on the ARM processor inside the FPGA on the supervision module. Users can configure the conditioning chips on the left side of the GUI. The RF power and phase information is displayed on the right of the GUI. Progress bars were used to show the relative relationship between channels.
Figure 3: The supervision module (left). The heating experiment setup (middle): a) water cooling system, b) 8-channel clock distributor (CDA-2990, National Instruments, TX, USA), c) RF signal generator, d) RF power amplifier, e) panel filter, f) directional coupler (BDC0810-50/1500, BONN Elektronik, Holzkirchen, Germany), g) power splitter (ZFSC-2-1W-S+, Mini-Circuits, NY, USA), h) network router, i) supervision module, j) oscilloscope (DPO7254, Tektronix, OR, USA), k) power sensor (NRP18T, R&S, Munich, Germany). The rectangular phantom (178x163x116 mm$^3$) (right).

Figure 4: Power and phase monitoring without (left) and with (right) regulation. The blue curves are power levels measured using the supervision module; the red curves are the power levels measured with the power sensor; the green curves are the recorded signal phases using the supervision module. The RF signal power level at the output of the amplifier was set to 45dBm. The RF signal phase with respect to the reference was set to zero at the beginning and changed to 90° after 150 seconds. Both the supervision module and the power sensor were set to averaging over 1024 samples.
Figure 5: MR thermometry results with the feedback control loop open and closed. A transversal slice in the middle of the phantom aligned with the center of the RF applicator was selected for MR thermometry. The left figure shows the temperature mapping without the supervision module regulating the power amplifier. A maximum temperature rise of 7.0°C was observed. The right figure shows the result with the supervision in the loop. A maximum temperature rise of 8.5°C was observed.

Identifying radiation therapy effect on cardiac function using ultrahigh field 9.4T MRI

El-Sayed Ibrahim¹, Dhiraj Baruah¹, Jason Rubenstein¹, Rachel Schlaak¹, Anne Frei¹, Carmen Bergom¹

¹Medical College of Wisconsin

Introduction

Lung cancer is the leading cause of cancer-related deaths, accounting for about 25% of all cancer deaths. About one-third of lung cancer patients are treated with radiation therapy (RT), where the incidence of cardiac complications in lung cancer patients after RT is as high as 33%. The current paradigm for cardiotoxicity detection and management relies primarily upon the assessment of LV ejection fraction (EF), which may not reflect the underlying advancement of subclinical cardiovascular disease. Therefore, there is a need for identifying new markers capable of early detection of RT-induced cardiotoxicity in lung cancer. In this study, we investigate the capabilities of ultrahigh field MRI for identifying early development of RT-induced subclinical cardiac dysfunction in a small-animal model of lung cancer RT.

Methods

A total of 22 salt-sensitive adult rats were divided into two groups: control (n=7) and RT (n=15). The RT group received image-guided localized whole-heart RT to 24 Gy using 3 equally-weighted fields, and then was divided in two groups that were imaged at 8 weeks post-RT and at 10 weeks post-RT. All rats (control and RT) were imaged when they are around the same age of 20 weeks on a Bruker 9.4T Biospec MRI scanner with 30-cm bore diameter and equipped with 4-element surface coil. The MRI scan included cine and tagging sequences. The cine images were analyzed to measure EF, end-diastolic volume (EDV), and myocardial mass. The tagged images were analyzed to measure myocardial circumferential (Ecc) strain, radial (Err) strain, and longitudinal (Ell) strains.

Results

Global cardiac function was normal in all rats (Figure 1), with increased EF and myocardial mass in the RT rats compared to controls. EF and mass were 67±7%, 78±2, 79±3% and 0.38±0.04g, 0.49±0.04g, 0.56±0.04g in the control, 8-week post-RT, and10-week post-RT rats, respectively. EDV values were slightly smaller in the RT rats. EDV = 0.29±0.02ml, 0.26±0.03ml, and 0.26±0.02ml in the control, 8-week post-RT, and10-week post-RT rats, respectively. Despite normal global function,
strain analysis (Figure 2) showed reduced (absolute) values in the RT rats compared to controls, where changes post-RT in Ecc were more than changes in Err or Ell. Global Ecc = -14.1±2.2%, -10.2±0.7%, and -8.4±0.5%; global Err = 23.3±4.0%, 21.7.2±3.7%, and 20.9.2±6.0%; and global Ell = -15.6±1.8%, -12.3±1.0%, and -12.7±1.9% in the control, 8-week post-RT, and 10-week post-RT rats, respectively. The strain measurements showed larger change between the control and the 8-week post-RT rats compared to the change between the 8-week and 10-week post-RT rats. Err showed wider range of values, especially at the basal and apical sites, compared to Ecc and Ell ranges of values.

Discussion

The most interesting finding in this study is the increased EF post-RT, where EF increased from 67% in the control rats to 78% and 79% in the 8-week and 10-week post-RT rats. This was accompanied by significant ventricular hypertrophy: 29% and 47% corresponding increases in myocardial mass, compared to control values. This reflects the nature of cardiac remodeling to maintain global function in the face of acute injuries from RT. Despite the normal global function, the MRI tagging-generated regional cardiac function parameters revealed deteriorated myocardial contractility. Specifically, myocardial strain showed to be a sensitive marker for detecting subclinical cardiac dysfunction, where different strain components helped characterize the nature of abnormal contractility patterns.

Conclusion

In conclusion, regional cardiac functional imaging and tissue characterization by MRI provides detailed information about myocardial contractility pattern post-RT and allows for early detection of induced cardiotoxicity before global cardiac function is affected.

Figure 1. Cine images showing end-diastolic (ED) and end-systolic (ES) images in both control and RT rats. The images show preserved cardiac function post-RT, along with cardiac remodeling and hypertrophy (solid arrow) compared to controls. Note pleural and pericardial effusions in RT (dotted arrows).
Figure 2. Tagged images with tracked probes at different heart regions in control and RT rats.

Cardiac functional imaging using ultrahigh field 7T MRI

El-Sayed Ibrahim\textsuperscript{1}, Arpinar V Emre\textsuperscript{1}, Muftuler L Tugan\textsuperscript{1}, Nencka Andrew\textsuperscript{1}, Koch Kevin\textsuperscript{1}

\textsuperscript{1}Medical College of Wisconsin

Introduction

Cardiac functional MRI has been established in clinical practice on 1.5T and 3T scanners. Nevertheless, the capabilities of ultra-high field (UHF) MRI have not been fully exploited in cardiac functional imaging. UHF MRI incorporates several advantages as well as some limitations. As signal-to-noise ratio (SNR) is proportional to magnetic field strength, 7T MRI provides \( \sim 2.3 \) times SNR compared to 3T imaging. Enhanced SNR can be traded for improved image quality, higher temporal or spatial resolution, or shorter scan time. In this study, we provide preliminary results of using a multi-channel transceiver modular coil and a dielectric pad towards optimizing MRI cardiac functional imaging at 7T and improving image quality while alleviating artifacts associated with UHF imaging.

Methods

Ten healthy subjects were scanned on a 7T GE MRI scanner using a 32-channel transceiver coil (MRI Tools, GmbH, Berlin, Germany). The modular coil array consists of 8 independent blocks, where each block contains 4 transceiver elements, whose phase settings were optimized based on simulations for a multi-oblique plane mimicking a standard cardiac view. The effect of the imaging flip angle on image quality was assessed in vivo using a gradient-echo cine sequence. Image acquisition was repeated with flip angles ranging from 1° to 120°. Forward simulation was conducted on the resulting images to generate an estimate of the B1 transmission frequency field in the imaged slice using actual imaging flip-angle (AIF) B1 mapping. Both cine and tagged cardiac images were acquired in the scanned subjects Optimal imaging parameters for cine images were: TR=8ms, TE=4ms, flip angle=60°, matrix=256x256, FOV=380x380 mm\(^2\), slice thickness=8mm, acquisition bandwidth=244Hz/pixel, #averages =1, #cardiac phases =25. Images with higher spatial and temporal resolutions were also acquired to assess capabilities of UHF cardiac functional imaging. Optimal imaging parameters for tagged images were similar to cine images, except: TR = 4.9 ms, TE = 2 ms, flip angle = 15°, acquisition bandwidth = 488 Hz/pixel. The effect of using a dielectric pad to improve B1 homogeneity was investigated in six subjects (three normal-weight and three overweight) with the pad placed at different positions close to the imaged region-of-interest.
Results
With proper settings and imaging parameters optimization, we were able to achieve sufficient RF penetration and B1 homogeneity across the heart, which allowed for successfully scanning all subjects with decent image quality. Figure-1 shows results from an in-vivo scan to estimate the B1 field. The figure shows variable signal intensity and regions of signal loss across the acquired slice, where the signal intensity profile changes with the imaging flip angle. Adding a dielectric pad close to the imaged slice could help improve B1 homogeneity. Moving the pad around the thorax area affects the presence and location of the signal nulling regions, where in most cases placing the pad anteriorly improved signal homogeneity. Exploiting the capabilities of UHF imaging allowed for achieving high-spatial resolution of 0.75x0.75x2 mm3, which is ~16 times better than conventional cine imaging at 1.5T (Figure-2). The elevated T1 value of normal myocardium at 7T results in slower magnetization recovery towards equilibrium, and thus helps reduce taglines fading during later phases of the cardiac cycle (Figure-3).

Discussion
Adjusting the imaging flip angle and adding a dielectric pad to the imaged region-of-interest, especially when imaging subjects with small body habitus, could help improve B1 homogeneity and reduce signal nulling resulting from standing-wave effects. In conclusion, through proper scan settings and imaging parameter optimization, 7T cardiac MRI would allow for improved cardiac functional imaging. This is expected to open the door for more cardiac applications of UHF MRI and potential adoption in clinical practice in the near future.

Figure 1. Estimation of the B1 transmission field in a volunteer scan. (a) Gradient-echo short-axis image. (b) B1 scale factor map. (c) Proton density (PD) distribution map. (d) R2 fitting map shows excellent simulation fittings. (e) Example of signal intensity measurements at different flip angles (dots) and the fitting curve inside the heart region (red circle). The results show altered B1 field across the imaged slice.
Figure 2. Improved image resolution achieved at 7T cardiac MRI. High signal-to-noise ratio (SNR) at 7T allows for achieving high spatial resolution with 16-fold reduction in voxel size (a) compared to standard clinical resolution in (b). Small voxel size illustrates anatomical details, such as the trabeculations and right ventricle details (arrows), that are not clearly visible at standard clinical resolution. Alternatively, high SNR can be traded for high temporal resolution (~20ms) imaging at conventional spatial resolution as in (b).

