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Safety and Efficacy of MR-guided Pediatric Musculoskeletal Procedures

Janice Wang, Ethan Dyer, Moustafa Abou Areda, Bao Chau Ly, Roberto Blanco Sequeiros and Jan Fritz

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Nathan Poulin and Robert Singer

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Lena Sonnow, Wesley D Gilson, Arne Hengerer, Clifford R Weiss, Himanshu Bhat, Frank Wacker and Jan Fritz

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Enrico Pannicke, Urte Kaegbein and Ralf Vick

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Marco Kalmar, Axel Boese and Michael Friebe

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Juan Sebastián Sánchez López, Sinja Lagotzki, Axel Boese, Robert Odenbach, Michael Vogele, Heinz-Werner Henke and Michael Friebe

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Robert Odenbach, Parisa Parsanejad and Michael Friebe

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Ernst Stille, Marieke Voet and Jurgen Füetterer

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Ahmed Mahran, Franklin King, Ravi Seethamraju, Nobuhiko Hata and Junichi Tokuda

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Tina Kapur

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Michael Bock

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Kemal Tuncali

MRI-Guided Cryoablation as an Immunotherapy for Canine Osteosarcoma
Brian Ladle, Rebecca Krimins, Byung-Hak Kang, Yingli Fu, Zachary Millman, Jan Fritz, Edward McCarthy and Dara Kraitchman

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Erica Knavel, Krzysztof Gorny, Chris Favazza, Aiming Lu, Joel Felmlee, Haraldur Bjarnason, Emily Bendel, Brian Welch, Megha Tollefson and David Woodrum

Evaluation of 2D simultaneous multi-slice EPI at 1.5T for MR-thermometry in presence of motion
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Motion Correction for PRF-based Thermometry during Tumor Ablation
Urte Kägebein, Marcus Prier, Enrico Pannicke, Oliver Speck, Frank Wacker and Bennet Hensen

Versatile system for 2D/3D temperature imaging during MR-guided thermal therapeutic procedures
Sunil Patil, Henrik Odén, John Roberts, Bradley Bolster Jr., Florian Maier, Himanshu Bhat and Dennis L. Parker

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Urte Kägebein, Marcus Prier, Enrico Pannicke, Oliver Speck, Frank Wacker and Bennet Hensen

09:50-10:20 Poster Session 12A: Ablation Therapies and Thermal Imaging

Initial Results of Image-Guided Percutaneous Ablation as Third-Line Treatment for Symptomatic Venous Malformations
Sjoerd F.M. Jenniskens, Christiaan G. Overduin and Jurgen J. Fütterer

Clinical workflow for MRI guided microwave ablation and thermometry in the liver
Bennet Hensen, Urte Kaegebein, Enrico Pannicke, Oliver Speck and Frank Wacker

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Brian Welch, Erica Knavel, Thomas Atwell, Joel Felmlee, Krzysztof Gorny, Matthew Callstrom, Nick Kurup, Michael Moynagh and David Woodrum

MR Guided Cryoablation of Invasive Breast Carcinoma: Feasibility and Safety
Brian Welch, Erica Knavel, Krzy Gorney, David Woodrum, Matthew Callstrom, Joel Felmlee and Thomas Atwell

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Erica Knavel, Krzysztof Gorny, Sean Dowdy, Jamie Bakkum-Gamze, Andrea Mariani, Carrie Langstraat, Bobbie Gostout, David Woodrum and Brian Welch
Improving MR-thermometry during MR-guided microwave ablations

Christopher Favazza, Krzysztof Gorny, Aiming Lu, Joel Felmlee, Ashley Anderson, Theodore Ormsby and David Woodrum

Improved MR thermometry during Microwave ablation by correcting for electromagnetic interference

Aiming Lu, Krzysztof Gorny, Christopher Favazza, Joel Felmlee and David Woodrum

Percutaneous MRI-Guided Hepatic Tumor Cryoablation: Experience and Long-term Outcomes

Dania Daye, Daniel Glazer, Kemal Tuncali, Vincent Levesque and Paul Shyn

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Michael Unger, Lisa Landgraf, Johann Berger, Thomas Neumuth, Thies Jochimsen, Bernhard Sattler, Osama Sabri and Andreas Melzer

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Ehud Schmidt, Akbar Alipour, Eric Meyer, Charles Dumoulin, Gregory Olson, Jeffrey Schweitzer, Henry Halperin and Akila Viswanathan

[Invited Talk] Tools for closed-loop MRI-guided prostate interventions

Junichi Tokuda

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Harald Busse, Thomas Kahn and Michael Moche

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Andrew Zheng and Pedro Moreira

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Pedro Moreira, Kemal Tuncali, Clare Tempany and Junichi Tokuda

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Kareem Elfatairy, Christopher Filson, Adeboye O. Osunkoya and Sherif Nour

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Kareem Elfatairy, Christopher Filson, Adeboye O. Osunkoya and Sherif Nour

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Dian Ren, Longquan Chen, Junichi Tokuda and Kemal Tuncali

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Stephan Katarina, Alireza Mehrtash, Nobuhiko Hata and Kemal Tuncali

14:20-14:50 Poster Session 15B: Focused Ultrasound

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Advanced drug delivery systems are having an enormous impact on human health. We start by discussing our early research on developing the first controlled release systems for macromolecules and the isolation of angiogenesis inhibitors and how these led to numerous new therapies. This early research then led to new drug delivery technologies including nanoparticles and nanotechnology that are now being studied. We also discuss the development of super long acting (weeks or more) oral delivery systems as well as ultrasound enhancement of drug delivery. Finally, we examine mammalian cells as drug delivery systems as well as novel microfluidic methods of squeezing cells to insert materials into them.
Speaker Biography

Robert S. Langer is one of 13 Institute Professors at MIT; being an Institute Professor is the highest honor that can be awarded to a faculty member. Dr. Langer has written more than 1,400 articles. He also has over 1,300 issued and pending patents worldwide. Dr. Langer’s patents have been licensed or sublicensed to over 350 pharmaceutical, chemical, biotechnology and medical device companies. He is the most cited engineer in history (h-index 259 with over 269,000 citations according to Google Scholar).

He served as a member of the United States Food and Drug Administration’s SCIENCE Board, the FDA’s highest advisory board, from 1995 — 2002 and as its Chairman from 1999-2002.

Dr. Langer has received over 220 major awards. He is one of 4 living individuals to have received both the United States National Medal of Science (2006) and the United States National Medal of Technology and Innovation (2011). He also received the 1996 Gairdner Foundation International Award, the 2002 Charles Stark Draper Prize, considered the equivalent of the Nobel Prize for engineers, the 2008 Millennium Prize, the world’s largest technology prize, the 2012 Priestley Medal, the highest award of the American Chemical Society, the 2013 Wolf Prize in Chemistry, the 2014 Breakthrough Prize in Life Sciences and the 2014 Kyoto Prize. In 2015, Dr. Langer received the Queen Elizabeth Prize for Engineering. Among numerous other awards Langer has received are the Dickson Prize for Science (2002), the Heinz Award for Technology, Economy and Employment (2003), the Harvey Prize (2003), the John Fritz Award (2003) (given previously to inventors such as Thomas Edison and Orville Wright), the General Motors Kettering Prize for Cancer Research (2004), the Dan David Prize in Materials Science (2005), the Albany Medical Center Prize in Medicine and Biomedical Research (2005), the largest prize in the U.S. for medical research, induction into the National Inventors Hall of Fame (2006), the Max Planck Research Award (2008), the Prince of Asturias Award for Technical and Scientific Research (2008), the Warren Alpert Foundation Prize (2011), the Terumo International Prize (2012), the Benjamin Franklin Medal in Life Science (2016) and the Kabiller Prize in Nanoscience and Nanomedicine (2017). In 1998, he received the Lemelson-MIT prize, the world’s largest prize for invention for being “one of history’s most prolific inventors in medicine.” In 1989 Dr. Langer was elected to the National Academy of Medicine, in 1992 he was elected to both the National Academy of Engineering and to the National Academy of Sciences, and in 2012 he was elected to the National Academy of Inventors.

Forbes Magazine (1999) and Bio World (1990) have named Dr. Langer as one of the 25 most important individuals in biotechnology in the world. Discover Magazine (2002) named him as one of the 20 most important people in this area. Forbes Magazine (2002) selected Dr. Langer as one of the 15 innovators worldwide who will reinvent our future. Time Magazine and CNN (2001) named Dr. Langer as one of the 100 most important people in America and one of the 18 top people in science or medicine in America (America’s Best). Parade Magazine (2004) selected Dr. Langer as one of 6 “Heroes whose research may save your life.” Dr. Langer has received 33 honorary doctorates. They include degrees from Harvard University, the Mt. Sinai School of Medicine, Yale University, the Memorial Sloan Kettering Cancer Center Gerstner Graduate School, the University of Maryland, the University of Western Ontario (Canada), ETH (Switzerland), the Technion (Israel), the Hebrew University of Jerusalem (Israel), the Universite Catholique de Louvain (Belgium), Rensselaer Polytechnic Institute, Willamette University, the University of Liverpool (England), Bates College, the University of Nottingham (England), Albany Medical College, Pennsylvania State University, Northwestern University, Uppsala University (Sweden), Tel Aviv University (Israel), Boston University, Ben Gurion University (Israel), the University of Laval (Canada), Carnegie Mellon University, Drexel University, Hanyang University (South Korea), the University of New South Wales (Australia), Karolinska Institutet (Sweden), Hong Kong University of Science and Technology (Hong Kong), the University of Limerick (Ireland), the University of Illinois and the University of California – San Francisco Medal. He received his Bachelor’s Degree from Cornell University in 1970 and his Sc.D. from the Massachusetts Institute of Technology in 1974, both in Chemical Engineering.

[Excerpt from Dr. Langer’s website http://langerlab.mit.edu/langer-bio/ in August 2018]
iMRI Guided Neurosurgical Gene Delivery for Parkinson’s Disease

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Background Gene therapy approaches for Parkinson’s disease (PD) have previously been evaluated in clinical trials involving direct infusion of adeno-associated viral vectors (AAV); insufficient clinical efficacy was attributed in part to poor distribution of gene transfer via conventional stereotactic procedures. Techniques using interventional MRI to monitor intracranial infusions in real time and convection enhanced delivery (CED) devices were refined in non-human primate studies and provided the basis for the ongoing aromatic L-amino acid decarboxylase (AADC) gene therapy clinical trials.

AADC is required to convert oral levodopa (L-Dopa)—the most efficacious therapy for the motor symptoms of PD—to dopamine. As PD progresses, less AADC is available in the brain, and L-Dopa becomes less efficacious with more side effects.

Non-clinical studies in large animal models of PD demonstrated that infusions of AAV2-hAADC covering approximately 35% of the putamen led to enhanced AADC activity and improved clinical responses (Hadaczek, 2010). Initial clinical trials of AAV2-hAADC likely did not achieve this targeted anatomical coverage of the putamen, which may explain why they did not achieve the desired response (Bartus, 2014).