Figure 3. Strain analysis throughout the whole cardiac cycle at 7T CMR. A series of tagged images acquired at different timepoints of a mid-ventricular short-axis slice throughout a 1200ms cardiac cycle, showing tagging persistence until the last timeframe (arrows), which allows for measuring strain throughout end-diastole, which is not feasible at low magnetic field strength where the tagging pattern fades before the end of the cardiac cycle.

Rapid Mapping of Radiofrequency Coil Fields with Computer Vision

Egor Kretov\textsuperscript{1}, Kaixuan Zhao\textsuperscript{1}, Charles Grassin\textsuperscript{2}, Thoralf Niendorf\textsuperscript{1}

\textsuperscript{1}Berlin Ultrahigh Field Facility (B.U.F.F.), Max Delbruck Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany,
\textsuperscript{2}Independent Researcher, Paris, France

Introduction

One of the most common techniques of characterization and assessment of MRI coils is near-RF field mapping. This method reveals possible problems even before the RF coil will be placed inside an MR scanner and it provides information in a non-invasive manner without the need to disassemble the RF coil. However, field mapping procedures require expensive high-precision positioning equipment, which is not always available to researchers. While there are numerous attempts to build such a system using robots\textsuperscript{1} or 3d printers\textsuperscript{2}, we propose an alternative cost-effective approach\textsuperscript{3} based on computer vision which facilitates tracking of a field probe position with a standard webcam.

Material & Methods

The core elements of our experimental setup are demonstrated in Fig.1. We employed a webcam with standard specifications (Trust Trino HD) at 640p resolution mode and a frame rate of 30 fps installed on a stand. The Webcam detects a QR-code with the use of the OpenCV\textsuperscript{4} library. The QR-code marker was attached to the symmetrical RF magnetic field probe\textsuperscript{5} allowing the webcam to track its position within the image frame. The RF magnetic field probe was connected to software-defined radio (SDR) receiver USB dongle which measures RF noise level. In that way, the measurement system is passive and doesn't contain any RF sources. The correlation between the noise level and magnetic field value allows us to use this quantity for the H-field estimation. For each new frame obtained from the camera, the root-mean-square magnitude of the noise level is calculated and stored as a value for the RF field map. As a proof-of-principle, we used a square-shaped resonant loop tuned to 114 MHz and the anterior section of a 4-channel torso RF coil array customized for 7.0 T MRI (f=297.5 MHz). The positioning of the probe was done (Fig.2(b)) manually and (Fig.2(c)) by using a low-cost robotic arm with two degrees of freedom.
Results
The results of field mapping performed by a human and a robotic arm for the resonant loop element are shown in Fig.2. The scan plane position was placed about 30 mm above the surface of the measured loop. The measurements display a higher RF noise level value in the center of the loop since its working as an efficient magnetic antenna at the resonant frequency. Figure 3 demonstrates a manually measured H-field distribution for the 7.0T torso RF coil array. For this purpose, the field probe was placed right on a top of an RF coil cover. Mapping the arrays fields with computer vision revealed the geometry and number of internal RF elements.

Discussion & Conclusion
During the scanning procedure, the human hand cannot hold a strict position for a long time, which significantly affects the measurement results. This is the main limitation of the method if it is applied for manual field mapping. Yet, this can be offset with software improvements. Another issue dealt with the necessity of direct visual contact between the camera and the field probe and proper light conditions during the measurement. Despite this constraint, our results demonstrated the suitability of our cost-effective approach for rapid RF coil field mapping and RF coil characterization. Additionally, it can serve as an accuracy enhancement feedback for low-cost positioning systems like a robotic arm used here.

Figure 1. Experimental setup. Field probe connected to the USB SDR receiver.
Figure 2. a) single resonant loop as a test object, manual (b) and robotized (c) measurements of RF noise level (dBm) which correlated with the magnetic field near the loop.

Figure 3. a) anterior section of a 7.0T torso RF coil array with indefinite internal structure b) manual field measurements reveal two RF coils elements and their geometry c) RF coil array with the housing removed.


Towards carotid arteries characterization: Time-resolved 3D Flow-MRF implementation at 7T

Lisa Leroi, Sebastian Flassbeck, Sebastian Schmitter

1Physikalisch-Technische Bundesansalt (PTB), Braunschweig and Berlin, Germany,
2Medical Physics in Radiology, German Cancer Research Center (DKFZ), Heidelberg, Germany,
3Department of Radiology, Center for Biomedical Imaging, New York University School of Medicine, New York, NY, USA,
4Center for Advanced Imaging Innovation and Research, New York University School of Medicine, New York, NY, USA

Introduction
Atherosclerotic plaque composition is a key factor to determine the risk of future cardiovascular events. Therefore, recovering simultaneously blood flow in vessels and relaxation times of surrounding tissues may lead to improved diagnostics and follow-ups. To that end, Magnetic Resonance Fingerprinting (MRF) has been adapted to enable time-resolved blood flow quantification within vessels for 2D acquisitions. Recently, a 3D implementation was proposed at 3T in the carotids. In this work, we demonstrate the feasibility of 3D Flow-MRF at 7T to retrieve time-resolved 3D blood velocity vector fields as well as M0, T1 and T2 values of static tissues.

Materials & Methods
MRF acquisitions
A stack-of-stars FISP sequence was implemented with bipolar flow-encoding gradients in three directions, as illustrated in Fig.1. Here, pseudo-random first gradient moments (m₁) between +/-20mT/m.ms were applied (Fig.1c) to quantify velocity in three directions simultaneously with M₀, T₁ and T₂.

Scanning was performed at 7T (Magnetom, Siemens, Germany), using a 1Tx/8Rx neck-coil (MRI.Tools GmbH, Berlin, Germany). Data was acquired in transverse orientation with following parameters: 300x300mm² FOV, 0.4x0.4mm² voxel size, 8 slices of 1mm thickness, TR/TE=13.38ms/7.06ms, BW 420Hz/px. Undersampled k-spaces were retrieved using a radial multi-shot approach with 1000 timeframes acquired per shot. 5 shots rotated by golden angles (137.51°) were acquired per partition. An 8s delay was inserted between shots for thermal equilibrium recovery, leading to a total acquisition time of 14min38s.
The presented 3D Flow-MRF sequence was used to scan a healthy volunteer (female 34y.o.), in accordance with local ethics committee and written informed consent.

**Quantitative extraction**
The quantitative analysis was performed using MATLAB (The Mathworks, Natick, USA). Voxel-wise estimates for M0, T1 and T2 were determined using a low-rank alternating direction method of multipliers\(^7\) approach. The range of simulated values for T1 and T2, and B1\(^+\) were [300:5:3000]ms, [10:2:180]ms and [0.2:0.03:1.5], respectively. The reconstruction included coil sensitivity maps calculated with the ESPRiT method\(^8\).

To recover temporal 3D velocity fields, the acquisition was synchronized with ECG signal. Projections from the same cardiac phase were used jointly to assess time-resolved velocities as described by Flasbeck et al.\(^4\) with a temporal resolution of 50.2ms.

**Results**
Figure 2a displays magnitude overlaid with the through-slice velocity. Temporal velocities assessed in the different slices are reported in Figure 2b. The velocity pattern corresponds to the expected velocity shape in the carotids. An ROI placed closely within the sternocleidomastoid muscle reflects T\(_1\) and T\(_2\) estimates of 1459±138 and 31±16ms over 8 slices. Associated T\(_1\) and T\(_2\) maps are depicted in Figure 2c,d.

Due to limited scan time, no reference velocity or relaxometric measurement was performed in this first acquisition. However, T\(_1\) and T\(_2\) literature obtained at 3T are listed in Table 1. Retrieved values at 7T are in the range of expected values at such B\(_0\)-field strength, considering that T\(_1\) increases with B\(_0\) field strength, and T\(_2\) is less sensitive to this effect\(^9\).

**Discussion**
These results demonstrate the feasibility of 3D Flow-MRF to quantify 3D time-resolved velocity vector fields in the carotid bifurcation and 3D relaxometric maps of the surrounding static tissues at 7T. Compared to the previous 3T acquisition\(^5\), the resolution was doubled (voxel size reduced 8-fold), while TA was shortened by 40%. A large standard deviation was observed for relaxometric values, which might be explained by the strong flip angle heterogeneity encountered at 7T. Moreover, flow encoding in combination with high resolution yields long TE, which may yield increased sensitivity to Eddy currents and diffusion. Larger slice coverage could be achieved in future work using this framework, which will be particularly beneficial for plaque characterization at 7T.

Table 1: Mean T<sub>1</sub> and T<sub>2</sub> values retrieved in the sternocleidomastoid muscle (neighbouring the carotids arteries) over 8 slices. The muscle is depicted in by a white region-of-interest in Figure 2.

<table>
<thead>
<tr>
<th>Method</th>
<th>T&lt;sub&gt;1&lt;/sub&gt; (ms)</th>
<th>T&lt;sub&gt;2&lt;/sub&gt; (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow-MRF (7T)</td>
<td>1459±138</td>
<td>31±16</td>
</tr>
<tr>
<td>Flow-MRF&lt;sup&gt;+&lt;/sup&gt; (3T)</td>
<td>1169±68</td>
<td>41±12</td>
</tr>
<tr>
<td>Literature&lt;sup&gt;+&lt;/sup&gt; (3T)</td>
<td>1137±110</td>
<td>34±12</td>
</tr>
</tbody>
</table>

Figure 1: Flow-MRF sequence diagram used in this work: A slice-selective adiabatic pulse is first applied, followed by a stack-of-stars FISP sequence with varying FA<sup>10</sup> and pseudo-random m<sub>f</sub> flow-encoding gradients pattern. Figure adapted from Flassbeck et al.<sup>4</sup>.

Figure 2: In vivo results for the magnitude (sum of all MRF timeframes) overlaid with the retrieved Z-velocity map at t=301.2ms after the ECG-trigger is displayed in (A). The corresponding flow over all the slices in a 10pixels-ROI in the right carotid artery is shown in (B). Associated Flow-MRF T<sub>1</sub> and T<sub>2</sub> maps are displayed in (C) and (D), where the ROI used for the sternocleidomastoid muscle is contoured in white. A certain T<sub>2</sub> heterogeneity is observed, due to FA heterogeneity at 7T.
Kinetic Oscillatory Stimulation in the Nasal Cavity Elicits Functional Brain Activation in the Limbic System of the Brain

Xia Li¹, Masaki Fukugawa², Tie-Qiang Li³

¹Key Laboratory of Electromagnetic Wave Information Technology and Metrology of Zhejiang Province, College of Information Engineering, China Jiliang University, Hangzhou, 310018 China,

²Division of Cerebral Integration, School of Life Science, National Institute for Physiological Sciences, The Graduate University for Advanced Studies, Japan,

³Department of Clinical Science, Intervention and Technology, Karolinska Institutet, S-17177 Stockholm, Sweden

Introduction

Brain stimulation in general and non-invasive brain stimulation in particular has become an attractive treatment for a number of disorders, such as Parkinson's disease and epilepsy. Taking advantage of the rich innervations and inter-nerve communications in the nasal cavity, we have recently devised a non-invasive nerve stimulation method for exploring its efficacy in treating chronic inflammatory diseases (1-3). This kinetic oscillation stimulation (KOS) method provides an alternative approach to stimulate autonomic nerve system (ANS) without the need of invasive procedure to implant a pacemaker and electrode. Small-scale clinical trials [1,2] have demonstrated that KOS in nasal cavity is effective for relieving symptoms for migraine and rhinitis. For better understanding of the mechanisms underlying this treatment efficacy, we used a 7T MRI system equipped with simultaneous multiple slice (SMS) imaging techniques to study the brain activation during a robust block design of KOS.