Methods Subjects with idiopathic PD who were candidates for surgical intervention due to disabling motor complications were enrolled in clinical trials PD-1101 (n=15, dose escalation over 3 cohorts; NCT01973543) and PD-1102 (n=8; NCT03065192). CED infusions in conjunction with intraoperative MRI-monitored neurosurgery were used to directly administer VY-AADC01 (AAV2-hAADC viral vector) admixed with 1-2 mM gadoteridol (ProHance) for MRI visualization. The Clearpoint® Neuro Navigation System (MRI Interventions, Irvine, CA) was used in interventional MR scanners to simultaneously align and place SmartFlow® cannula (MRI Interventions) bilaterally into the putamen. Repeated MP-RAGE sequences were acquired during administration of VY-AADC01 to monitor inaparenchymal distribution, with the goal of covering as much of the post-commissural putamen as feasible. Intraoperative MRI visualization of the delivery procedure allowed for real-time modification of infusion parameters and incremental adjustments and evaluation of the surgical approach. The delivery procedure evolved from multiple transfrontal cannula trajectories (PD-1101) with fixed point infusions, to a single transparietal trajectory per putamen (PD-1102). Progressive advancement of the cannula tip throughout the CED infusion was employed in the last 8 subjects in PD-1101 and all subjects in PD-1102. Segmentation of the putamen and hyperintense gadoteridol signal was performed on end-of-infusion MP-RAGE images to quantify coverage of the putamen. ¹⁸F-Dopa PET scans were acquired pre-surgery and 6 months after VY-AADC01 infusion to measure changes in AADC activity. Subjects were followed clinically for up to 3 years.

Results In PD-1101, putamen coverage was 21% in Cohort 1 (n=5), 34% in Cohort 2 (n=5), and 42% in Cohort 3 (n=5). This increasing coverage of the targeted putamen region reflected (1) an increase in infusion volume from 0.45 mL in Cohort 1 to 0.9 mL in Cohorts 2 and 3, and (2) an evolving surgical procedure providing increased surgical control over distribution. Coverage of the putamen was significantly correlated with change in AADC enzyme activity 6-months post VY-AADC01 administration (r=0.84, p=0.0002), with dose-dependent clinical outcomes.

Further enhancement of putamen coverage to 53% was achieved in PD-1102, where a single transparietal trajectory traversing the long axis of the putamen was utilized to infuse up to 1.5 mL per putamen. This surgical approach resulted in considerably greater distribution within the relatively thin post-commissural region of the putamen, and an ability to limit distribution outside the putamen. Additional data from the PD-1102 trial will be presented.

Conclusions iMRI-monitored surgery allowed for the rapid evolution of the neurosurgical delivery of VY-AADC01 over two clinical trials, resulting in increased target coverage and clinical outcomes. A randomized, double-blind, placebo-surgery controlled trial is planned utilizing iMRI and the lessons learned from PD-1101 and PD-1102 to more efficiently and accurately administer VY-AADC to the post-commissural putamen of subjects with PD.

A phase 1 trial of oncolytic HSV-1 mutant rQNestin 34.5v.2 delivered to patients with recurrent glioblastoma by an intraoperative MRI-guided intratumoral injection

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Background: Glioblastoma is a deadly brain cancer with a median survival of about 15 months despite standard treatment\(^1\). At time of tumor recurrence, survival drops to 6-10 months, depending on the choice of second and third line options. rQNestin is an oncolytic virus derived from HSV-1, which has displayed strong antitumor effect in preclinical animal models of glioblastoma\(^2\). The primary objective of this study is to evaluate safety and feasibility of rQNestin administration to patients with recurrent glioblastoma, through a minimally invasive, MRI-guided stereotactic approach.

Methods A dose-escalation protocol of rQNestin 34.5v.2, delivered by intratumoral injection under intraoperative MRI guidance is currently under way in the Advanced Multimodality Image Guided (AMIGO) suite at the Brigham and Women's Hospital. Patients with a history of glioblastoma, presenting with radiological evidence of tumor progression are eligible for the trial. Initially, a stereotactic biopsy is performed for confirmation of tumor recurrence. Intraoperative MRI is then used to plan an ideal tumor region for virus inoculation, different from the initial biopsy site. The ClearPoint\(^\text{®}\) system is used to stereotactically administer 1 ml of vehicle containing different amounts of virus particles, according to the experimental cohorts. Axial T2 Flair and axial T1 with Gadolinium scans are performed for intraoperative confirmation of appropriate targeting before virus administration, and repeated immediately after virus injection, for confirmation of appropriate delivery to the selected tumor region.

Results. To date, nine patients have received rQNestin 34.5v.2 (3 patients in cohort 1 were inoculated with 1x10^6 virus particles, 3 patients in cohort 2 received 3x10^6 particles and 3 patients in cohort 3 received 1x10^7 particles). On average, the length of the procedure was 180 minutes. There were no complications associated to either the surgical procedure itself, or related to the virus injection. No grade 3-5 adverse events have been observed to date. Two patients had the tumor resected within 6 weeks after virus inoculation, providing histopathological confirmation of virus replication and also of profound intratumoral immune infiltrate. One patient in cohort 2, inoculated at the tumor edge, has shown tumor response by progressive decrease of tumor size and enhancement with serial follow up imaging and is currently alive 8 months after treatment. MRI imaging obtained immediately after virus injection provided novel evidence of interstitial accumulation of virus vehicle at the injection site.

Conclusions: Intratumoral administration of rQNestin 34.5v.2 via an intraoperative MRI-assisted stereotactic injection protocol is safe, well tolerated and of simple execution. This approach allows to target specific regions of the tumor (in particular the proliferative edge) which are expected to be more favorable to virus replication, and also allows for a more accurate radiological and histological follow up of the changes observed in the infected vs non infected regions. Finally, the ability to acquire images immediately after virus inoculation demonstrates for the first time the formation of a localized interstitial virus collection, suggesting the creation of a pressure gradient favoring virus penetration into the tumor.

References

Modulation of brain neural networks by targeted delivery of neurotransmitter chemicals through the disrupted blood-brain barrier

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Background

Neuromodulation refers to the selective enhancement or suppression of neuronal activity in targeted brain regions and represents an important tool for both basic science research and clinical applications. A variety of neuromodulation techniques have been developed, such as optogenetics or transcranial magnetic stimulation, each with their own advantages and limitations.

Here we present a novel approach to non-invasive neuromodulation that affects neuronal activity by delivering neurotransmitter chemicals to targeted areas of the brain. This is achieved by using focused ultrasound (FUS) to transiently open the blood-brain barrier (BBB) in a targeted brain region such that a systemically injected neuroactive chemical will leak out of the vessels and into the brain parenchyma only at the intended site. This work shows initial results demonstrating the proof of concept in a rodent model using targeted delivery of GABA to inhibit the brain’s functional response to an external stimulus.

Methods

Functional MRI was used to assess brain activation in N = 7 Sprague-Dawley rats undergoing hind paw stimulation. A 2 x 2 study design was used to evaluate conditions of BBB Closed vs BBB Open and No GABA vs GABA.

Stimulation: Bilateral hind paw electrical stimulation (4 mA, 0.3 ms duration, 6 Hz) was used for activation of the somatosensory network. Stimulation was performed in 5 blocks of 40 seconds OFF, 20 seconds ON.

BBB opening: Rats underwent actual and sham BBB opening on different days. BBB disruption was targeted to the right hemisphere only and confirmed via MRI T1-weighted contrast imaging.

GABA/Glutamate delivery: A systemic tail vein injection of GABA was delivered as a 50 mg/kg bolus immediately before imaging plus a 50 mg/kg continuous infusion during imaging.

Functional MRI: Rats underwent four total fMRI runs, one for each of the conditions of the 2 x 2 study design. Functional activation was measured according to changes in the blood oxygen level-dependent (BOLD) signal.

Results

Results from the BOLD signal measurements show: 1) GABA injection without BBB opening does not affect the functional response; 2) FUS-mediated BBB opening alone reduces the functional response to the stimulus; 3) the combination of FUS-mediated BBB opening and GABA injection further inhibits the response to the stimulus.

Conclusions

The data support the thesis that FUS-mediated opening of the BBB can be used to achieve non-invasive delivery of neuroactive substances for targeted manipulation of brain function.
Title Feasibility of MR-guided 8MHz RF capacitive hyperthermia
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Abstract Electromagnetic interference between a pair of capacitive electrodes and an MR scanner was evaluated in numerical simulations to examine feasibility of MR-guided RF (8MHz) capacitive hyperthermia. In a 1.5-T scanner with a horizontal B₀, B₁ field rotating in x-y plane suffered marked inhomogeneity of 67% of the original field from the eddy current generated on the electrode. The inhomogeneity was reduced to 33% by dividing the electrode disk into small strips. In a 0.3-T with a vertical B₀, the deviation of B₁ field was only 7% indicating that the vertical B₀ scanner is suitable for RF capacitive hyperthermia.

Purpose Radio frequency (RF) capacitive hyperthermia systems operating at 8MHz are commonly used for cancer treatment in Asian countries. This is because a relatively thinner subcutaneous fat layer prevents excessive heating from the RF electric field, which penetrates perpendicularly to the abdominal wall. Unlike the other heating modalities such as microwave, high intensity focused ultrasound, or laser, MR thermometry for monitoring and controlling the 8MHz capacitive hyperthermia has not been examined, mainly because generation of eddy current on the large electrode diameter (~30 cm) will shade the B₁ field of an MR system. In order to reduce the shading effect to achieve the combination of RF capacitive heating and imaging, we devised the shape, size and geometrical configurations of the pairs of electrodes relative to the B₁ field based on numerical simulations.

Methods A numerical model comprising an elliptical cylinder mimicking a human trunk with electrical properties equivalent to muscle, a pair of electrode discs with boluses filled with physiological saline was created. The model was placed in the isocenter of a 1.5-T scanner with a B₁ field orthogonal to horizontal B₀. Three types of capacitive electrodes were examined: a normal full disk, radially segmented disk and stripped disk. The electromagnetic field created by a high pass 8-element birdcage coil covering the capacitive electrodes was estimated with finite difference time domain (FDTD) method(1). The identical trunk model was also placed in a similar birdcage coil but orthogonally to mimic the horizontal B₁ field operating at 12.8 MHz in a 0.3-T scanner with a vertical B₀. In this case, the electromagnetic field was simulated with finite element method (FEM).

Results In the horizontal 1.5-T MR scanner, strong eddy current was generated on the full disc electrodes, and thus a large deviation (67% of the incident value) of B₁ field appeared. In the case of the stripped electrode, the deviation was halved (33%) because of the reduced eddy current loops on the strip structure. In the vertical 0.3-T scanner, the B₁ field remains homogeneous with the maximum deviation of 7%, because the capacitive electrodes are parallel to B₁ field and thus the eddy current was hardly generated.

Discussion Feasibility of the hybrid configuration of MRI and RF capacitive hyperthermia apparatus was examined from the view point of B₁ inhomogeneity. The results suggested that the B₁ field rotating in the vertical plane like in a 1.5-T scanner with a horizontal B₀ suffers significant non-uniformity due to the eddy current generated on the capacitive electrode. Even if the electrode is divided into the strips, the non-uniformity remains. This indicates that proton resonance frequency shift (PRF) thermometry based on gradient echo imaging will be problematic. In addition, large deviation around the edge of the strips appeared as an adverse effect. In the case of B₁ field rotating in the horizontal plane like in a 0.3-T scanner with a vertical B₀, the eddy current and thus the B₁ non-uniformity was drastically suppressed.

Conclusion The present results suggested that the vertical B₀ scanner will be a suitable choice for combining the RF capacitive hyperthermia system.

Experimental Determination of Transfer Functions using an Electro-Optic Sensor Setup

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Introduction: Due to the increased use of pacemakers, deep brain stimulators (DBS), and other implanted devices, methods are needed to study the response of devices to the radio-frequency (RF) fields in the MR environment. In the presence of an active device, maximum RF power limits must be determined to ensure patient safety. To characterize the response to an arbitrary incident electric RF field, the transfer function (TF) approach has been proposed [1], and methods have been described to measure the TF based on electrical coupling to the implant [2]. In this study, an electro-optical sensor (EOS) is used to measure TFs, which offers sub-millimeter spatial resolution, high SNR and full electrical isolation. To demonstrate feasibility, the E-field distribution of a straight wire excited by a monopole antenna was measured and simulated, and sampling strategies to determine TF were investigated.

Methods: The EOS measurement principle is based on the Pockels effect: the polarization of a laser beam is rotated proportional to an external E field when passing through an electro-optical crystal (LiNbO$_3$), which is measured by a polarization-sensitive detector [2]. The (1mm)$^3$ electro-optic crystal is mounted on the tip of a non-metallic sensor probe, which can measure the normal component of the E-field. Copper wires with different lengths (L=10cm, 20cm, 30cm) and Polyurethan isolation (1cm removed at both ends) were placed in distilled water ($\epsilon_r = 81, \sigma = 5 \cdot 10^{-5}$/m), and EOS data were acquired at a sampling rate of 4 Hz. The wires were excited at one tip by a small monopole antenna, and the resulting E-field was measured with a 1 mm resolution around the wire for $^1$H frequencies of 1.5 T and 3 T (i.e., 64 and 123 MHz). For comparison, simulations were performed with the software Sim4Life Version 3.4 (ZMT AG, Zürich, Switzerland). The 10cm-long excitation source was modeled with a voltage source driving the coaxial cable. Simulation time was between 1 and 1.5 hours per setting. From these simulations the TF was calculated via Ampere’s law. Each data point was normalized relative to the magnitude of the of the excitation field.

Results: The measurement times of the E-field measurements for 10cm, 20cm and 30cm were 35min, 48min, and 62min for 1x1mm$^2$ resolutions. Single line measurements were performed below 2min. Figure 1 shows the E-field maps acquired at 123 MHz next to the simulation results. The theoretical dipole behavior of the structure was confirmed. The calculated TF (Figure 2) is in good agreement for the measured cases for 64 MHz and 123 MHz as well as with the literature.

Discussion: In general, TFs derived from the E-field measurements are in good agreement with the simulations – observed differences can be attributed to uncertainties in material parameters and dimensions. The current study is only based on the measurement of the z component since the measurements are performed in the vicinity of the sample where the E-field is perpendicular to conducting structures. The presented setup is able to validate E-field distributions and transfer functions within relatively short measurement times, and it does not need electrically conducting elements such as dipoles, which can cause additional systematic errors.

References
Safety of Active Catheters in MRI: Termination Impedance vs. RF-induced Heating
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Introduction RF-induced heating is the result of the electric (E) field distributions along a conducting wire (1,2). To calculate RF-induced heating at the electrode of an implant lead (3), the transfer function (TF) approach was proposed. Alternatively, analytical modeling is a complementary approach that simplifies the heating problem but offers insights into the effects of individual parameters, which might affect the MR safety characteristics of implants/devices. In this work we analyze the effect of the termination impedance of an active catheter on the tip heating using a simplified analytical model.

Methods
In Fig 1, a two-conductor transmission line model is shown. Here, one conductor is formed by the outer shield of the coaxial cable, and the second virtual conductor is formed both by the surrounding lossy medium and the coaxial’s inner conductor. Applying Maxwell’s equations to this geometry, equations for coupling of an arbitrary electromagnetic field to the transmission line were derived in (4):

\[
\frac{\partial I(z)}{\partial z} + ZI(z) = j\omega \int_{0}^{d} B_{y}(x, z) \, dx + E_{0}(0, z) \]

\[
\frac{\partial U(z)}{\partial z} + YU(z) = -V \int_{0}^{d} E_{x}(x, z) \, dx
\]

where \(U(z), I(z), Z \) and \(Y \) are distributed voltage, current, impedance and admittance along the transmission line, respectively. Incidental fields are denoted by a superscript ‘i’. These differential equations can be solved by the Green’s function approach (5).

To test the analytical model, at first an active catheter was constructed for a 3 Tesla MR system (i.e., at 128 MHz) The analytical model was implemented in MatLab R2017a (The MathWorks, Inc. Natick, MA) to calculate the TF for a 110cm-long catheter completely immersed in lossy medium. The following incident field configurations \(E_{0}(x, z)\) were considered: a uniform E field \((E(z) = E_{0} = 1 \text{ V/m})\), and a worst case E field function \((E_{\text{worst}})\) such that the contributions of the E field along the line add constructively at the tip (3). As a reference, TF measurements were performed with the active catheter at 128 MHz using the commercial setup for TF analysis (pX, ZMT Zurich Med Tech AG, CH). \(SAR_{\text{tip}}\) values calculated from the TF measurements for the various incident fields were plotted on the Smith chart in color, and interpolated to cover the whole Smith chart.

Results
In Fig 2 color-coded Smith charts are shown that plot \(SAR_{\text{tip}}\) as a function of the input reflection coefficient \((Z_{\text{in}} - 50)/(Z_{\text{in}} + 50)\) for different incident fields. Figs 2a-b represent the analytical model, and Figs 6c-d display the TF measurements, respectively. The color-coded Smith charts show that \(SAR_{\text{tip}}\) depends strongly on \(Z_{\text{in}}\) – when the real part of the reflection coefficient approaching infinity SAR also increases. A quantitative comparison between the charts is given in Figs 2e-f, where the 22 measured SAR values are plotted against calculated values for the same \(Z_{\text{in}}\). Within each field configuration the analytical model always overestimated the SAR value: the mean \(SAR_{\text{tip}}\) from the measured TFs is lower than that of analytical model by 25%, and 49% for \(E_{0}\) and \(E_{\text{worst}}\), respectively.

Conclusions
This study introduces an analytical formulation to describe the interaction of an incident E field and a transmission line, specifically an active catheter. The TF model expresses for the voltage and current distribution in terms of the incident E field, medium properties, transmission line characteristics, and the input and output reflection coefficients. The results show that the RF-induced heating can be reduced by adapting the input impedance.

References

12th Interventional MRI Symposium 8 October, 2018 Boston, MA
Nursing Care Assistance is vital to successfully & safely treat prostate patients using MRI Guided Prostate Focal Therapy (FUS, Laser, Cryo)

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Abstract

Purpose

To create a multilevel nursing care model for efficient work-up and treatment of patients presenting for MRI guided prostate ablation. MRI Guided Prostate Ablation procedures are steadily increasing at our institution due to better targeting and ablation monitoring under MRI especially for localized prostate cancer.

Methods

Through trial and error multiple different methodologies of nursing involvement have been tried. The seven key aspects identified by our team are as follows: 1. Patient enquiries concerning candidacy, 2. Workup orders, 3. Clinic visit, 4. Procedural listing, 5. Intraprocedural nursing role, 6. Immediate post-procedural nursing role, 7. Long-term followup.

Results

The results of our team from years of clinical treatments and a steady interval growth are a very strong integrated team with select nurses, MR technicians, MR Physicists, and Physicians. Our MR ablation nurses are a key component of initial patient contact and information delivery to the patient. Patients are presented at dedicated multidisciplinary conference specifically for prostate ablation patients with the entire treatment team present. After conference review, nurses will then make sure the appropriate studies and labs are input for each patient prior to the clinic visit. Physicians and nurses see the patient in clinic together with the physician discussion the treatment and risks associated with it, while the nurse discusses the practical aspects of patient arrival and overall timing of events on the procedure day. During the ablation, nurses serve as surgical assistant during needle placement and run the ablation equipment at the direction of the physician. After the ablation procedure, the nurses will round with or without treating physician to check on the patient. Nurses provide key educational information concerning the follow-up care and subsequent imaging with PSA checks. Physicians and nurses will see the patient together in clinical follow-up.

Conclusions

Practical evolution of MR guided ablation over time has demonstrated that integral nursing involvement is key to an efficient and successful ablation practice at our institution. The role of nursing in the ablation practice is tremendous from the educational aspect prior to and after the procedure.
Technical testing prior to introduction of ancillary electronic equipment inside a newly-constructed 1.5T iMRI suite.

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Purpose: To safely introduce electronic equipment into iMRI suite, assess its impact on MR image quality and interactions with the magnetic environment.

Methods: The following devices were assessed prior to clinical use inside the iMRI scanner room hosting 1.5T MRI (Ingenia, Philips, Eindhoven, Netherlands): EPIQ 7 ultrasound scanner (Philips, Bothell, WA), in-room monitor (NordicNeuroLab, Bergen, Norway), LED procedure lamp (AADCO Medical, Randolph, VT), and in-room video and audio communication system (Image Stream Medical, Littleton, MA). Spatial maps of magnetic field and field gradients in zone 4 were first measured with a Gauss meter. Each device was individually interrogated using a hand-held magnet and subsequently tethered and advanced to the proposed clinical use position (see Fig. 1A), where magnetic pull forces were further evaluated. Once in position, the effects of the device operation on MR image quality were determined using the “small-sample” and ACR2 SNR tests. The effects of the MR environment on the function of each device were also evaluated.

Results: All devices were safely positioned at the proposed clinical use locations. The effects of the device operation on the MR image quality were minor (see Figure 1B). Operation of the LED lamp and EPIQ scanner (with probe near magnet bore opening) caused ~ 20% and 10% reduction in image SNR, respectively. Except for the LED lamp MRI environment had no impact on devices’ operation. Magnetic field caused the lamp to shut off near the bore of the MR scanner. The lamp’s function would resume once the lamp was moved beyond 50cm from the bore.

Conclusions: Clinical use locations for electronic equipment were established and assessed for safety and impact on MR image quality and device function. The LED lamp was to be switched off for MR imaging and operated to a minimal distance of 50cm away from scanner bore. During MR imaging the US probes were to be positioned on the US scanner in a sleep mode.

Figure 1: A. Experimental setup with devices at clinical use locations. B. "Small sample" test results.

A Measurement Setup for Ablation at the Larmor Frequency

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Background or Purpose: Commercially available Radio Frequency (RF) and Microwave ablation generators interferes the MR imaging process [1]. Gerlach et al. has shown that it is possible to destroy proteins with an MRI-Ablation hybrid system [2]. In this case, an electrode was connected to the internal RF amplifier of the MRI device to ablate tissue with the high power pulse sequences. This would make a separate ablation generator obsolete. However, different conditions must be met for this system, e.g. calibration of the transmitted B1 field when the electrode is connected to the MRI device. Furthermore, the generation of signal reflections during the ablation must be avoided. Therefore, it is recommended to study the behavior of the ablation at the Larmor frequency outside the MR device, first. Such a test setup will be shown in this abstract.

Methods: The setup is shown in figure 1. A bipolar ablation electrode was made from a semi rigid coaxial cable and placed in a polyacrylamide phantom [3]. The electrode was connected to an RF amplifier, which amplified a 123 MHz signal. The 123 MHz signal corresponded to the Larmor frequency of a 3T-MRI device. A Continuous Wave (CW) sequence was compared with a pulsed ablation sequence. The CW sequence had a voltage amplitude of 80 V. The pulsed sequence was designed similar to a Turbo-Spin Echo sequence: turbo factor = 100, pulse length = 2 ms, echo time = 10 ms, repetition time = 2000 ms and voltage amplitude = 90 V. Both ablations were performed for 400 s.

Results: During the CW ablation soot formations and carbonizations were formed next to the tip of the inner conductor and at the boundary between the inner conductor and the outer conductor (figure 2). The ablation area was formed mainly in the area of the inner electrode. Even though the mean voltage of the pulsed ablation sequence was lower than the mean voltage of the CW ablation, the ablation areas of both sequences were approximately equal.