Methods

Eight adult male volunteers (age=38±12) were recruited. The fMRI measurements were conducted using a 7T MAGNETOM Terra system (Siemens, Erlangen) equipped with a 32-channel phased-array detector for brain imaging. A single-shot 2D GRE-EPI pulse sequence was used for data acquisition with the following acquisition parameters: 85 slices of 1.6 mm thick, TR/TE=1000/22.2 ms, FOV=208 mm, matrix size=130x130, flip angle=45°, GRAPPA acceleration factor=2 and SMS acceleration factor=5. Each fMRI session lasted 26min corresponding to 1560 dynamic timeframes.
We conducted at least one session of BOLD fMRI per participant based on a block design. The stimulation paradigm consisted of 7 epochs of inactive resting periods interleaved with 6 blocks of active stimulations. The block duration was 2 minutes. The KOS device was acquired from Choodate Medical AB (https://www.chordate.com). The original operation interface and power supplier were stripped and replace with a relay controlled by a microprocessor that was programmed to generate the block paradigm described above. A clear polyethylene plastic tube (ID=8mm) was used to extend the nasal catheter through the penetration panel. The catheter was inserted into the nasal cavity during the entire session. For active stimulation, the catheter was inflated at the pressure of 100 mbar with an oscillation frequency of 68 Hz.

The fMRI data underwent a standard preprocessing pipeline that was performed with AFNI and FSL programs in a bash wrapper[3]. The procedure included the following main steps: Temporal de-spiking, six-parameter rigid body image registration for motion correction, spatial normalization to the standard MNI template using a 12-parameter affine transformation, re-sampled to isotropic resolution using a Gaussian kernel (FWHM=2), nuisance signal removal by voxel-wise regression using 16 regressors based on the motion correction parameters, average signal of the ventricles, average signal of the core white matter and the 1st order derivatives of the above regressors, baseline trend removal up to the 5th order polynomial, low-pass filtering at 0.08Hz.

Individual activation map was generated by Pearson's correlation calculation using the block activation paradigm as the reference function. The group activation results were assessed by one-sampled t-test and a threshold at t>9.87 (p<0.05 interconnected voxels).

Results
Figure 1 depicts the group activation maps. The locations of the significant clusters and their corresponding amplitudes of the BOLD responses are detailed in Table 1. As shown, the activated brain regions are mainly located in the limbic system including the prefrontal cortex, anterior cingulate cortex, caudate, insula, hypothalamus, and parahippocampal gyrus. As illustrated by the average time course, both positive and negative BOLD responses were observed. Most interestingly, positive response in the dorsal nucleus of vagus nerve was also detected.

Discussion
Previous KOS studies of clinical patients indicate that the KOS has a positive impact on the functioning of ANS possibly by restoring its homeostasis through short-term regulation from the central nervous system (CNS) control network [3]. The findings from the current study demonstrate that KOS in nasal cavity is indeed as-
associated with robust functional responses in the limbic system and dorsal nucleus of vagus nerve. This implicates that KOS treatment may has similar impact as the electric stimulation of vagus nerve [4,5]. It explains the anti-inflammatory efficacy of KOS treatment for chronic inflammatory diseases.

**Conclusion**

Taking advantage of the high contrast-to-noise ratio for BOLD fMRI at 7T and the acquisition efficiency of SMS techniques, we were able to detect robust brain activations in response to KOS in nasal cavity. The results demonstrate that KOS is effective to induce regulatory response of the CNS control network to restore the neurophysiological homeostasis in the ANS.

![Brain regions with significant BOLD signal change assessed with one-sampled t-test at p3.2 and the minimum cluster size > 100 voxels](image)

**Fig. 1** Brain regions with significant BOLD signal change assessed with one-sampled t-test at p3.2 and the minimum cluster size > 100 voxels. The inflated displays depict the cortical activations (top row), whereas the cross-sectional displays demonstrate the activation at the dorsal nucleus of vagus nerve. The crossing green lines indicate the location of the cross sections. The underlay is a T1-weighted MNI template of 0.25mm resolution. The colour bar indicates z-score of the t-test.

SAR distribution for the Transceiver Array for Human Cardiac MRI at 7T: Variations due to Displacement on Thorax.

Terekhov Maxim1, Elabyad Ibrahim1, Theresa Reiter1, Schreiber Laura1

1Department of Cardiovascular Imaging, Comprehensive Heart Failure Center, University Hospital Wuerzburg, Wuerzburg, Germany

Motivation

MRI at ultra-high field (UHF) is a rising modality to improve the signal-to-noise ratio (SNR) compared to clinical MRI. Different types of RF coils including, multichannel Tx (mTX) loops and dipole antenna arrays are used for mitigating these inhomogeneities performed by adjusting phases of the driving voltage for the individual elements ($B_1^+$-shimming). One of the critical factors which must be accounted by using mTX arrays is energy deposition in the human body characterized by a specific absorption rate (SAR). The individual human thorax anatomy varies in shape and dimensions influencing the position of the array allocation which may lead to deviation of the SAR from the precomputed values. The aim of the study was to simulate the variation of SAR for 8Tx/16Rx cardiac array prototype caused array displacement and using different $B_1^+$-shimming setting.

Materials and Methods

Both the anterior and posterior parts of the new cardiac array prototype are composed of eight loop elements. For SAR safety and $B_1^+$-field optimization, EM-simulations were performed using CST-Software. The simulations were performed using Duke and Ella human voxel models. The final total number of mesh cells was 40.9 million. The local averaged 10g SAR values were evaluated in CST-MWS using IEEE/IEC-62704-1 standard averaging method. In this paper, we analyzed the variation of the SAR which comes from two sources:

1) Adjustment of phase of individual elements needed to provide homogeneous $B_1^+$-profile. Four phase vectors $\{\Phi\}_1 - \{\Phi\}_3$ preliminary pre-computed to provide optimized $B_1^+$-profile in Duke and Ella models were considered.

2) Variation of SAR due to different positioning of the anterior part of the array on the human subject thorax. The anterior array position was shifted from the central allocation on 50 mm to the right, left, head, foot, diagonal directions (e.g ‘left-head’) and tilted on 10 degrees from the horizontal allocation.

From the 3D SAR maps simulated for each of the phase vectors, the primary maximal intensity projection (MIP) maps within the slabs of 20mm distance from the
anterior part were computed (Figure 1b). Then the secondary SAR MIP positions were computed using a stack of the above determined MIPs for each of 3 phase vectors (Figure 1c). The relative variation of SAR MIP positions with respect to the reference position was analyzed to determine the worst-case situation.

**Results**

Fig. 1(a) demonstrates a sketch of the multichannel 8Tx/16Rx coil array prototype and with default position on the human subject thorax and shifted on 50mm to the right respectively. Fig. 1(b) shows the coronal slabs used to evaluate 10g SAR for MIP computation and the scheme of computing anterior MIP position SAR from 3 phase vector. Fig 1d demonstrates a variation of MIP SAR due to the change of the position of the array on the thorax normalized to the maximal value at a centered position.

**Discussion and Conclusion**

Maximal variation of 10g SAR due to the changes of the position of the anterior array part was observed for horizontal (left-right) shift being of 37%. However, a more significant increase of SAR in the new hot spot with an increase up to 50% from the initial position was observed at the same time at a non-displaced posterior array. Usually, without such an analysis the conservative safety margins for the worst-case SAR (and therefore k-factor) use to be applied (typically factor 2 from the modeled value). Knowing the variation originated from the array displacement allows for using it for setting less conservative safety limits for the maximal driving voltage, thus, providing more flexibility for the array usage.

**Acknowledgment**

Financial support was obtained from the German Ministry of Education and Research (BMBF) under grants: 01EO1004 & 01EO1504.
Figure 1(a) A sketch of the novel multichannel 8Tx/16Rx coil array prototype. Blue contours mark the default centered position on the human subject thorax, white contours denote shifted position. Panels (b) shows slabs used for computation of anterior and posterior SAR MIPs which in turn was used to calculate MIP through array positions (panel (c)) at each analyzed phase vector.

Panel (d) demonstrates variation of MIP$_{\text{position}}$ SAR maps for different phased vectors array at both anterior and posterior parts. The values are normalized to the MIP SAR computed for the reference position “zero shift” position. The maximal increase of SAR on 37% at anterior and up to 50% at posterior array.
Postmortem human brain 9.4T ultra-high field magnetic resonance imaging: the UTAP study.

Stijn Michielse¹, Jackson Boonstra¹, Alard Roebroeck², Yasin Temel¹,³, Ali Jahanshahi¹

¹School for Mental Health and Neuroscience, Department of Neurosurgery, Maastricht University Medical Center, the Netherlands,
²Department of Cognitive Neuroscience, Faculty of Psychology & Neuroscience, Maastricht University, the Netherlands,
³Maastricht University Medical Center, Department of Neurosurgery, the Netherlands

Magnetic resonance imaging (MRI) is a non-invasive medical imaging modality used to visualize and quantify anatomical and microstructural characteristics of the human brain. The emerging field of ultra-high field MRI (UHF-MRI) provides the opportunity to investigate human brains at a higher resolution and with higher signal-to-noise ratios compared to the more widely available 1.5 and 3T scanners. Scanning postmortem tissue additionally allows for greatly increased scan times and less artifacts leading to improvements in image quality. Typical postmortem scanning methodologies involve vacuum sealing tissue in plastic bags to remove surface and ventricular air bubbles from the sample, but this method is liable to leaks, border susceptibilities (artifacts from air-tissue boundaries), and reproducibility concerns.

The UTAP-study provides a better understanding of Parkinson’s Disease (PD) at the sub-millimeter level with UHF-MRI. This will be done with the use of a dedicated brain jar to obtain T2* quantitative and Diffusion Weighted Imaging (DWI) data. A representation of the DWI outcomes by means of white matter tracts will be provided as well as the T2* maps. A further translation towards the cellular level will be made by conducting histological staining on sections of postmortem tissue and link this with MRI findings. The UTAP-study will ultimately help to better understand PD. Therefor PD subgroups of rigid and tremor dominant will be compared against healthy controls.