Conclusion: The design of the ablation sequence has a big influence on the behavior of the ablation. It is therefore recommended to test the ablation system and sequence first outside the MRI to find optimal parameters for ablation. This test setup gives also the possibility to verify the performance of components which can be added to the MRI-Ablation hybrid system, like an automatic matching circuit for ablation.


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Figure 1: Set-up for ablation at the 3T-Larmor frequency

Figure 2: Comparison of the CW ablation (above) and the pulsed ablation (below)
Evaluation of a Luxtron FOT Lab Kit for MR-Compatible Temperature Measurements

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Background. The Luxtron FOT Lab Kit (LumaSense Technologies, CA) is an MR-compatible fiber-optic thermometer that is widely used in the MR community. The performance of our Luxtron FOT Lab Kit was evaluated for a range of 1 °C to 70 °C, as preliminary experiments with this device indicated irregularities in temperature measurements.

Methods. A temperature-controllable water bath was used as a suitable measurement environment (Haake C25, ThermoFisher Scientific, MA). After one-point calibrating the Luxtron FOT with ice water, its performance was compared to two reference thermometers (1 °C to 70 °C in 1 °C increments). In another experiment, the temperature range of 1 °C to 35°C was investigated again to check the reproducibility of the results. The following three thermometers were used as reference devices: the GTH 175/PT (GHM Messtechnik GmbH, Germany), the HI98509 Checktemp 1 (Hanna Instruments, RI) only in the first experiment and the DET3R (Conrad Electronic SE, Germany) only in the second experiment. According to the manufacturer, the resolution of the GTH 175/PT is 0.1 °C with an accuracy of ±0.1% of the measured value ±2 digits of the first decimal place for a range of -70 °C to 199 °C.¹ The resolution of the DET3R is 0.1 °C with an accuracy of ±0.5 °C.² For the HI98509 Checktemp 1, the manufacturer states a resolution of 0.1 °C with an accuracy of ±0.2 °C for a range of -30 °C to 120 °C.³ The HI98509 was calibrated ex-factory in 2015. For the Luxtron FOT Lab Kit (STF-2 probe with SST-10 extension cable), the manufacturer estimates an accuracy of 0.5 °C within 50 °C of the calibration temperature.⁴

Results. Fig. 1 shows the temperature estimated with the Luxtron FOT plotted versus the temperature that was measured with the GTH 175/PT resistance thermometer. Offsets in measured temperature of up to (1.0 ± 0.2) °C were found. For temperatures below 10 °C, there was a negative offset, for temperatures above 10 °C, the offset was positive. The difference in temperatures measured with the GTH 175/PT and the HI98509 Checktemp 1 was not significant for any of the measurement points (< 1σ). In a conducted second experiment (range of 1 °C to 35°C), similar offsets in temperature were found (not shown).

Conclusions. Discrepancies of up to 1 °C between the Luxtron FOT Lab Kit and three reference thermometers were measured. Assuming the three reference thermometers fulfilled their specifications, this implies that the device specifications of the Luxtron FOT Lab Kit stated by the manufacturer (accuracy of 0.5 °C within 50 °C of calibration temperature⁴) were apparently not fully achieved by the specimen investigated in this work. Further investigation will be needed to clarify whether the measured deviations were solely an issue with the investigated device or whether other Luxtron thermometers show similar behavior. For accurate measurements, the use of a lookup table can be a feasible workaround, as the found offsets proved to be reproducible in a second experiment.

Figures.

Figure 1: (a) shows the temperature inside the Haake C25 water bath recorded with the Luxtron FOT Lab Kit (4 fibers) plotted versus the temperature recorded with the GTH 175/PT resistance thermometer. The temperature recorded with the HI98509 Checktemp 1 is also plotted. (b) shows the measured offsets between the GTH 175/PT and the fibers of the FOT.

Saline Displacement of the Rectal Wall for MRI-guided Cryoablation of Primary and Recurrent Prostate Cancer
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Purpose: To describe safety and efficacy of saline displacement of the rectal wall during cryoablation of primary and recurrent prostate cancer.

Methods: A retrospective review of patients who underwent MRI-guided cryoablation for primary and recurrent prostate cancer (January 2016–December 2017) was conducted. Under general anesthesia and MRI guidance (wide-bore 1.5T MRI), 2-6 cryotherapy probes were placed in or around the prostate cancer lesion by transperineal approach and cryoablation was performed. One to three saline infusion needles were placed under MRI guidance and sterile normal saline was infused via gravity or pressure bag. Pre- and post-ablation rectal wall displacement distances were measured on MRI. Distances were measured from the edge of the lesion for focal lesion ablation and from the edge of the prostate for hemic-gland ablation. Saline volumes were estimated based on area of tissue expansion at the level of the lesion after the final thaw. Immediate and long-term complications were recorded as well as evidence of recurrence in the treatment field on follow-up imaging.

Results: MRI-guided cryotherapy with saline displacement was performed on 23 patients. Median age at time of ablation was 70. All men had biopsy proven adenocarcinoma of the prostate within the targeted ablation zone. Three patients underwent cryoablation for primary treatment of prostate cancer while 20 had it as a salvage therapy. Of the 20 salvage patients, 13 had undergone prostatectomy (11 primary, 2 salvage), 21 had received radiation therapy (9 primary, 12 salvage), and 2 had undergone previous salvage cryoablation. Median saline displacement distance was 4.6 mm (Range: 0-26.5) Median area of tissue expansion was 1634.7 mm² (Range: 298.2-3560.0). Median follow-up was 12 months (Range: 5-26). Two patients had imaging evidence of recurrence within the treatment zone, but also demonstrated imaging findings concerning for metastatic disease so systemic therapy was recommended. No patients underwent repeat cryoablation. There were no intra procedural complications. There was one reported rectal complication occurring in patient with history of rectal cancer and low anterior resection. This patient experienced anterior rectal wall breakdown at the anastomosis which was successfully managed conservatively with drain placement.

Conclusions: Saline infusion at the time of MRI-guided cryoablation of prostate cancer resulted in increased distances between the target lesion and the rectum and is a useful technique when ablating areas close to the rectal wall.

Figure 1. MRI Images from saline displacement during MRI-guided cryoablation for radiorecurrent prostate cancer. A Pre-Treatment Axial DWI imaging showing lesion (white arrow). B Pre-Treatment Axial imaging showing measurement from rectal wall to edge of lesion C Immediate post-treatment Axial Imaging showing distance from rectal wall to lesion edge after saline displacement. D Post-treatment Axial Imaging showing area of saline infused
Evaluation of Needle Heating during Interventional Magnetic Resonance Imaging at 3 Tesla

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Abstract
We aimed to quantify the heating of MR-conditional needles during imaging with pulse sequences commonly used in 3T interventional MRI procedures. Our study provides preliminary evidence that heating of needles during interventional 3T MRI is minimal for 10 cm long needles, suggesting minimal risk for thermal injury.

Background or Purpose
Testing for MR-conditional needles often includes the assessment of traction forces and image artifacts, but may not include the degree of heating during interventional pulse sequences. Therefore, the objective of our study was to quantify the heating of interventional MRI needles at 3T.

Methods
We used a standard ASTM gel phantom and a clinical 3T MRI system. MR-conditional 20G 10cm cobalt-chromium needles were placed at the center and equidistantly on each side to account for spatial variations of radiofrequency power deposition. Fiber optic sensors measured the temperature changes at the needle tips. The interventional sequences tested included unaccelerated Turbo Spin Echo (TSE), accelerated TSE, Slice Encoding for Metal Artifact Correction (SEMAC) TSE, Compressed Sensing SEMAC TSE, Half-Fourier Acquisition Single-Shot TSE (HASTE), HASTE Inversion Recovery (IR), as well as fluoroscopic and static gradient sequences. All sequences had clinical acquisition times of < 1 min. However, in order to accentuate subtle temperature changes and emulate the effects of successive image acquisition during procedures, each sequence was acquired continuously for 5 min. Measurements were obtained with the needles at 90° and 45° angles relative to B0. Finally, the needles were removed and temperature changes were rerecorded in order to calculate local background specific absorption rates (LBSAR) at each position.

Results
For 90° needle orientation, the maximum heating measured across all nine protocols during 5 min of continuous scanning was 0.2 °C, which was equal to the temperature rises without the needles. For 45° oblique needle orientation, the maximum heating was 1.8 °C, which occurred with the accelerated TSE sequence. The maximum background heating in the absence of needles for 45° orientation was 0.2 °C, seen with the accelerated TSE and HASTE IR sequences. Temperature increases were generally higher with the needles at a 45° angle compared to 90°, with 5/9 (56%) sequences showing a 1°C increase or greater at 45° and 0/9 (0%) at 90°.

Conclusions
In our experimental setting at 3T, the temperature increases around 10 cm long MR-conditional needles were < 2 °C during continuous acquisition of nine commonly used interventional MRI sequences, which is within the physiologic range.
Benefits of Integrated Staffing Model in iMR

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**Purpose:** To build an integrated staffing model within the procedural MR practice and suite to maximize patient care across the continuum of care.

**Methods:** Multiple iterations of team members have developed over time in the interventional MR practice and suite. These have been based on determining the best combination of specialties and skill sets to optimize patient care during procedures including ablations and biopsies of prostate cancer, liver nodules, arteriovenous malformations, nerve tumors, and soft tissue tumors, as well as the review and intake of new patients. Because of the nature of the cases and complex equipment needs depending on the type of procedure or modality of ablation, a variety of staff members are needed for the following activities: to run procedural equipment, obtain images, provide sedation and analgesia, assist in the introduction and testing of needles and patient care supplies, and monitor the safety of the patient, staff, and room at all times. Often, additional imaging modalities are also used during the procedures, adding the need for additional specialists and equipment in the room. The importance of the integrated team approach also carries over into the preparation and follow-up for patients and their families for patient education, setting up additional services, and follow-up for procedures.

**Results:** The interventional MR team within our facility is comprised of Interventional Radiologists, Surgical Urologists, MR technologists, Registered Nurses, Certified Registered Nurse Anesthetists (CRNA), Anesthesiologists, Medical Physicists, Sonographers, and a Research Study Coordinator. The Interventional Radiologist is the team leader and in prostate cases works collaboratively with the Urologist to maximize care in both planning and treatment phases. Generally, our team has three MR technologists present to function as a safety officer to monitor and assess safety within the equipment room, scanning room, and control room; a scanning technologist who focuses on scanning and adjusting imaging as appropriate; and a circulating technologist to assist with imaging technology and equipment within the procedure room. The nurses assist with positioning the patient, monitoring patient safety, sterile set-up, and assisting the providers with the hands-on care of the patient within the room. In addition, the nursing team provides patient education and follow-up leading to and following the actual procedure. The Medical Physicist is monitoring equipment for use in the scanner, optimizing treatments in collaboration with the providers, and assisting with real-time safety and procedure needs regarding MR safety within the suite. In addition, the physicists play an integral role outside of the procedures in developing new methods to use the equipment and ensure what is planned for use in the suite is safe and effective. The sonographer assists in imaging during procedures requiring ultrasound assistance. In addition to these team members within the suite during cases, the team also relies on an administrative team who assist with scheduling and follow-up, as well as a study coordinator for study-related procedures and research consent. The entire team is also involved in reviewing patients for candidacy into a focal therapy plan during a weekly review meeting. The multidisciplinary team is extremely helpful in capturing all aspects and potential contributing factors that may affect patient care.