An image of the dedicated brain jar is provided as attachment to the abstract. It can hold two brain hemispheres and can be filled with proton-free liquid via the valves.
The dedicated brain jar can hold two hemispheres, has a spacer in between and two valves to add liquid. It basically mimics the human skull and fits nicely in a standard head coil.
Introduction

Pediatric patients with neuroinflammatory disease such as acute disseminated encephalomyelitis (ADEM) are at risk of impaired brain growth, with profound long-term neuropsychiatric consequences. ADEM patients have reduced brain volume and increased ventricle volume (VV) compared to age-matched controls.1 In this study we examined VV changes in ADEM, investigating longitudinal MRI scans of pediatric ADEM patients, to distinguish temporary VV expansions (reflecting acute disease activity) from persistent ones (reflecting brain atrophy).

Methods

Scans from patients with confirmed ADEM were obtained from 7 neurology clinics in Germany and Austria: n=14; 8/14 female; mean age=7.2 years (range 0.7-17.6). Brain VV was obtained from routine native T1-weighted scans (using FreeSurfer v6.04 for scans with 1mm-isotropic resolution; for lower resolution scans using FMRIB Software Library FSL v5.05 with manual correction. The same method was used for all scans of the same patient, to allow for consistent intra-individual comparisons.

Discussion

Brain VV of ADEM patients showed a heterogeneous mixture of expansion and contraction, which generally stabilized over the long-term follow-up period (Fig1). The majority of patients (11/14) showed VV contractions ≥10%; 3/14 patients showed exclusively expansion of VV (including one patient with >300% increase), although these three patients had only one follow-up scan. VV changes occurred
in different age groups, and indicate that VV did not merely increase monotonically over time (Fig 2). Images from a representative patient show VV expanded beyond the initial level by the second timepoint, and subsequently contracted, reaching a value lower than baseline after 1y follow-up (Fig 3).

The expectation for pediatric patients is that VV increases over time, with normal brain growth. In fact, the majority of these patients showed decreases in VV, either directly following the initial clinical event, or following subsequent VV expansion – often stabilizing during long-term follow-up. This suggests that, in some patients, the VV expansion was not a consequence of irreversible brain atrophy, but rather likely reflected some process associated with acute disease. In one notable case, the VV expanded during the course of the investigation, but did not return to baseline levels during the follow-up period, suggesting neurodegeneration and permanent brain damage. Monitoring VV could be a crucial marker to differentiate between transient processes and permanent damage, and plan treatment strategies accordingly.

Fig.1: VV in ADEM patients change dynamically over time. VV is depicted as percent of baseline. In the acute phase, there was a complex mixture of VV contraction, expansion, and oscillation, which had generally stabilized in the long-term phase.

Fig.2: VV changes plotted with respect to patient age. Dynamic VV changes occur across all ages in the cohort. Images from the patient marked in red are shown in Fig 3.
Fig. 3: Images from a representative patient show that VV had increased by d21 compared to baseline, and decreased by d143. At 1y follow-up VV was lower than at baseline, suggesting that the initial VV represented an expansion over the physiological volume.

Deep CEST MR Fingerprinting at 7T Reveals Tumor Apoptotic Response to Oncolytic Virotherapy In Vivo

Or Perlman1, Hirotaka Ito2, Kai Herz3,4, Naoyuki Shono2, Hiroshi Nakashima2, Moritz Zaiss3,5, E. Antonio Chiocca2, Ouri Cohen6, Matthew S. Rosen1,7, Christian T. Farrar7

1Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA, USA,
2Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, United States,
3Magnetic Resonance Center, Max Planck Institute for Biological Cybernetics, Tübingen, Germany,
4IMPRS for Cognitive and Systems Neuroscience, University of Tübingen, Tübingen, Germany,
5Department of Neuroradiology, University Clinic Erlangen, Erlangen, Germany,
6Memorial Sloan Kettering Cancer Center, New York, USA
7Department of Physics, Harvard University, Cambridge, MA, USA

Introduction
Oncolytic virotherapy (OV) is a promising treatment for high mortality cancers.1 Non-invasive monitoring of OV is essential for optimizing the clinical outcome and providing an improved understanding of the interactions between the virus and its tumor-host. Chemical exchange saturation transfer (CEST) MRI is a molecular imaging technique that may shed new light on OV, as it is capable of detecting protein concentration and pH changes. However, clinical translation of CEST methods has been hindered by the qualitative nature of the image contrast and the long image acquisition times.

Objective
The goal of this work was to develop a deep-learning-based CEST MR fingerprinting (MRF) method for quantitative and rapid multi-pool imaging of OV treatment response. The approach was evaluated in mice undergoing virotherapy treatment and translated to clinical scanners.

Methods
CEST-MRF Two SE-EPI CEST-MRF acquisition protocols (105s each) were employed sequentially, designed for obtaining MT and amide proton exchange-rate and volume-fraction maps. Both protocols varied the saturation power, but employed different saturation offsets (first: 6-14 ppm, second: 3.5 ppm). T1, T2, and B0 maps
were acquired using variable repetition-time, multi-echo spin-echo, and water saturation shift referencing, respectively.

**CEST-MRF Dictionary Generation** The CEST-MRF signal trajectories for 184,800 and 70,224,000 multi-pool parameter combinations were synthesized for the two protocols using a numerical solution of the Bloch-McConnell equations.

**Deep Reconstruction Networks** To avoid the exceedingly long dictionary matching-time required for conventional dot-product MRF and to improve the multi-parameter reconstruction ability, image reconstruction was performed using a series of two Deep RecOnstruction NEtworks (DRONEs), trained on the synthesized data. The pixel-wise signal trajectories from the MT specific MRF schedule were input to the first DRONE, together with the water T1, T2 and B0 values. The two MT exchange parameter outputs, together with the water pool and B0 parameters were then input into the second DRONE, together with the pixel-wise signal trajectories from the amide-pool MRF schedule.

**In Vivo Imaging** U87 tumors were implanted in the brain of 16 mice (25% used as control). The mice were imaged at 8-11 days after implantation, using a 7T preclinical MRI (Bruker, Germany). Next, a herpes simplex-derived oncolytic virus, NG34, was inoculated, and the mice were imaged 48hrs and 72hrs later. For clinical translation, the continuous wave saturation pulse was replaced by a train of spin-lock saturation pulses and the read-out was done using GRE-EPI. A healthy volunteer was recruited and imaged at 3T (Siemens Healthineers, Germany).

**Results**

Before virus inoculation, the semi-solid and amide proton concentrations were both decreased in the tumor, consistent with increased edema decreasing the protein concentrations. The tumor amide proton exchange-rate was increased, indicative of increased intracellular pH. Following OV, the core of the tumor presented significantly lower amide proton concentration and exchange-rate compared to the tumor rim and the contralateral region. Both effects are indicative of apoptosis as it is known to inhibit protein synthesis and decrease cytosolic pH. At baseline, control mice demonstrated similar MT and amide effects as OV-treated mice, however, no apoptotic process was evident. The preclinical MRI findings were in good agreement with the histology and immunohistochemistry findings (HSV antibodies, H&E, Caspase-3, Coomassie). The normal human subject parameter maps yielded MT volume fraction and exchange-rate values in good agreement with the literature. The amide proton exchange-rate was in good agreement with previous water exchange spectroscopy-based measurements. The total reconstruction time for the 4 molecular maps using the neural-network scheme was 94 ms, compared to 2.3 hrs for conventional dot-product reconstruction.
Conclusions
The deep CEST-MRF technique successfully and rapidly quantified pH and molecular concentration changes, potentially serving as important biomarkers for OV-induced apoptosis.

Introduction
Siponimod is a trifluorinated anti-inflammatory drug indicated for multiple sclerosis (1) that could be potentially tracked in pharmacokinetic studies by fluorine-19 (\(^{19}\text{F}\)) MR techniques (2) in order to support therapeutic monitoring. In this study, we investigated the \(^{19}\text{F}\) MR properties of siponimod and its dependency on environmental factors for achieving best SNR efficiency in vivo.

Methods
Siponimod (Sigma) was dissolved in DMSO and human serum to model an in vivo situation (2 ml syringes), with measurements at room temperature (20 °C; RT) and at 37 °C. All MR experiments were performed on a 9.4 T MR scanner (Bruker Biospec) using a dual-tunable \(^{19}\text{F}/^{1}\text{H}\) mouse head RF coil (3). Global single pulse MR spectroscopy was used for \(^{19}\text{F}\) signal detection and measuring T\(_1\). A CPMG sequence was used for measuring T\(_2\). Also, T\(_1\) mapping was performed using a saturation based RARE technique and T\(_2\) mapping using a multi-slice multi-echo technique. We optimized RARE, FLASH, UTE (4) and bSSFP (5) sequences to compare SNR efficiencies (SNR/\(\sqrt{\text{time}}\)). Image processing and spectral analysis were performed in MATLAB R2018a and ImageJ (6).

Results
In DMSO Siponimod revealed a single peak spectrum with chemical shifts of -55.47 ppm at RT and -55.36 ppm at 37 °C (Fig.1A).

At 20 °C, T\(_1\) was 680 ms (spectroscopy; Fig. 1B), matching T\(_1\) obtained with RAREVTR (T\(_1\)=638 ms). At 37 °C, T\(_1\) was 928 ms (spectroscopy; Fig.1B), matching the RAREVTR acquired T\(_1\) of 907 ms.
T₂ obtained with CPMG yielded 320 ms (Fig. 1C) and with MSME 219 ms. At 37 °C, T₂ values increased to 547 ms using CPMG (Fig. 1C) and 328 ms for MSME, resulting in an increase of 9.9 ms/°C.

In the presence of serum, siponimod showed a single peak spectrum with chemical shifts of -59.06 ppm at 20°C, and -58.85 ppm at 37 °C (Fig. 1D).

Both T₁ and T₂ of siponimod were shortened in serum. T₁ was shortened to 326 ms at 20 °C and 380 ms at 37 °C (Fig. 1E). T₂ was substantially reduced to 7 ms at 20 °C, and 17 ms at 37 °C (Fig. 1F), resulting in a relative T₁ shortening of 52% (59% at 37 °C) and T₂ shortening of 98% (97% at 37 °C).

The SNR efficiency measured in DMSO revealed the highest value for the optimized RARE sequence (100%), followed by bSSFP (67%), UTE (20%), and FLASH (11%). At 37 °C, the SNR efficiency for RARE was highest (90%), followed by bSSFP (56%), UTE (14%) and FLASH (7%)(Fig. 2A).

SNR efficiencies in serum at RT revealed a superiority of UTE (100%) over RARE (18%), bSSFP (25%) and FLASH (19%) at 20°C. UTE was still most efficient (86%) at 37 °C, compared to RARE (48%), bSSFP (51%) and FLASH (35%) (Fig. 2B).

**Discussion**

The characterization of siponimod revealed an influence of temperature and environment on its ¹⁹F MR properties. (7). RARE and bSSFP techniques performed best in DMSO but were outperformed by UTE in serum. T₂ is also expected to be shortened in vivo. Therefore, sequence and parameter selection for achieving maximally high SNRs in vivo need to be adapted according to the compound of interest and its environment.

Technological developments such as cryogenically-cooled coils (8), higher field strengths (9), and compressed sensing will aid in further lowering detection limits. The goal of ¹⁹F MR detection is to enable ¹⁹F MR imaging of low drug concentrations in different tissues for non-invasively informing clinical studies and aiding patient-tailored drug dose modifications.

**Acknowledgements**

This study is funded by Novartis as well as the Deutsche Forschungsgemeinschaft to S.W. (DFG-WA2804)
Figure 1. Characterisation of the 19F MR properties of siponimod dissolved in DMSO and serum, at RT (blue) and at 37°C (red), A. 19F MR single peak spectrum of siponimod in DMSO at -55ppm, B. T1 relaxation of siponimod in DMSO determined by 19F MRS using different TRs, C. T2 relaxation of siponimod in DMSO using a CPMG sequence, D. 19F MR single peak spectrum of siponimod in serum at -59ppm E. T1 relaxation of siponimod in serum determined by 19F MRS using different TRs, F. T2 relaxation of siponimod in serum using a CPMG sequence.

Figure 2. Comparison of the SNR efficiencies of different optimized sequences for imaging siponimod dissolved in DMSO and in human serum, at RT (blue) and at 37°C (red), A. Comparison of the SNR efficiencies of different optimized sequences in DMSO (normalized to RARE at RT), B. Comparison of the SNR efficiencies of different optimized sequences in serum (normalized to UTE at RT).

Implementation, validation and comparison of three $B_1$ inhomogeneity correction methods for RARE MRI with transceive surface RF probes

Paula Ramos Delgado$^{1,2}$, Andre Kuehne$^3$, Jason M. Millward$^1$, Joao S. Periquito$^{1,2}$, Andreas Pohlmann$^1$, Sonia Waiczies$^1$, Thoralf Niendorf$^{1,2,3}$

$^1$Berlin Ultrahigh Field Facility (B.U.F.F), Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany,
$^2$Experimental and Clinical Research Center, a joint cooperation between the Charité Medical Faculty and the Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany,
$^3$MRI.TOOLS GmbH, Berlin, Germany

Introduction

Surface RF coils and SNR-efficient imaging techniques such as RARE are used in (pre)clinical MRI to enhance SNR$^1$. The use of transceive (TxRx) surface RF coils is rapidly growing due to cryogenically-cooled RF technology (CRP)$^2$ and ultrahigh-field MRI. However, transceive surface RF coils show variation in the excitation field, impairing quantification and $T_1$ contrast. Therefore, there is an increasing need for correction of both excitation ($B_1^+$) field and coil sensitivity ($B_1^-$)$^1$ inhomogeneity. Here, we implemented, validated and compared 3 retrospective $B_1$ correction methods tailored for RARE$^3$ used in combination with TxRx surface RF coils.

Methods

Sample preparation and MR measurements

Experiments were performed on a Bruker 9.4T animal MR scanner (Bruker BioSpin, Germany). A healthy SJL/J mouse was scanned in compliance with local animal welfare guidelines. Four phantoms (50-mL flasks) were filled with two $^1$H-atom concentrations (100% water, 1:1 water/deuterium oxide) and two $T_1$ values (490 ms, 1525 ms; adding gadolinium).

RARE images (TE/TR=5.1/1000ms, ETL=8, centric encoding, resolution=(273×273)$\mu$m$^2$, 3 axial slices, 30min) were acquired with a CRP (*in vivo*, using flipback) and a TxRx surface loop RF coil (flasks, with/without flipback). Reference images and $T_1$ maps (RARE: 8 TRs, 200-9000 ms) were acquired with a volume RF coil.

Correction methods

Three correction methods were implemented (Fig. 1A). A sensitivity ($B_1^-$ correction) method$^1$ multiplying by the inverse of a normalized RARE image (same param-
eters) of a homogeneous phantom (15-mL tube, $T_1$: 280 ms); a model-based $B_1$ correction method computing a $B_1^+$ map\(^4\)\(^-\)\(^5\) and a $B_1^-$ map\(^6\)\(^-\)\(^7\) using the same phantom and the surface RF coils. SI models (RARE same parameters, FA: 5°-160°, NMR tubes with $T_1$: 170-2600 ms) were acquired using a volume RF coil as described\(^8\).

The hybrid $B_1$ correction was performed using a model-based $B_1^+$ correction followed by a sensitivity $B_1^-$ correction. A reference image was acquired (same parameters) using a volume resonator.

Performance assessment
Pre- and post-corrected images (Fig. 2A-E) were compared and their image homogeneity was evaluated on the in vivo image using a central SI profile perpendicular to the RF coil surface (Fig. 2F). ROIs were placed in cortex and left/right basal ganglia/thalamus and the percentage integral uniformity (PIU)\(^9\) was calculated (Fig. 2G).

The 50mL-flasks were used for SI quantification and $T_1$ contrast evaluation. To evaluate SI quantification, pairs of phantoms with different water content (same $T_1$ value) were used. Pairs of phantoms with different $T_1$ values (same water content) were used to assess the $T_1$ contrast performance (Fig. 1B). Five ROIs were drawn on corrected, uncorrected and reference images (Fig. 1C). For each of the flask image pairs, mean SI ratios were calculated using all ROI combinations. Mean errors and mean standard deviations were computed: $\text{Ratio error} = \frac{\text{abs}(\text{mean(SI}_{\text{reference}}) - \text{mean(SI}_{\text{corrected}}))/(\text{mean(SI}_{\text{reference}}) * 100\%}{\text{)}$. A non-parametric one-way ANOVA Friedman repeated measures test followed by Dunn’s test was performed (all corrections compared to original, p

Results
All 3 correction methods show a substantial improvement in image homogeneity (Fig. 2), SI quantification (Fig. 3A-B) and $T_1$ contrast (from mean errors>40% in the original images to in vivo images showed a percentage image uniformity comparable to that of reference images (PIU>80% corrected vs >87% reference, Fig. 2G). These results indicate 17 mm as the maximum distance from the RF coil up until which $B_1$ correction is feasible.

Discussion
While we demonstrated the correction methods in conventional $^1$H imaging, these results open the way for $T_1$ measurements and X-nuclei quantification using surface TxRx surface RF coils and MR imaging techniques for which no analytical SI equation exists.

Acknowledgements
Deutsche Forschungsgemeinschaft WA2804 (S.W.) and PO1869 (A.P.)
Fig1. A Pipeline description of the 3 retrospective B₁ correction methods. B Experimental setup used for SI quantification and T₁ contrast validation. C ROI placement of 5 randomly-selected locations used for performance assessment.

Fig2. A-E B₁ correction for *in vivo* CRP MR images of a mouse head. F Normalized signal intensity profiles perpendicular to the RF coil surface. G Percentage image uniformity (PIU) of anatomical
Fig3. Relative quantification and contrast errors for RARE with/without flipback (high T₁ and 100% H2O shown) for the original images and those corrected with each of the three B₁ correction methods. Whiskers represent the 5-95 percentiles.

References
1. Axel L, Hayes C. Arch Int Physiol Biochim 1985;93(5):11-18
First \textit{in vivo} $^{19}$F signal quantification in a mouse model of brain inflammation using a $^{19}$F cryogenic transceive surface RF probe and RARE MRI

Paula Ramos Delgado$^{1,2}$, Christian Prinz$^{1,2}$, Jason M. Millward$^1$, Helmar Waiczies$^3$, Ludger Starke$^1$, João S. Periquito$^{1,2}$, Laura Boehmert$^{1,2}$, Andreas Pohlmann$^1$, Thoralf Niendorf$^{1,2,3}$, Sonia Waiczies$^1$

$^1$Berlin Ultrahigh Field Facility (B.U.F.F), Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany, $^2$Experimental and Clinical Research Center, a joint cooperation between the Charité Medical Faculty and the Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany, $^3$MRI.TOOLS GmbH, Berlin, Germany

Introduction

Fluorine ($^{19}$F) MRI supports \textit{in vivo} quantification of exogenous fluorinated compounds\textsuperscript{1}. However, the low SNR inherent to fluorine ($^{19}$F) MRI necessitates sensitivity-boosting methods. Surface RF coils\textsuperscript{2} and SNR-efficient imaging techniques (e.g. RARE\textsuperscript{3}) are used in (pre)clinical MRI to enhance SNR. Cryogenically-cooled transceive surface RF antennas (CRP) provide substantial SNR gains compared with room temperature RF coils\textsuperscript{4}. However, the $B_1$-field inhomogeneity of transceive surface CRP hampers quantification\textsuperscript{4}. Quadrature CRP technologies are only offered as single-tuned for some X-nuclei (e.g. $^{19}$F), complicating registration on anatomical images\textsuperscript{4}. Previously, we showed a $B_1$ correction method\textsuperscript{5} using $^1$H-MRI in which we modeled RARE’s signal intensity (SI) as a function of flip angle (FA) and $T_1$. Here we have established a workflow to facilitate $^{19}$F quantification for $^{19}$F-CRP and RARE imaging to monitor and quantify inflammation in the experimental autoimmune encephalomyelitis (EAE) mouse model.

Methods

Sample preparation

Experiments were performed on a Bruker 9.4T animal MR scanner (Bruker BioSpin, Germany). Four capillary tubes filled with perfluoro-15-crown-5-ether nanoparticles (NP) (10/10/25/50mM) were embedded in a 15mL-tube. EAE was induced in \textit{n}=4 SJL/J mice and 10μM of NP was administered i.v. for 12 days\textsuperscript{6}. Mice were euthanized, fixed and the skull embedded in 15mL-tubes (\textit{n}=3).
MR measurements

$T_1$ values of two NP preparations (20/300mM in 2% agarose) and ex vivo samples were computed using non-localized spectroscopy (block pulse: 10 TRs, 250-10000ms). $T_1$ values in the brain after NP administration were achieved using localized spectroscopy (PRESS) ex vivo (12 TRs, 250-15000ms) and in vivo (n=2, 8 TRs, 413-13000ms). All $T_1$ measurements were performed with a 35mm-volume resonator. Anatomical images (FLASH: TE/TR=3.72/120ms, resolution=(260×260)$\mu$m², 5 axial slices, 14min) were acquired with a 72mm-volume RF coil placed around the center tube of the $^{19}$F-CRP using an in-house built system to keep positioning consistent between measurements (Fig.1B). $^{19}$F MRI (RARE: TE/TR=5.08/1000ms, ETL=32, centric encoding, flipback, same geometry; 30/50min phantom/mouse) was acquired with the $^{19}$F-CRP and a volume RF coil. A flexible reference containing 300mM NP in 2% agarose was placed on top of phantoms/mouse head for reference power adjustments and quantification.