**Conclusion:** This collaborative and integrative approach has been vital to building a highly successful and growing interventional MR practice with successful care of these patients.
Considerations for design of interventional MRI environment to optimize workflow and procedure times


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Teaching points

Due to excellent tissue contrast and capability of near real-time visualization of ice boundaries MRI is well-suited for image-guided cryo ablations of subtle post-prostatectomy prostate cancer recurrences. However, adapting a dedicated diagnostic MRI space for image guided procedures presents unique challenges, both in terms of equipment used and procedural workflow, which could potentially impede the procedures and result in unnecessarily complicated and lengthy treatments. MR-guided prostate ablations performed by our interventional MRI (iMRI) group were initially performed on a diagnostic MRI scanner. Since then, knowledge gained during this experience was used to design a dedicated iMRI suite. The teaching points of this presentation provide review of the following solutions implemented in order to reduce complexities and improve efficiency of the iMRI procedures:

1. **iMRI space design (Figure 1):** Dedicated iMRI suite consists of scanner room with adjacent work and equipment rooms on one side, and intubation and control rooms on the other, see Figure 1. Audiovisual communication system enables communication between all locations of the suite. The scanner room includes storage cabinets placed near clinical use locations for small procedure-related objects (biopsy needles, introducers, applicators, etc.).

2. **Equipment layout (Figure 1):** Galil cryo-ablation unit and urethral warmer were located inside the workroom. The Galil unit was connected with the MR-safe cryo needle tripod inside the scanner room via the filter box on the pen panel. The urethral warmer lines were fed into the scanner room via the waveguide. The need for Ar and He gas tanks was eliminated using a dedicated cryo-gas supply system linking the outlet in the workroom with tank storage room in the basement. Mobile anesthesia machine and ultrasound scanner were moved into clinical use locations through the specified routes inside zone 4. The mobile sterile cart was placed in scanner room near the entrance to workroom for ease of access. Intubation room was designed to store all necessary anesthesia supplies.

3. **Staffing solutions:** our staffing model requires presence of at least one radiologist, 3 MR technologists (which includes one designated to be a MR-safety officer), anesthesia team, 2 nurses, and one physicist. Depending on the details of the procedure, a urologist and an ultrasound technologists may also be required.

Overview:

1: Introduction – Overview of iMRI procedures
2: Organization of iMRI space, additional ancillary equipment, internal staffing support: comparison between dedicated diagnostic and interventional suites.
3: Comparison of treatment times between the two sites.

Summary:

Careful design of iMRI suite that addresses unique challenges of iMRI procedures can result in significant improvements to treatment times.
MR Guided Implantation of DBS Electrodes
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Background or Purpose – Deep brain stimulation (DBS) therapy requires that electrodes be precisely placed in brain structures such as theglobus pallidus interna (GPI) or the subthalamic nucleus (STN). High targeting accuracy (within~1mm) is necessary, so conventional stereotactic methods are commonly supplemented with invasive physiological tests, including micro-electrode recordings (MER) and test stimulation. This requires that the patient be awake during surgery and off any medications that might mask their condition. Procedures can be long and arduous for the patient and technically challenging for the surgeon. Intraoperative MR guidance affords the possibility to achieve high anatomic targeting accuracy and can be performed in anesthetized patients. We report on the technical outcomes of over 250 MR guided DBS surgeries; clinical outcomes and complication rates associated with MR guided DBS electrode implantations will also be addressed.

Methods – MR guided DBS implantations were performed in patients with movement disorders. All procedures were performed under institutional review board approved protocols and criteria for surgical intervention were comparable to DBS patients undergoing conventional implantations. The surgical procedure [1] utilized the ClearPoint platform (MRI Interventions, Irvine, CA) and involves the use of a trajectory guide (Fig 1A), which is mounted to the skull over a 15 mm burr hole. The entire procedure is performed within the magnet bore (Fig 1B) and intraoperative imaging is used to identify the anatomic target (Fig 1C) and to bring the trajectory guide into alignment with the selected target (Fig 1D). Once aligned a rigid ceramic mandrel within a peel-away sheath is inserted through the trajectory guide to the target depth. Imaging is then performed to assess anatomic positioning and determine targeting error. The primary accuracy assessment is radial error, which is the difference between the target location and the center of the ceramic mandrel in the axial plane in which the target was selected. Once acceptable placement is confirmed, the mandrel is removed and replaced by the DBS electrode. Finally, the electrode is anchored, the peel-away withdrawn, and the excess lead length is coiled beneath the scalp. Implantation of a pulse generator (IPG) is performed later in a separate procedure. We report on the targeting accuracy, number of brain penetrations, procedure durations and complication rates, including hemorrhage and post-operative infection of MR guided DBS implantations. Preliminary assessment of clinical outcome measures will also be presented.

Results – A total of 414 DBS electrodes were implanted in 256 surgical procedures (157 bilateral, 99 unilateral). Patients suffering from Parkinson’s disease (219), Dystonia (32), Tourette’s Syndrome (3) and Essential Tremor (2) were treated. Implantations targeted the GPI (157), STN (92), Vim (4) or thalamus (3). The radial error between planned and actual lead placement averaged 0.55±0.33 mm and acceptable positioning was obtained on the first past into the brain 98% of the time (2 passes required in all other cases). Procedure times, measured from skin incision to skin closure, have averaged 178±29 minutes for bilateral and 135±29 minutes for unilateral implantations. Both are trending down, with the last 50 bilateral procedures averaging 165 minutes and the last 30 unilateral procedures averaging 123 minutes. Hemorrhage rates were 2.4%/electrode or 3.9%/surgery, with symptomatic and/or clinically significant hemorrhage occurring at a rate of 1.1%/electrode or 1.7%/surgery [2]. An infection rate of 2.6% was found in this cohort, all of which occurred at the IPG site and not the intracranial electrode [3]. Both of these complication rates are comparable or superior to those reported for conventional procedures. Clinical outcomes have been assessed with standardized disease rating scales on sub-groups of both Parkinsonian [4] and dystonia patients [5]. These analyses have similarly demonstrated at least comparable clinical efficacy to conventional surgical approaches.

Conclusions – MR guided implantation of DBS electrodes has proven to be a viable alternative to conventional surgical approaches. High anatomic targeting accuracy can be achieved with a single brain penetration in a high fraction of procedures. Procedure durations are comparatively short and complication rates and clinical outcomes are comparable to physiological-guided DBS surgery.

The third decade of iMRI for neurosurgery: where do we go from here?  
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Intraoperative MRI was first developed at Brigham and Women's Hospital in the early 1990s. The first decade of iMRI saw the advent of specialized MRI-compatible instrumentation and workflows for increasingly complex neurosurgical cases. The original double donut MRT was the site for the development of iMRI guided stereotactic biopsies, craniotomies for tumor, transphenoidal pituitary tumor resection, spine surgery, and the initial studies of interstitial laser hyperthermia; over 1000 craniotomies were performed in the MRT. Intraoperative MRI allowed the updated acquisition and display of imaging to reflect the changes occurring during surgery in order to more accurately guide the clinician. In particular, iMRI was able to demonstrate brain shift and the updated location of the tumor and was also able to demonstrate areas of residual tumor thereby helping the clinician to maximize the extent of resection and improve the rate of gross total resection. The establishment of instrumentation, workflows, and imaging paradigms not only aided neurosurgical procedures, but also was able to inform the adoption of iMRI for numerous other interventional specialties.

Since then, intraoperative MRI has been adopted by numerous centers, with most dedicated largely to neurosurgical applications. Tumor resection remains the mainstay and laser interstitial thermal therapy (LITT) is emerging as an alternative, minimally invasive, standard of care for selected tumor and epilepsy cases. iMRI guided placement of electrodes for DBS treatment of movement disorders is rapidly gaining acceptance due to shortened surgical times and easier tolerability for patients of surgery under general anesthesia. An emerging area of iMRI is its use to guide and confirm direct drug delivery into the CNS. As development of neuro- and onco-therapeutics advances, local delivery to circumvent the blood brain barrier will become increasingly viable. Viral vectors, nanoparticles, drug loaded polymers, stem cells, and biologics hold promise to treat brain tumors, neurodegenerative diseases and potentially neurobehavioral illnesses not previously considered surgical targets. In order to fully realize these potentials, technological developments will be required in the speed and resolution of intra-operative imaging. Devices to improve access when the surgical site is at isocenter in the scanner and relatively inaccessible to the clinician. Alternatively, dedicated interventional imaging systems designed to allow more direct access by the clinician to the surgical site will be needed. A number of robotic devices are under development for specific clinical applications. Such devices will need to be MRI compatible, easily and accurately deployable, and able to be guided by real time location feedback with iterative positioning. In order to maximize the accuracy of both in-bore and out-of-bore iMRI interventions, the ability to incorporate pre-operative images including functional images, advanced imaging such as microstructural imaging, and non-MR imaging such as PET, will require approaches for non-rigid registration to account for brain shift. An important workflow challenge is the difficulty for a clinician to select and display relevant images, and to interpret the numerous images which are produced during the intervention while focusing on the patient and technical steps. Improved computational capabilities and expert systems to handle the processing, display and interpretation of data will be increasingly important. Finally, the close integration of imaging and tissue sampling in iMRI allows unprecedented opportunities for the development and validation of imaging to detect clinical relevant biomarkers. All of these advances will require close partnership between clinicians, engineers, physicists, computer scientist and commercial entities working closely with patients within clinical systems.
Interventional MR Neurography in the Age of Precision Medicine

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Precision medicine aims to provide individualized patient care that is designed to optimize accuracy, efficiency and therapeutic benefit for particular groups and individual patients with specific conditions. Interventional pain management is a field where the application of precision medicine has an enormous impact through direct visualization of variant course and anatomy of submillimeter interventional targets, instrument placement under direct visualization of the target without the need to rely on anatomic landmarks, and direct process monitoring ranging from visualization of injectants to temperature during ablation processes in conjunction with targeted and non-targeted structures. Interventional MR Neurography represents a minimally invasive precision medicine technique that combines all the aforementioned criteria, including the targeting of small nerves in challenging areas of the human body for highly accurate nerve blocks, intramuscular injections, and ablations (1). This cross-sectional technique uniquely combines highest tissue contrast and high spatial resolution anatomic detail, which enables the precise identification and selective targeting of peripheral nerves, accurate needle guidance and navigation of the tip of injection and cryoablation needles within the immediate vicinity of a nerve (2). Based on T2 and T1 properties, Interventional MR Imaging is able to directly visualize injected drug for the assessment of appropriate drug distribution without the need of an artificial contrast agent and documentation of the absence of spread to confounding nearby nerves (3). Similarly, Interventional MR Neurography provides the unique ability to visualize and monitor the ice ball during cryoablation. 3-Tesla field strength offers high spatial and temporal resolution for improved visualization of small targets and increased efficiency (4). MR Neurography guidance exclusively combines the absence of procedure-related exposure to ionizing radiation with the capability to resolve small nerves in deeply situated locations. This talks will discuss techniques as well as diagnostic and interventional procedures of high-field Interventional MR Neurography of various small peripheral nerves and complex pain syndromes.

References

Bringing Causality to fMRI through MR-Guided Pharmacological Intervention

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Introduction: Cognitive and behavioral functions are mediated by distributed networks of neurons involving multiple cortical and subcortical brain regions. Functional magnetic resonance imaging (fMRI), a technology for observing such networks while the subject is at rest or performing specific tasks, has served as the bulwark of human brain mapping for the past twenty years. The spatial and temporal resolution limits of fMRI provide correlative information on brain connectivity but makes determination of how one region causally modulates and mediates activity in other regions difficult. Therefore, the ability to alter local brain regions and then link ensuing changes in neural dynamics and behavior is highly desired to demonstrate causality in neuroscience research. We demonstrate here how techniques developed first for therapeutic delivery can be used to guide and monitor pharmacologic alteration of a local brain region in a Rhesus monkeys while monitoring changes in functional brain connectivity throughout all brain networks.