$B_1$ correction

The acquisition and post-processing pipeline is described in Fig.1A. $B_1$ maps of the $^{19}$F-CRP were computed using a homogeneous phantom (15-mL tube, $T_1$; 280ms) and the double angle method$^{7-8}$ ($B_1^+$) and the low FA approximation$^{9-10}$ ($B_1^-$). A SI model was calculated from RARE scans (same parameters, FA=5º-165º, NMR tubes with $T_1$=190-2870ms) using a volume RF coil$^5$. The corrected images were calculated as described$^5$ and overlaid on the anatomical images.

Results

$T_1$ values for PFCE-NPs agreed with published values$^{9-10}$ (Fig.2A). In vivo $T_1$ values (Fig.2B-C) differed largely from ex vivo values (Fig.2D). We corrected $^{19}$F-CRP images of a phantom (Fig.3B-D) and in vivo (Fig.3E-J). Errors in corrected capillary phantom images (Fig.3C) were reduced when compared to original images (Fig.3B) (errors relative to volume RF reference coil, Fig.3D). Using the reference band, we calculated concentration maps for two exemplary in vivo slices (Fig.3G-J).

Conclusion

Here we show the first in vivo $^{19}$F images of the inflamed EAE mouse brain using a $^{19}$F-CRP in combination with RARE. We also report the first in vivo $T_1$ relaxation times obtained for $^{19}$F NP in the EAE brain under physiological conditions. Finally, we computed concentration maps and established a workflow that enables $^{19}$F and anatomical imaging with a single-tuned CRP. These results provide the foundation for future studies using a $^{19}$F-CRP to quantify inflammation or $^{19}$F compounds in in vivo longitudinal studies.
Acknowledgements
Deutsche Forschungsgemeinschaft WA2804 (S.W.) and PO1869 (A.P.)

Fig1. Workflow description. AMR measurements needed for B₁ correction, B anatomical and ¹⁹F MR imaging setups, C ¹⁹F image post-processing (SNR thresholding and B₁ correction) and overlay with anatomy.

Fig2. T₁ curves of A 20mM and 300mM NPs in 2% agarose at 20°C with non-localized spectroscopy, B ex vivo with non-localized spectroscopy and C with PRESS (n=3, each a different color), and D in vivo with PRESS (n=2, each a different color).
Fig3. Phantom: A scheme, B-C original and corrected $^{19}$F-CRP images, D reference image. SI ratios were calculated for pairs of tubes. *In vivo*: E-F/H-I original and corrected images and G-J concentration maps. The dashed lines show the RF coil position.
In-vivo repeatability of SPECIAL based single-voxel spectroscopy using different adiabatic inversion pulses

Layla Tabea Riemann¹, Christoph Stefan Aigner¹, Ralf Mekle², Sebastian Schmitter¹, Bernd Ittermann¹, Ariane Fillmer¹

¹Physikalisch-Technische Bundesanstalt (PTB), Braunschweig und Berlin, Germany,
²Center for Stroke Research Berlin, Charité-Universitätsmedizin, Berlin, Germany

Introduction
For single-voxel spectroscopy, the use of short TEs is favorable, since effects due to T₂ relaxation and J-coupling can be minimized¹. One way to achieve this is to use the SPin ECho, full Intensity Acquired Localized (SPECIAL)², ³ which consists of a slice-selective 90° and a 180° pulse in perpendicular slices, generating a spin echo in the intersecting column. Localization in the third dimensions achieved by a slice selective adiabatic inversion pulse, which is applied before excitation in alternating measurements.

To assure reproducible and comparable results at UHF, the influences of B₀ and B₁ inhomogeneities should be minimized⁴. This is particularly important for the adiabatic inversion pulse used in SPECIAL, since it is switched on and off in alternating scans, which are subsequently subtracted from each other to achieve full localization.

The aim of this work is to determine the test-retest repeatability of neurochemical profiles using three different adiabatic inversion pulses with the SPECIAL sequence at 7T, namely the originally implemented hyperbolic secant (HS)⁵ pulse, a gradient-offset independent adiabaticity (GOIA)⁶ pulse, and a wideband, uniform rate, smooth truncation (WURST)⁷ pulse.

Methods
A SPECIAL sequence with HS, GOIA and WURST pulses was used to obtain spectra from the posterior cingulate cortex (PCC) of six healthy volunteers, using a 7T Magnetom Scanner (Siemens Healthineers, Erlangen, Germany) together with a 1Tx/32Rx-channel head coil (Nova Medical Inc., Wilmington, MA, USA). Figure1 shows the implemented SPECIAL sequence diagram (Fig. 1a), the scan scheme (Fig. 1b) and an example voxel positioning (Fig. 1c). Table1a and b summarize the pulse parameters of the adiabatic pulses and sequence parameters, respectively. Each volunteer was scanned four times, twice on the first day, with repeated measurements including repositioning, and twice one week after with repeated mea-
measurements without repositioning to assess the intrA-, intEr- and Week-Between-Session Repeatability (ASR, ESR and WBSR, respectively). Bland-Altman plots were generated for each pulse and repetition scenario over all spectral points. Coefficients of variance (CVs) were determined for all valid metabolite results for each volunteer over the four sessions and then averaged over all subjects.

**Results**

Figure 2 shows the acquired spectra of subject 2 (Fig. 2a) and quantitative Bland-Altman plots for ASR, ESR and WBSR (Fig. 2b) using adiabatic HS, GOIA and WURST inversion pulses. Whereas the spectral quality of all three pulses is high and comparable, Bland-Altman plots indicate more accurate results using adiabatic GOIA and WURST pulses. For same-day repetitions, GOIA and WURST perform similarly and both appear to have improved performance compared to HS. With one week between repetitions, all three pulses perform on a similar level. Expectedly, repeatability is best, the shorter the time in between measurements, i.e. ASR ≤ ESR ≤ WBSR.

For all RF pulses and all selected metabolites, similar concentrations and inter-subject variance were measured (Fig. 3a). Both Concentrations as well as CRLBs are comparable with literature values from the same region. The CRLBs are highest for the HS pulse and lowest, i.e. best, for the GOIA pulse (Fig. 3b). In Fig. 3c, the HS pulse shows the highest mean CV across most metabolites, while GOIA shows the lowest for Gln, Glu, GSH, Ins, NAA, NAAG, tCho, tCr and Tau. The CVs for HS are up to 2.5 times higher than the ones for GOIA. CVs of the measurements using a WURST pulse appear to be comparable to the performance of GOIA measurements, with a potential tendency to be slightly higher for some metabolites.

**Discussion and Conclusion**

The overall variation between intra-subject measurements is highest for the HS pulse, indicating that both GOIA and WURST allow for a more robust metabolite quantification than the originally used HS pulse in the SPECIAL sequence.

It was demonstrated that the GOIA pulse provides the lowest variance throughout all reproducibility scenarios.
Fig. 1: a) Pulse sequence diagram of SPECIAL with the HS (blue), GOIA (orange) and WURST (green) pulse is shown. b) Scan scheme (exemplary): On the first day in the first session (1_1) SPECIAL with HS, GOIA and WURST was measured. After repositioning the volunteer (1_2), the sequences were measured in the same order as in 1_1. On the second day (i.e. one week later) in the first session (2_1), HS und GOIA were measured twice without any repositioning. In the second session on day two (2_2), the SPECIAL application using the WURST pulse was measured twice without repositioning. c) Exemplary voxel position in the posterior cingulate cortex (PCC) of a volunteer.

Tab. 1: a) Adiabatic inversion pulse parameters: The red lines indicate the parameters that were fixed. All parameters were obtained by an in-house built MATLAB based Bloch simulation tool. The power was derived by the Integral of the absolute B1(t). b) Parameters of the SPECIAL sequence for in-vivo measurements.

Fig. 2: a) Measured spectra between 0.8 and 4.2 ppm for all pulses from session 1_1 for subject 2 are shown. The obtained spectra were postprocessed using in-house written MATLAB software and quantified with LCMedel⁹. Metabolite concentrations were corrected for relaxation and individual tissue composition using SPM12¹⁰. b) Bland-Altman plots for HS, GOIA, WURST (left to right) for ASR (top), ESR (middle) and WBSR (bottom) to visualize the test-retest reproducibility. The black points represent each volunteer. On the x-axis the integral of the absolute of the difference for each spectral point is shown. The y-axis represents the integral of the averaged spectrum. The dashed red line indicates the inter-subject mean and the dashed gray lines show the confidence interval.
Fig. 3: Inter-subject metabolite quantification plots for all pulses are shown. a) The averaged absolute metabolite concentrations calculated using the unsuppressed water signal, b) averaged CRLBs and c) the inter-subject CVs for all subjects and every repetition are depicted. The CVs were first calculated for each subject over the four sessions and then averaged over all volunteers. The concentrations and the CRLBs were averaged over every subject and each session. Results with Cramér-Rao lower bounds (CRLBs) exceeding 20% were discarded.

Towards Non-Invasive Imaging of MS Disease-Modifying Drugs

Fatima Sherazi1, Ludger Starke1, Christian Prinz1, Jason Millward1, Paula Ramos Delgado1, Mariya Aravina1, Thoralf Niendorf1,2,3, Sonia Waiczies1

1Berlin Ultrahigh Field Facility (B.U.F.F.), Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany,
2Experimental and Clinical Research Center, a joint cooperation between the Charité Medical Faculty and the Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany,
3MRI TOOLS GmbH, Berlin, Germany

Introduction

Siponimod is an anti-inflammatory drug indicated to treat secondary progressive multiple sclerosis (SPMS) [1]. Siponimod contains a trifluoromethyl (CF₃) functional group in its molecular structure. The addition of fluorine-19 (¹⁹F) atoms typically improves pharmacological activity [2]. It also enables detection by ¹⁹F MR techniques, which would be invaluable for non-invasive pharmacokinetic studies and therapeutic monitoring [2]. We previously reported that siponimod suffers from short T₂ under in vivo like conditions and we identified UTE as an SNR efficient MR pulse sequence for this compound [3]. In the present study we performed in vivo MRI of siponimod in the healthy mouse stomach using an optimized UTE sequence and studied the drug in ex vivo samples.

Methods

All MR experiments were performed on a 9.4T MR scanner (Bruker Biospec) using a cryogenic ¹⁹F transceive quadrature RF probe (¹⁹F CRP) [4]. Global single pulse MR spectroscopy (TR=1s) was used to detect the ¹⁹F signal and make frequency adjustments for in vivo and ex vivo measurements. We optimized a UTE sequence according to its T₁ value (slice thickness=6mm, averages (NA)=20, Ernst flip angle=28°).

Healthy B6 mice (n=3) were first anaesthetized (100mg/kg ketamine; 7.5mg/kg xylazine) and subsequently given a single dose of 400μl of 10mg/ml siponimod (Sigma) in carboxymethyl cellulose, delivered orally through an intubation tube. Anatomical images of the mouse (m) were acquired using a ¹H volume coil and RARE (ETL=4, TR=1.2s). Following oral application, global spectroscopy acquisitions (n=11 for m1, n=20 for m2, n=10 for m3) were interleaved with UTE scans (n=10 for m1, n=19 for m2, n=9 for m3).
After the *in vivo* experiment, mice were sacrificed and perfused with 4% PFA in PBS. *Ex vivo* phantoms were prepared in 5ml tubes (liver, brain; filled with PFA) and 1.5ml tubes (mouse serum). Global $^{19}$F spectroscopy was performed on each phantom (NA=2700, TR=1s). Acquisition (acq.) and excitation (exc.) bandwidths were adjusted for liver (acq.BW=50kHz, exc.BW=50kHz), serum (acq.BW=50kHz, exc.BW=30kHz) and brain (acq.BW=30kHz, exc.BW=50kHz) phantoms. In brain phantom from m2, acq.BW=50kHz.

We used MATLAB R2018a and ImageJ [5] for image processing and spectral analysis.

**Results**

$^{19}$F MRI of siponimod revealed a clearly localized fluorine signal in the mouse stomach stable over time when using UTE (*Fig. 1*). In mouse 1 a distribution of $^{19}$F signal could be seen over time. Quantification of the $^{19}$F MR spectroscopy signal at -59.4ppm indicated an initial increase that stabilized over time (*Fig. 2*). In some cases (mouse 1 and 3) a drop in signal intensity was observed after 2 hours. *Ex vivo* investigations of serum phantoms revealed a single peak at -85.5ppm (*Fig. 3A*). This peak was accompanied by a larger single peak at -59.9ppm in the liver phantom (*Fig. 3B*). In brain phantoms, particularly for mouse 1, a major peak was measured at a chemical shift of -77.2ppm (*Fig. 3C*).

**Discussion**

We imaged the MS drug siponimod *in vivo* using UTE $^{19}$F MRI. A lack of *in vivo* $^{19}$F signal distribution over time could be an indication of reduced absorption due to anaesthesia effects on gastrointestinal physiology. *Ex vivo* studies on liver, brain and serum validated the presence of siponimod in pharmacological relevant organs. Stark variations in signal intensities and chemical shifts suggest variations in drug uptake, changes in the chemical environment and metabolite formation. These results set the path for non-invasive drug localization in pharmacologically relevant organs including the brain. In situations of low SNR, localized single-voxel spectroscopy might be a compromise instead of $^{19}$F MRI. Sensitivity limitations in $^{19}$F MRI might be overcome by implementing measures such as compressed sensing [6] and higher field strengths [7].
Figure 1: *In vivo* monitoring of the fluorinated MS drug siponimod over time. $^{19}$F signal (red) progression after oral administration over the course of the experiment for mouse 1 and 2. Each image corresponds to a 30-minute UTE measurement and shows $^{19}$F-signal from the same coronal slice.

Figure 2: Spectroscopic quantification of the $^{19}$F-MR signal intensity for all three mice.

Figure 3: Spectroscopic measurements of *ex vivo* phantoms. (A) For all three animals, the spectrum of ex vivo serum shows a major peak with highest signal intensity for mouse 2, followed by mouse 1 and mouse 3. (B) Liver phantoms all show a major single peak spectrum along with an additional peak. The highest signal intensity was measured for mouse 3, whereas mouse 2 showed the lowest signal intensity. (C) Ex vivo brain phantoms all reveal a single peak spectrum. Here, mouse 1 shows highest signal intensity whereas similar intensities are demonstrated by mouse 2 and 3.


Serum and urine NMR metabolomics study in acute spinal cord injury (ASCI): A possible recovery pathfinder as indicated in a prospective case-control study

Alka Singh¹, RN Srivastava¹, Lavini Raj¹, Raja Roy²

¹Department of Orthopaedic Surgery, King George’s Medical University, Lucknow, India,
²Centre of Bio-Medical Research (CBMR), Lucknow, India

Introduction
A prospective case-control study based on serum and urine biofluids with 1H NMR spectroscopic metabolic profiling was carried out to evaluate metabolites perturbations and its relationship with recovery and to see the role of stem cells in facilitating neurological recovery.

Methodology
A total of 135 subjects were enrolled in the study; 65 ASCI subjects, divided into 2 groups. Fixation alone (FA, n=34). Fixation with stem cell therapy (FST, n=31). Seventy healthy subjects (HCs) were enrolled. Serum and urine samples were collected at admission, 6 weeks, 3, and after 6 months. NMR data of serum and urine samples were quantified and subjected to multivariate analysis using supervised OSC-PCA followed by OPLS-DA was performed in the full study. This finding was further validated in the VIP scores.

Result
An OSC-PCA and OPLS-DA model was created for investigating the role of metabolites in differentiation amid all ASCI subjects against healthy control at baseline as well as at the final follow-up. The 3D scattered score plots represented the shifting of more ASCI subjects towards healthy control in the final follow-up, which is an indicator of better prognosis.

Conclusions
Serum and urine NMR spectroscopy reveals certain metabolites perturbations having a clear correlation with pattern of recovery in treated ASCI subject. Stem cells treatment group had a comparatively effective recovery.
1H NMR based serum and urine bio-fluids metabolic profile correlates with the neurological recovery in treated acute spinal cord injury (ASCI) subjects: A prospective case control study

Alka Singh¹, RN Srivastava¹, Raja Roy², Lavini Raj¹

¹Department of Orthopaedic Surgery, King George's Medical University, Nabiullah Road, Daliganj, Lucknow, U.P., India,
²Centre of Biomedical Research, formerly Centre of Biomedical Magnetic Resonance (CBMR), Sanjay Gandhi Postgraduate Institute of Medical Sciences Campus, Rae Bareli Road, Lucknow, India

Objective
A prospective case control study with serum and urine 1H NMR spectroscopic metabolic profiling was carried out to evaluate metabolites perturbations and its relationship with recovery and to see role of stem cells in facilitating neurological recovery.

Methodology
A total of 135 subjects were enrolled in the study; 65 ASCI subjects, divided into 2 groups. Fixation alone (FA, n= 34). Fixation with stem cells therapy (FST, n= 31). Seventy healthy subjects (HCs) were enrolled. Serum and urine samples were collected at admission (baseline), 6th week, 3rd month and after 6th month (follow-up). NMR data of serum and urine sample were quantified and subjected to multivariate analysis using supervised OSC-PCA followed by OPLS-DA was performed in the full study. This finding was further validated in the VIP scores.

Results
Gender analysis revealed that out of 135 participants were male. The age group of 18 to 30 years was found most prone to SCI. Fall from height and road traffic accidents were the two most common modes of injuries. Most common injured
segments of thoraco-lumbar spine were T10-L2 levels. On AIS grading, highly significant improvement was observed in FST group in comparison to FA group. In FST group, 61.29% subjects remained in AIS A and the percentage improvements to AIS B, C and D were 12.90%, 16.13% and 9.68% respectively, whereas in FA group these values were 67.65%, 17.64%, 11.76% and 2.94% respectively. At the 6th month follow-up, improvements in sensory and motor scores were observed in both cases groups (FST and FA), but FST group showed better results. In the spectra of urine biofluid, forty three metabolites were identified and assigned and twenty-eight metabolites were identified and assigned in serum biofluid. Predominantly amino acids and ketone bodies played vital role in the differentiation of groups. An OSC-PCA and OPLS-DA model was created for investigating the role of metabolites in differentiation amid all ASCI subjects against healthy control at baseline as well as at final follow-up. Statistical comparison was validated by OSC-PCA as well as OPLS-DA methods and multivariate data analysis resulted in to R2 value of 0.91 and 0.81 and Q2 value of 0.81 and 0.67 respectively. The generated model was robust enough for evaluating the differentiation among the present data set. The 3D OSC-PCA model generated resulted to the total explained variance of 50.21% and 50.67% respectively. The 3D scattered score plots represented the shifting of more ASCI subjects towards healthy control in the final follow-up, which is suggestive of improved health status and an indicator of better prognosis in ASCI subjects.

**Conclusions**

Serum and urine NMR spectroscopy reveals certain metabolites perturbations having clear correlation with pattern of recovery in treated ASCI subject. Stem cells treatment group had comparatively effective recovery.
Characterization of fluorinated pesticides using fluorine ($^{19}$F) MR methods

Salina Skenderi¹, Jason M. Millward¹, Ludger Starke¹, Paula Ramos Delgado¹, Fatima Sherazi¹, Christian Prinz¹, Joao dos Santos Periquito¹, Thoralf Niendorf¹,²,³, Sonia Waiczies¹

¹Berlin Ultrahigh Field Facility (B.U.F.F.), Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany,
²MRI TOOLS GmbH, Berlin, Germany,
³Experimental and Clinical Research Center, a joint cooperation between the Charité Medical Faculty and the Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

Introduction

The use of fluorinated agrochemicals has increased tremendously in recent years [1]. Fluorination changes the physicochemical properties of compounds, for example an increased lipophilicity is expected [2], implying increased bioaccumulation. An in vivo non-invasive imaging method would be beneficial to study the extent of bioaccumulation. Fluorine ($^{19}$F) MRI is a method that could be used to detect fluorinated compounds in vivo [2, 3]. Since there is a lack of endogenous fluorine in living organisms, there is no background signal and thus fluorinated compounds can be detected with high specificity [2]. In order to achieve the best SNR efficiency for in vivo $^{19}$F MRI the best acquisition method and scan parameters need to be determined following a thorough $^{19}$F MR characterization. Here we studied the $^{19}$F MR properties of chlorfenapyr, fipronil, fluopicolide and trifloxystrobin. These fluorinated pesticides have been frequently notified by the European Commission (EC) [4] to seriously exceed maximum residue levels (MRL) allowed in food products (Figure 1).