Methods: Two untrained monkeys slated for euthanasia at the Wisconsin National Primate Center were used for initial testing. As shown in Fig. 1A, pre-surgical MRI was used to determine skull locations for craniotomies for installation of Navigus™ brain ports. After installation (Fig. 1B), real-time control of the scanner was garnered with the RHawk portal (HeartVista, CA). The ports were aligned in real-time (Fig. 1D) to provide trajectories aimed at the central nucleus of the amygdala (CeA) using methods previously presented at the NCIGT Workshop [1]. Fused silica 0.7 mm catheters are then inserted into the CeA where 24 µg of muscimol (inhibitory agent) was infused in 24 µl of buffered solution under pressure over 12 minutes, first on the right side of the image in Fig. 1F and then later on the left side. Resting state-functional connectivity MRI studies (rs-fcMRI) were done for 45 minutes prior to the unilateral infusion, after the unilateral infusion, and after the bilateral infusion.

Results: Significant functional connectivity (p<0.001) was observed between bilateral CeA prior to infusion (Figure 2, left). This is consistent with prior studies, which have shown that the CeA is most strongly connected to the contralateral CeA [2]. This connectivity was significantly reduced following both unilateral and bilateral injections of muscimol into CeA, demonstrating the effectiveness of the muscimol infusions (Fig. 2 center, right).

Discussion: Though demonstrated in anesthetized NHP models for feasibility, we believe permanent brain ports can be affixed to skulls in a surgical setting which can provide later access for repeated studies in awake behaving models that we have trained to do cognitive tasks in the magnet. The intermittent insertions of MR catheters are actually smaller than the electrodes typically inserted in the field.

Conclusion: The first feasibility studies for causally examining the functional organization and dynamics of brain networks have been completed. Further development will allow us to test hypotheses about network topology and information flow, as well as to further the understanding of the mechanisms underlying the signals provided by fMRI.

Intraoperative imaging modalities to compensate for brain shift in tumor resection surgery

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Background or Purpose Intraoperative brain shift during neurosurgical procedures is a well-known phenomenon caused by gravity, tissue manipulation, cerebrospinal fluid drainage and use of diuretics. This phenomenon greatly affects the accuracy of image-guided neuronavigation systems [1]. The introduction of intraoperative magnetic resonance imaging (iMRI) into neurosurgery opened new opportunities to increase the accuracy of neurosurgical procedures by providing frequent image updates with high soft tissue resolution for the neurosurgeon [2]. A major drawback of iMRI methods stems from the cost and time it adds to a specific procedure. Intraoperative ultrasound (iUS) provides inexpensive image data in real-time and is widely available [3]. We present a novel feature-based method for achieving robust, fully automatic deformable registration of intraoperative neurosurgical ultrasound images. Our goal is to use IMRI as a validation tool for the proposed 3D intraoperative ultrasound feature-based registration model.

Methods A sparse set of local image feature correspondences is first estimated between intraoperative 3D ultrasound image pairs, after which rigid, affine and thin-plate spline models are used to estimate dense mappings throughout the image. Correspondences are derived from 3D features, distinctive generic image patterns that are automatically extracted from 3D ultrasound images and characterized in terms of their geometry (i.e., location, scale, and orientation) and a descriptor of local image appearance. Feature correspondences between ultrasound images are achieved based on a nearest-neighbor descriptor matching and the Hough transform probabilistic voting model. Figure 1 presents a summary of the proposed feature-based registration for intraoperative 3D-ultrasound.

Results Experiments demonstrate our method on iUS images acquired before and after opening of the dura mater, during resection and after resection in nine clinical cases. A total of 1,620 automatically extracted 3D feature correspondences were manually validated by eleven experts and used to guide the registration. Using manually labeled corresponding landmarks in the pre- and post-resection ultrasound images, we show that our feature-based registration reduces the mean target registration error from an initial value of 3.3 to 1.5 mm

Conclusions This result demonstrates that the 3D features promise to offer a robust and accurate solution for 3D ultrasound registration and to correct for brain shift in image-guided neurosurgery. We are currently working on brain shift correction, using non-linear deformation models between preoperative MR / intraoperative US and preoperative MR / intraoperative MR.

References
Intraarterial chemotherapy of glioblastoma following hyperosmolar opening of the blood-brain barrier under real-time MRI guidance

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Background The presence of the blood-brain barrier (BBB) is a main obstacle for effective chemotherapy of brain tumors. Intra-arterial (IA) injection of hyperosmotic mannitol has been widely used to permeabilize the BBB. However, the reproducibility of IA BBB manipulation has been low and therapeutic outcomes vary. We previously showed in large animal models that the variability can be reduced or even eliminated when the procedure of BBB opening (BBBO) is performed under real-time MRI. Here we adapted and optimized this approach for a mouse glioblastoma model enabling high-throughput cost-effective efficacy studies. The targeted and localized BBBO was induced as predicted by interventional MRI and following IA chemotherapy showed with good treatment responses in the mouse model.

Methods: BBBO: Scid mice (20-25) were anesthetized with 2% isoflurane. Mice were catheterized with a microcatheter in the common carotid artery and imaged with a Bruker 11.7T horizontal bore MRI scanner. Baseline T1- and T2-w and dynamic GE-EPI images were acquired. IA Feridex (0.1 mg Fe/ml) was infused under dynamic GE-EPI to predict the perfusion territory for different injection speeds. 25% mannitol was delivered via IA over one minute at the optimal speed determined by prior Feridex perfusion study for each animal. MRI and histology were used to assess the status of the BBB and any consequences compromising the safety of the procedure.

IA chemotherapy: Mice were inoculated with luciferase-expressing human glioblastoma (GBM1) cells. Three weeks after glioblastoma induction, mice were subjected to BBBO as described above and melphalan, (0.05 mg/mouse) or temozolomide (1 mg/mouse) was injected IA. Mice were serially imaged with bioluminescence imaging (BLI) to monitor tumor growth.

Results Dynamic susceptibility contrast MRI during transcatheter IA infusion of SPIO contrast demonstrated that at a rate below 0.1 ml/min cerebral perfusion was inconsistent. However, when the speed was increased from 0.15 ml/min to 0.2 ml/min, desired brain perfusion was obtained as visualized by the reduction in signal intensity during injection of the Feridex bolus. IA mannitol infused at predetermined rate over 60 s resulted in BBBO as verified by gadolinium-enhanced T1 weighted MRI, showing hyperintensity in the region previously highlighted by the Feridex infusion. The SPIO perfusion MRI showed an average signal change area of 26.00±5.60%, while Gd-enhanced MRI showed an average signal change area of 26.52±5.33%, in good agreement (r=0.879). On histopathology, iv injected Evans Blue (marker for BBBO) and rhodamine (surrogate marker of therapeutic agent demonstrated a pattern of extravasation that was consistent with that observed by MRI. T2-w MRI acquired on day 3 post BBBO showed no obvious abnormalities, nor Gd-enhanced MRI. Immunohistochemistry showed no increased number of GFAP+ activated astrocytes or IBA-1+ microglia, nor NeuN+ neuron loss. Altogether, these data indicate an excellent safety profile of our BBBO procedure.

The tumor-bearing mice received melphalan treatment with or without BBBO showed a gradual increase of BLI signal. However, six days after treatment, the signal intensity in the BBBO groups was much lower than that without BBBO, indicating a treatment response. After this initial reduction the signal in treated mice continued to grow, indicating a single dose can’t completely regress tumor growth.

Conclusions Real-time MRI-guidance enables a precise fine-tuning of the infusion rate to achieve a safe and effective local BBBO at a high reproducibility. Bypassing the BBB resulted in treatment response, but the effect was transient indicating the need for further studies on more effective treatment plans.
Feasibility Study of MR Image-Guided Intracerebral Clot Evacuation
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Purpose: Typically, the current clinical treatment of intracerebral hemorrhage (ICH) merely stabilizes the patient’s condition, resigning them to a lifetime of considerable cognitive deficits, motor deficits, loss of independence, and extended care costs. However, a recent large-scale NIH trial, termed MISTIE (Minimally Invasive Surgery Plus rt-PA for Intracerebral Hemorrhage Evacuation) [1], shows promise in minimizing the brain damage by lysing the interior of the clot with a minimally invasive catheter, inserted through a small burr hole not much wider than the catheter, which slowly delivers clot-busting drugs and drains the lysed blood. CT surveillance is used daily to plan dosages and catheter movements that will avoid dangerously lysing the exterior of the clot and creating a new bleed. The inability of CT to visualize the clot components or the spatial distribution of the clot buster drug leads to very conservative dosing, slowly administered over 3-5 days, with highly variable patient outcomes.

![Figure 1: Vision for MR-Guided ICH Evacuation](image1)

**Figure 1:** Vision for MR-Guided ICH Evacuation

A) MR depicts bright plasma in T2-w image which can be extracted prior to clot lysing through aspiration. B-D) MR improves safety and cuts procedure time by displaying location of clot busting drugs relative to clot boundaries.

We investigate here whether the soft tissue contrast of MR would advance the MISTIE approach by spatially visualizing blood clot components and the location of administered drugs, as illustrated in Figure 1. We hypothesize that T2-W imaging will clearly show plasma components which could be immediately aspirated under MR guidance to reduce intracranial pressure. We also hypothesize that co-infused Gd, or simply T2-W imaging, would differentiate the administered clot buster and lysed blood from rigid blood clots, as the lysing agent is distributed (illustrated in Fig. 1B), acts upon the clot (Fig. 1C), and is drained (Fig. 1D).

Methods: We mimicked ICH clots in vitro by drawing 50 mL of fresh blood from a swine donor, transferring the blood to a thin plastic bag, and burying it in soft dough to approximate the mechanics of surrounding brain tissue. By several hours after collection, the blood had separated into distinct volumes of free plasma and rigid clot, as shown in Fig 2A. We simulated plasma extraction by inserting a catheter into the plasma under MR guidance. We also operated on large solid clots that filled the 5×5×7 cm³ experimental boxes (Fig. 3) and were taken from multi-liter blood samples collected at a slaughterhouse during routine swine exsanguination. We simulated (1) manual surgical injection of tPA clot buster into the clot with dose volumes (1—2 mL) and catheter diameter (3 mm) similar to techniques used clinically for MISTIE today, and (2) similar dose volumes delivered via pressurized infusions through a 0.7 mm fused silica catheter at flow rates of 12, 20, or 50 µL/min, in accordance with methods used for intraparenchymal brain cancer treatments. This infusion technique is known as convection-enhanced delivery (CED).

**Figure 2:** In vitro feasibility study of plasma extraction. A) Bright plasma in T2-w image surrounds fibrin-rich dark clot. B) After plasma aspiration, volume of clot is significantly reduced.

![Figure 3: Simulation of surgical practice of manual injection](image2)

**Figure 3:** Simulation of surgical practice of manual injection (Col. A) shows highly asymmetric and dangerous clot buster distribution. MR guided infusion (Col. B-D) shows ability to monitor and control distribution.