Methods

Experiments were performed on a 9.4T animal MR scanner (Bruker BioSpin, Ettlingen, Germany) using a dual-tunable $^{19}$F/$^1$H mouse head RF coil. Chlorfenapyr, fipronil, fluopicolide, trifloxystrobin (all from Sigma Aldrich) were dissolved in MetOH (Roth 99.9%, HPLC grade) and transferred into 2ml-syringe phantoms. The concentrations were 11.3 mg/ml, 25.5 mg/ml, 26 mg/ml, 85 mg/ml, respectively. All concentrations correspond to $\sim$4x10$^{20}$ $^{19}$F atoms in 2ml. $^{19}$F signal was detected with single pulse MR spectroscopy (TR=1000ms). $T_1$ was determined using RARE
with variable repetition times (RAREVTR) and T₂ using a multi-slice/multi-echo sequence (MSME) (Table 1). Parameters according to specific RF pulse sequence (RARE: TR, TE, ETL), (FLASH: FA) and (bSSFP: FA) were optimized to compare their SNR efficiencies (SNR/√time). FOV=28mmx28mm, matrix size=96x96 and slice thickness=5mm were kept constant. Data analysis was performed using MATLAB R2018a and ImageJ.

Results
The spectra and chemical shifts of all four pesticides are shown in Figure 2. Chlorfenapyr had the longest T₁ relaxation time (1762 ms), followed by fluopicolide (1599 ms), trifloxystrobin (1395 ms) and fipronil (1156 ms left peak, 1025 ms right peak) (Figure 3). Fluopicolide had the shortest T₂ (667 ms), followed by fipronil (739 ms and 717 ms for left peak and right peak, respectively), chlorfenapyr (843 ms) and trifloxystrobin (934 ms). The SNR efficiency analysis revealed the highest SNR for the optimized RARE sequence, followed by bSSFP and FLASH (Figure 4).

Conclusion and Discussion
Here we characterized the ¹⁹F MR properties (chemical shift, T₁, T₂) of four fluorinated pesticides to optimize RARE, FLASH and bSSFP pulse sequence methods. A comparison in SNR efficiency revealed the superiority of the RARE method to detect and image fluorinated pesticides at the conditions that these compounds were examined. These results will be valuable for future studies in which the distribution of fluorinated pesticides will be evaluated in vivo.

Figure 1 | Total number of serious alerts accumulated since 2012 for fluorinated pesticides in contaminated foods (4). Fipronil has the most alerts from all fluorinated pesticides.

Figure 2 | The spectra of the fluorinated pesticides and their associated chemical shifts. Chlorfenapyr shows a chemical shift of -54.46 ppm, fipronil shows two duplet peaks (right peak shown above at -74.63 ppm and left peak at -63.19 ppm), fluopicolide at -62.24 ppm, trifloxystrobin at -62.64 ppm.
Figure 3 | Relaxation times of examined fluorinated pesticides. (A) $T_1$ values from RAREVTR maps. (B) $T_2$ values from MSME maps. Each pesticide is colored in an individual color.

Figure 4 | SNR efficiency comparison between different MRI acquisition methods (bSSFP, FLASH and RARE). SNR efficiency is defined as SNR/√time. The acquisition time was four minutes. Each pesticide is colored in an individual color.

Table 1 | Parameters used for RAREVTR and MSME methods to estimate the $T_1$ and $T_2$ values of the fluorinated pesticides. The echo train length (ETL) was constantly 4 and the image matrix 64x64.

Performance of Compressed Sensing for detecting low SNR $^{19}$F MRI in Experimental Autoimmune Encephalomyelitis using Prospective Undersampling

Ludger Starke$^1$, Joao Periquito$^1$, Christian Prinz$^1$, Thoralf Niendorf$^{1,2}$, Sonia Waiczies$^1$

$^1$Berlin Ultrahigh Field Facility (B.U.F.F.), Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany,

$^2$Experimental and Clinical Research Center, a joint cooperation between the Charité Medical Faculty and the Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

Introduction

Fluorine-19 ($^{19}$F) MRI is an established tool for tracking inflammatory cells in vivo, yet low signal-to-noise ratios (SNR) remain a major challenge, especially when studying inflammation at high resolution in the brain. Compressed sensing (CS) increases $^{19}$F MRI sensitivity,$^{1,2}$ but false positives are observed in reconstructions at low SNR.$^2$ This work assesses the performance of CS to detect in vivo $^{19}$F signals with MRI.

Methods

Animal experiments were carried out in accordance with local guidelines (LaGeSo). EAE was induced in 4 SJL/J mice. Perfluoro-15-crown-5-ether rich nanoparticles were administered daily starting on day 5 following EAE induction.$^3$ In vivo data was acquired on day 12 to 14.

MR experiments were performed on a 9.4T animal scanner (Bruker BioSpin, Ettlingen, Germany). A purpose-built 2D-RARE CS protocol was employed for $^{19}$F MRI: TR=1020ms, TE=5.2ms, ETL=40, FOV=(20×20)mm$^3$, (128×128) matrix, 3.2mm slice thickness, 6 slices. 296, 592 and 1184 averages were acquired with no, 2-fold and 4-fold undersampling (TA=20min). Fully sampled measurements were repeated 4 times as reference (80min). A pure noise scan was acquired to determine the noise level.

CS reconstructions of undersampled data were computed using the accelerated alternating direction method of multipliers$^4$ with equally weighted isotropic total variation and image l$_1$-norm regularization. The discrepancy principle was used to determine the optimal regularization strength.
The SNR threshold for reference scans was 3.5 and outliers were defined as features with Undersampling patterns, reconstructions and analyses were programmed in MATLAB 2018a (The MathWorks, USA).

**Results**

Compared to conventional Fourier reconstructions, the number of detected $^{19}$F signal voxels was greatly enhanced by CS with 2-fold undersampling (Fig.1A and B). Slight blurring was only present at the edges of true positive features. The number of true positives was further increased with 4-fold undersampling, but so was the blurring effect. CS showed superior detection at all signal levels (Fig.2A). FDRs in CS reconstructions on the other hand were elevated at low signal levels, especially for 4-fold undersampling (Fig.2B). The RMSD from the reference was consistently reduced by CS (Fig.3A) and the effect size was independent of the undersampling factor. Similar reduction of the RMSD was measured when considering the full images, signal voxels only or background voxels only. When varying detection thresholds, CS offered superior results for conditions allowing overall FDRs >15%, with 2-fold undersampling consistently performing better than 4-fold undersampling (Fig.3B).

**Discussion / Conclusion**

These results confirm that CS with moderate undersampling improves detection performance and can be reliably applied to in vivo $^{19}$F MRI. CS outperformed conventional reconstructions, particularly at low SNR regimes. Conventional reconstructions can be advantageous for high SNR conditions if a very conservative analysis is desired. However, the absence of random false features in contrast to conventional reconstructions makes CS more reliable at low SNR, in addition to the improved sensitivity. Thus, CS holds promise particularly for those $^{19}$F MRI applications involving the detection of small quantities of $^{19}$F, such as studies investigating the distribution of CNS-acting drugs in the brain.
Exemplary slices comparing Fourier and CS reconstructions (TA=20min) with the reference (Fourier reconstruction, TA=80min). $\alpha$ denotes the factor of undersampling. The second line shows true positives, false negatives, and false positives.

(A) TPRs computed for different levels of the reference signal using a sliding window approach. The window had a width of $0.5\sigma_F$. (B) FDRs computed for different levels of the measured signal using the same method.

(A) Root-mean-square deviation (RMSD) from the reference. Plotted is the mean and standard deviation over the 4 datasets. (B) Modified ROC curve showing false discovery rates vs. true positive rates computed over all reconstructions.


Point spread function mapping eliminates image distortion from renal echo-planar imaging: preliminary results from a 9.4T animal MR system

Kaixuan Zhao¹,², João Periquito¹, Zhongbiao Xu², Min-Chi Ku¹, Andreas Pohlmann¹, Thoralf Niendorf¹

¹Berlin Ultrahigh Field Facility (B.U.F.F.), Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany,
²Southern Medical University, School of Biomedical Engineering

Introduction
Echo-planar Imaging (EPI) allows fast acquisition beneficial for quantitative renal MRI, e.g. arterial spin labeling (ASL) (1). B0 field inhomogeneities and susceptibility effects render renal EPI prone to image distortion and signal non-uniformities. These adverse effects constitute a challenge for the accuracy and reproducibility of quantitative renal MRI. Point spread function (PSF) mapping offers a distortion correction method that introduces an additional encoding gradient to obtain PSF along the distortion direction, e.g. mainly in phase encoding direction (2,3). In the present study, we examined the feasibility of PSF mapping for correction of image distortion in EPI based ASL of the in vivo rat kidney at 9.4 T.

Methods & Material

Theory
The pulse sequence used for PSF mapping is shown in Figure 1A. Because the phase encoding direction suffers severe distortion due to limited bandwidth compared to frequency encoding direction, the PSF encoding gradient is applied in phase encoding direction. Inverse Fourier transform was performed on the acquired 3-dimensional k-space data, and PSF reconstructed data that integrate the image domain data along the non-distorted direction (PSF-FE), the distorted direction (PF-FE), and the PSF kernel in (PSF-PF) direction were calculated as shown in Figure 1B.

In the present study, magnetic field inhomogeneity was assumed to be relatively stable in time. The PSF kernel was derived from a pre-scan and applied to the distorted EPI images. The PSF kernel was estimated by a homemade PSF-EPI sequence using a 9.4T small animal MR system. This approach consumes approximately 3 minutes using: matrix size = 96*96*96, TR = 2000ms, TE = 24ms. Afterward, the estimated PSF kernel was applied to an ASL-EPI sequence for distortion correction.
The ASL-EPI images were acquired with different contrast at 3 inversion times (TI=100,700,5000ms, TE = 24ms, TR=15000ms) with the geometry parameters being identical to the PSF sequence.

**Results**

Arterial spin labeling EPI images obtained with and without PSF mapping correction are shown in Figure 2. Our results demonstrate that the geometric distortion can be corrected after applying the PSF kernel to different T₁ contrast EPI images while maintaining signal intensity and image contrast.

**Discussion & Conclusion**

PSF mapping reduces if not eliminates geometric distortion in EPI based ASL imaging, and is recommended to be included in the data processing pipeline tailored for distortion correction of EPI based perfusion measurements.

![Image of Pulse Sequence](image1.png)

**Figure 1.** Pulse sequence used for PSF mapping (A) and reconstruction of acquired PSF mapping signal along the non-distorted direction (PSF-FE), the distorted direction (PF-FE) and the PSF kernel (PSF-PF)

![Image of EPI Images](image2.png)

**Figure 2.** Comparison of EPI based ASL images (with different image contrast acquired at TI=100 ms, 700 ms, 5000ms) before and after PSF correction.


The organizers gratefully acknowledge the symposium's sponsors who provided kind contributions to foster science and educational activities.