Results: The ability to aspirate plasma, thus decreasing clot volume and its deleterious mass effect on the brain, is shown in Fig. 2B. Manually injecting the clot buster, the actual surgical practice, creates escape routes along paths of least resistance, producing a highly asymmetric distribution with unwanted and potentially dangerous backflow along the catheter. Our initial experience using CED to infuse clots reveals a much more controlled and symmetric distribution of infusate (Fig. 3B) at 12 µL/min. At the higher flow rate of 50 µL/min, real-time monitoring shows the infusion fracturing the clot (Fig. 3C), which risks lysing at unsafe locations such as the exterior surface of the clot, where the failed vessel that was initially responsible for the hemorrhage is likely located. While Fig. 3A—C used co-infused Gd with T1 sequences, Fig. 3D demonstrates that T2 sequences without Gd show hyperintense infusion as well.

Conclusion: The ability of MR to visualize blood clot components and the spatial distribution of clot busting drugs within the clot holds significant promise for speeding the extraction of clots while visualizing whether the treatment is risking rebleeds by nearing the exterior of the clot.


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MR-safety within the Interventional MRI suite

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Background: MR-guided interventions (iMRI) differ from conventional diagnostic MRI procedures in that they are frequently performed by large multidisciplinary teams and require use of additional equipment in Zone 4. These complexities pose challenges to establishing a meaningful and robust MR-safety program within the iMRI practice.

Purpose: To develop, implement and maintain an MR-safety program within the complex environment of an iMRI suite.

Methods: A dedicated iMRI subcommittee of our institution’s MR-safety committee was formed to design iMRI site-specific safety/emergency procedures and iMRI-specific training documentation. The subcommittee was also charged with reviewing iMRI safety incidents and equipment safety testing, and developing workflow safety guidelines for equipment in the iMRI suite. An MR safety officer-of-the-day was designated prior to every procedure in the iMRI suite. A ferromagnetic detector was located in Zone 3. To ensure no ferromagnetic items were inadvertently introduced into Zone 4, a pocket-less scrubs policy was introduced. Required mobile tools and devices lacking MR-safe equivalents, but considered necessary for routine use during iMRI procedures, had to undergo safety assessments by the iMRI-dedicated physics team prior to introduction to Zone 4. Following testing, corresponding workflow safety guidelines, checklists, and training documents were developed and reviewed by the iMRI-safety subcommittee.

The 300 and 100 Gauss iso-lines were measured and delineated on the floor with red and blue tape, respectively. All mobile equipment in Zone 4 was correspondingly color-coded to the floor labeling. ACR-recommended labeling³ was adopted and further refined for the needs of iMRI practice. Objects determined to have ferrous components received additional labeling as follows: orange tape with diagonal black stripes – objects restricted from Zone 4; blue tape – objects restricted from within the 100 Gauss (blue) line; red tape – objects restricted from within the 300 Gauss (red) line. The labeling was repeated for storage containing small ferrous items. All safety incidents were analyzed for root-causes by the iMRI safety subcommittee, and appropriate safety recommendations were communicated with the institutional MRI-safety committee. An iMRI-independent institutional quarterly audit of all safety practices was also implemented.

Results: Since the implementation of the program in November 2017, 94 iMRI procedures involving iMRI-specific equipment were performed without incident. Within that time period, three minor safety breaches were recorded involving inadvertent operation of equipment outside the workflow safety guidelines. Each of these breaches was followed by root-cause analysis and recommendation for workflow improvements by the iMRI safety subcommittee.

Conclusions: We have implemented a consistent and robust iMRI safety program. Since iMRI-specific safety continues to evolve with new procedures and equipment, it is essential to continually review and update the program, particularly following any safety-incident.

References:
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Safety and Efficacy of MR-guided Pediatric Musculoskeletal Procedures

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Abstract

Purpose Pediatric interventional radiology represents a tremendous benefit for the diagnosis and treatment of a variety of musculoskeletal conditions of children and adolescents. X-ray fluoroscopic and computed tomography (CT) guidance are frequently used; however, the procedure-related exposure to ionizing radiation raises health concerns. Interventional magnetic resonance (MR) imaging offers imaging guidance for a wide variety of procedures without the use of ionization radiation, but there is limited data about efficacy and safety [1]. Therefore, we analyzed the technical efficacy and safety of MR-guided percutaneous musculoskeletal procedures in children and adolescents.

Methods A retrospective search of our radiology information systems derived 200 procedures, which were performed in 171 subjects (91 girls and 80 boys; median age: 14 years; range: 1-17 years) at 0.2-Tesla (39/200, 19.5%), 0.23-Tesla (51/200, 25.5%) and 1.5-T (110/200, 55%) MR imaging systems. Procedures were evaluated for a.) procedure type, b.) type of anesthesia, c.) technical success, defined as adequate drug delivery on post-procedural MR imaging, acquisition of an adequate tissue sample for diagnosis at pathologic analysis, or successful percutaneous therapy of an osseous condition confirmed during follow-up, d.) length of time of procedures, and e.) major complications, defined according to American College of Radiology guidelines.

Results The 200 procedures consisted of 113 (56.5%) targeted drug delivery [sacroiliac joint (35, 17.5%), epidural space (26, 13%), temporomandibular joints (24, 12%), spinal nerve (11, 5.5%), facet joint (6, 3%), shoulder injections (5, 2.5%), hip injections (3, 1.5%), and lumbar sympathetic nerves (3, 1.5%)] 33 (16.5%) osseous biopsies, 32 (16%) percutaneous osseous therapies [treatment of a focal lesion 19, 9.5%, drill resection of an osteoid osteoma (10, 5%), drill resection of a physal bone bridge (3/1.5%)], 16 (8%) soft tissue biopsies, 5 (2.5%) preoperative percutaneous tumor marking procedures, and 1 (0.5%) abscess drainage. 94/200 (47%) procedures were performed with local anesthesia, 77/200 (38.5%) with conscious sedation, and 29/200 (14.5%) with general anesthesia. Technical success was achieved in 200/200 (100%) procedures. The average total length of time of a procedure was 40 (range, 11-221) min, including 35 (11-90) min for targeted drug delivery, 72 (17-221) min for percutaneous osseous therapy, 58 (51-68) min for percutaneous tumor marking procedures, 66 (15-104) min for soft tissue biopsies, 49 (18-124) min for osseous biopsies and 29 min for the drainage. No major complications occurred. Two minor complications occurred. One minor local infection occurred around a percutaneous micro-catheter at post-procedural day 10, which healed after catheter removal and oral antibiotics without further intervention. One focal subcutaneous atrophy occurred after steroid injection of a temporomandibular joint.

Conclusions A wide variety of pediatric MR imaging-guided percutaneous musculoskeletal procedures are efficacious and safe for use in clinical practice.

References

Low-flow vascular malformations are congenital, non-neoplastic lesions that arise secondary to defects in vasculogenesis that do not include arterial components. The two primary types of low-flow vascular malformations are venous malformations and lymphatic malformations. Treatment is often indicated to ameliorate pain, cosmetic disfigurement, and functional impairment. Percutaneous sclerotherapy is the treatment of choice for VMs and LMs. Sclerotherapy, which is traditionally the first line therapy for treating low-flow vascular malformations, is an image-guided treatment that involves the injection of a sclerosant into a low-flow vascular malformation. This induces endothelial damage and fibrosis with the goal of eventual involution. Thermal therapies, including cryoablation involves heating or freezing of target tissue to induce cell death and necrosis. The choice of imaging modality employed is especially important for lesion characterization and treatment response (pre and post procedure) as well as for needle guidance and for monitoring of sclerosant during delivery. Conventionally, magnetic resonance imaging (MRI) is the modality of choice for pre- and post-intervention assessments, while ultrasound (US) is used to guide needle placement, and fluoroscopy is used to monitor the injection of sclerosant. While US offers adequate soft tissue resolution and real-time imaging with no exposure to ionizing radiation, certain lesions cannot be completely visualized with US due either to “depth” or to overlying anatomy that deflects soundwaves. To overcome the limitations of US and fluoroscopy, MRI has emerged as an alternative for needle guidance and sclerosant monitoring. MR can provide dynamic, multiplanar imaging that delineates surrounding critical structures such as nerves and vasculature. MR has the potential to replace X-ray fluoroscopy for needle guidance and sclerosant monitoring while reducing ionizing radiation exposure and improving intra-procedural tissue resolution. Multiple studies have demonstrated that MR-guided treatment of low-flow vascular malformations is clinically successful with very few complications. Although MR-guided intervention can be considered a secondary, salvage treatment for these patients it can be applied to treat a wide range of low-flow vascular malformations as primary therapy. This invited talk will outline procedural basics and will present a series of cases of MR-guided sclerotherapy and MR guided thermal ablation for low-flow vascular malformations at both 1.5T and 3T.
**Real-time MRI Endoscopy**

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**Background:** Traditional endoscopy provides real-time optical imaging from the frame-of-reference (FoR) of the probe-end, enabling routine assessment and minimally-invasive intervention in gastroenterology. While inexpensive, it can’t see through opaque tissue, blood or the vessel wall and thus cannot identify disease, target a biopsy or guide interventions in adjacent tissue lying outside of vessels that could otherwise afford immediate access. Traditional MRI is slow, lacks microscopic resolution and is bound to the laboratory FoR. MRI endoscopy employing tiny internal MRI probes in clinical 3Tesla MRI systems, could provide high spatial resolution (~200µm) from the FoR of the probe-end, and identify disease inside and outside vessel walls (1,2). But until now it has been limited to 1-2 fr/sec, which is not real-time endoscopy.

Accelerated MRI employing highly under-sampled radial pulse sequences and a temporally-regularized nonlinear inversion (NLINV) reconstruction algorithm (3) was recently implemented with high-speed graphics processing units (GPUs) to achieve truly real-time ultra-high-speed multi-channel MRI (4). We have adapted this technology for real-time single-channel MRI endoscopy at ~10 frames/s with 150-300µm in plane resolution and several cm effective field-of-view.

**Methods:** The MRI endoscope was fabricated from a 3mm outer-diameter (9Fr) 4½-turn spiral coil tuned with micro-capacitors on a coaxial lead. It is operated in transmit/receive mode using an under-sampled radial FISP and FLASH sequences in which selective excitation is replaced by adiabatic B1-independent rotation (BIR4) pulses applied in the absence of MRI gradients. The NLINV reconstruction, which jointly estimates the highly-nonuniform endoscope’s image and coil sensitivities, is implemented in a ‘SysGen TITAN Octuple-GPU’ computer (Sysgen, Bremen) equipped with 8 GeForce GTX 580, TITAN (Nvidia, Santa Clara) GPUs. This system is connected to the host computer of a Siemens 3T Prisma scanner via a single Ethernet cable and tested on fresh human carotid artery obtained from our Pathology Dept, and iliac and carotid specimens from porcine and canine studies in vitro and in vivo in the iliac vein. Cine frames from real-time endoscopy recorded at ≤10 fr/s were compared with fully-sampled endoscopy at 1-3s and at 6min/16 scans.

**Results:** Real-time MRI endoscopy at 10fr/s was relatively simple to implement with this real-time system developed for conventional MRI (3,4), and modified for adiabatic transmit/receive (1,2). At 10 fr/s, vessel wall and surrounding tissue up to ~5mm from the probe were depicted (Fig. 1). There was no evidence of thermal injury at the very low transmit power levels used, but some loss in contrast resolution and radial under-sampling artefacts were evident.

**Discussion:** MRI endoscopy performed with tiny internal detector coils can be combined with real time high-speed under-sampled iterative reconstruction to achieve frame-rates of ~10 fps, on a clinical 3T MRI scanner. This yields a tool that is potentially viable for applications currently done by conventional optical endoscopy with the added advantages that it can see through vessel walls and blood, and offer MRIs full complement of multi functional capabilities. Speed is currently limited by gradient strength and slew rate; the BIR4 pulse length and the limitation of a single MRI channel.

Reducing reconstruction artifacts, improving soft tissue contrast and mating it with therapy delivery are current works in progress.

**References**


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Intravascular MRI Guided Perivascular Ultrasound Ablation
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Background: The degree of involvement of cancerous tissue with adjacent blood vessels is a major factor determining whether pancreatic cancer is surgically resectable. Cancers extending >180° around critical vessels are considered non-resectable and have very poor survival rates compared to those that are resectable (1). Ultrasound ablation using tiny intravascular (IV) transducers has potential advantages for delivering therapy without the limitations imposed by ultrasound acoustic windows, while protecting vessel walls from injury via coolant circulation and a transducer design that can target perivascular tissue (2). If it could be combined with practical high-resolution image guidance and a means of titrated thermal therapy delivery, this technology has the potential for rendering non-resectable cancer resectable by ablating a tumor margin around a vessel while preserving vessel wall. Other cancers, such as hepatocellular cancer which has a high incidence of recurrence post-surgery (3), could benefit from new image-guided intervention technology that can visualize tumor at high resolution and precisely target and monitor therapy delivery.

IV magnetic resonance imaging (IVMRI) (4) combined with an IV ultrasound ablation probe can guide a catheter to a target and provide precision thermometry critical for ensuring accurate ablation outcomes. Here we demonstrate such technology with a high-intensity IV ultrasound catheter combined with an IVMRI loopless antenna deployed ex vivo and in vivo to verify ablation efficacy, vessel wall preservation and reproducibility.

Methods: A 3T MRI loopless antenna (4) was combined with a water-cooled Acoustic MedSystem ultrasound ablation catheter (Fig. A) (2). High-resolution anatomical imaging on a Philips Achieva 3T MRI system was used to precisely localize the transducer in ex vivo liver specimens. Ultrasound transducer power was applied at 14W for ~4mins and monitored by (Sonalleve) MRI thermometry from the IVMRI probe (5). Ablation efficacy was assessed by gross histology post-ablation. Repeat experiments were performed to monitor and measure vessel wall protection margins. Institutionally-approved in vivo ablations were performed in porcine inferior vena cava (IVC) accessed from the common femoral vein using high-resolution (0.3x0.3x2mm) anatomical MRI at muscle ablation targets, with ~7mins ablation times. Ablated tissues around vessel were sampled post mortem for histology.

Results The IVMRI/ablation transducer is clearly localized under high-resolution MRI in a pig liver ex vivo (Figs. B, C, E). MRI thermometry enabled titration of thermal dose (Fig. C) producing ablation lesions (Fig. D) consistent with thermal dose maps. In vivo high-resolution MRI shows an ablation target (Fig. F) and correct thermometry-guided ablation (Fig. G). No identifiable transvascular lesions were found in the IVC or aortic wall (F,G). At histology 7 of 8 ex vivo experiments exhibited vessel wall protection margins of 0.5–2mm (Fig. H) with one failure due to improper catheter positioning (predicted by thermometry).

Conclusions: The combined IVMRI IV ultrasound ablation/imaging catheter delivered perivascular thermal therapy while affording protecting to adjacent vessel wall. Porcine experiments verify that such results can be achieved in vivo.

Aerosol Jet-Deposited Double Helix Wireless Resonant Markers for MRI Catheter Tracking

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Keywords: wireless resonant circuits, tracking markers, double helix design

Background: Endovascular catheter-based procedures under MRI guidance for neurointerventional applications are inherently difficult. One major challenge is tracking the tip of the catheter under MRI, as standard fabrication methods for building semi-active markers are rigid and bulky. Semi-active methods are implemented as wireless resonant circuits, which work by inductively coupling to the MR system’s transmit coil, inducing a current in the circuit that is then amplified, increasing the surrounding magnetization and signal. Aerosol jet deposition is a new additive manufacturing process used to create 3D, conformal, micron size (10–100 µm) electronics and is CAD-file driven, making design practical and customizable. A prior study used aerosol deposition to print a solenoid inductor, which was then connected to a 100pF capacitor inside the catheter lumen for use at 1.0T, and recent work proposed an inductor geometry in the shape of a double helix, using wire-winding and a customized flexible capacitor sheet. We aim to extend upon these works by using aerosol jet deposition to print a complete LC circuit using the geometry of a double helix inductor on a polymer catheter for interventional MRI use at 3T.

Methods: A catheter was constructed using a custom 6Fr catheter PTFE substrate, and polyethylene ether ketone (PEEK) braidng (Penumbra Inc., Alameda, CA). The conductive traces of the double helix were printed with a 250 µm trace width, 10 turns with a 22.5° pitch, and a 5–7 µm trace thickness. The capacitor plates were printed measuring 180 mm long, with 280–300 µm trace width, with a similar 5–7 µm trace thickness, and 200 µm separation of the plates (Fig. 1a). All conductive prints were made using a water-based silver flake ink and polyimide dielectric ink (Aerosol Jet® 300P system, Optomec, Albuquerque, NM) (Fig. 1b). The catheter was placed in a water phantom doped with CuSO₄ and the phantom was oriented either parallel or perpendicular to B₀ at 3T (Discovery MR 750w, GE Healthcare) using an 8-channel cardiac coil. A balanced steady state free precession (bSSFP) sequence (TE/TR = 1.7/4.63ms, 30 mm FOV, slice thickness 20 mm, matrix 384 × 384) was acquired with flip angles 5°, 15°, and 75°. A 5° Bloch-Siegert B₁+ map was also acquired (TE/TR = 13.4/28ms, 30 mm FOV, slice thickness 20 mm, matrix 128 × 128). The mean signal of a manually drawn ROI of the marker was measured, and compared with the nearby water signal to measure the relative contrast ratio RCR = (C_{marker} – C_{water})/C_{water}.

Results: The low flip angle bSSFP sequence (5° and 15°) shows the signal amplification of the markers relative to the background signal, in comparison with the high flip angle (75°) sequence (Fig. 1c). In the parallel orientation, the RCR measured 5.26, 4.07, and 2.38 for 5°, 15°, and 75° flip angles respectively, and 0.53 for the 5° B₁+ map (Fig. 1c). In the perpendicular orientation, the RCR measured 1.6, 1.01, and -0.02 for 5°, 15°, and 75° flip angles respectively, and 0.64 for the 5° B₁+ map (Fig. 1d).

Conclusions: This preliminary data suggests that fabrication of complete 3D printed LC circuits for use as tracking markers on catheters is possible and that these markers can exhibit good tracking characteristics at 3T.

References
Cardiac radiofrequency ablation under real-time MRI thermometry and contact electrophysiology using actively tracked MR-compatible catheters

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Purpose: radiofrequency catheter ablation under x-ray fluoroscopy is a reference curative treatment of cardiac arrhythmia. Electrical isolation of pathologic tissue relies on induction of transmural coagulation necrosis by local heat deposition from the catheter tip using consecutive adjacent ablations to create a geometrical pattern. However, due to the lack of real-time lesion visualization, a high rate of arrhythmia recurrence is reported, requiring costly and time consuming redo procedures (up to 40% of patients). The development of real-time MR-thermometry may help in providing real-time assessment of the lesion and provide a therapeutic endpoint of the therapeutic procedure [1-3]. The purpose of this work is to present an integrated MRI solution combining contact electrophysiology mapping using an actively tracked MR-compatible catheter, a console for visualization of MR images and contact EP, an active catheter tracking MRI sequence for online visualization of catheter localization and electrical mapping within the cardiac chamber and real-time MR-thermometry for online visualization of lesion formation. The method was evaluated in vivo on a large animal model.

Methods: The experiment was performed on an anesthetized sheep (50 kg) under assisted mechanical ventilation. ECG electrodes were positioned on the thorax of the animal for MRI sequence synchronization using conventional MRI device. The experimental protocol was approved by animal care IRB. The MR-compatible electrophysiology (EP) recording system (Advantage-MR, Imricor, Burnsville, USA) and MR-compatible catheters with 2 active tracking coils (Vision-MR, Imricor) were interfaced with a dedicated prototype console (Monte Carlo station, Siemens Healthcare, Erlangen, Germany) with a prototype scanner interface module (Scanner Remote Control, Siemens Healthcare, Erlangen, Germany) controlling the MRI scanner (MAGNETOM Aera 1.5T, Siemens Healthcare, Erlangen, Germany). The combined system can receive intracardiac electrogroms, measure electrogram amplitude and duration, and display this information as electroanatomical maps on shells representing the cardiac anatomy. One catheter was positioned in the Right Ventricle (RV, venous access through femoral vein) for pacing the heart using the cardiac stimulator integrated into the EP recording system and a second catheter was placed in the Left Ventricle (LV, aortic access through femoral artery) for ablation. A prototype 3D MRI sequence CS_r1a3d_28 with TR/TE = 261,1.76 ms; matrix 288*288, FOV 320*320, Flip angle 90°, accelerator factor 5.1, 20 iterations, SLT 1.05*1.05*1.05, Acquisition time 9 min was acquired to provide a roadmap of the anatomy of the heart. 3D meshes were generated from this data set using in-house developed software (Music) and imported into the Siemens console. Every MRI-acquisition sequence could be switched from inside the MRI room using a pedal switch, allowing the operator to alternate between 1) tracking only acquisitions to visualize and position the catheter interactively for 3D contact EP mapping, 2) anatomical imaging (e.g. truefisp sequence) automatically centered on the tip of the electrode, 3) thermometry sequences based on an prototype ECG-gated Echo Planar Imaging combined with parallel acceleration (as previously described in [3]) with an in-plane resolution of 0.8 mm and 4 slices acquired continuously at each heartbeat. After mapping the LV, a RF ablation was performed using an ablation generator located inside the MRI room under real-time MR-thermometry. Raw-data from this sequence were streamed to the Gadgetron for real-time image reconstruction and processing of temperature images that were displayed on a separate visualization console (IGT SA, Pessac France) inside the MRI room.

Results: Figure 2 displays the contact electrogroms recorded by the LV (trace on the RV shows the pacing signal) at different times relative to the RF ablation (blue rectangle) 40W during 2 minutes. Residual minor artifacts (yellow ellipse) can be seen due to rapid gradient switching of the thermometry sequence, although electrograms can still be interpreted. The trace in C shows modification of the EP signal in the LV at the end of the RF deposition. The temperature image at the end of the RF deposition (Figure 2, right column) show substantial temperature increase (20°C or more) close to the catheter tip and the accumulated thermal dose was higher than a lethal threshold. Contact mapping performed in this region before and after ablation showed important modifications of the QRS voltage (5 mV vs 1mV) and duration (60 ms vs 120 ms).

Conclusions: an integrated solution is presented allowing real-time tracking of a catheter, online contact EP recording and visualization of the temperature distribution during radiofrequency ablation. Residual artifacts can be observed during the ablation due to the thermometry sequence, but with acceptable quality of the signal of the contact electrogroms.

MR-Guided Implantation of Bioresorbable Coronary Scaffolds at 3T

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Introduction: Recently, bio-resorbable vascular scaffolds (BVS) have been introduced for scaffolding of coronary arteries. BVS are free of metal and thus enable artifact-free MR imaging of the scaffolded coronary artery segment which is desirable for MR-guided PCI as the result of the intervention can be readily assessed via MR imaging. In this study, the feasibility of fully MR-guided implantation of BVS in at 3T is demonstrated.

Methods: Animal trials were performed in 6 adult Göttingen minipigs. The left coronary artery (LCA) was engaged using an 8F catheter with non-metallic braiding and Tiger tip shape. The catheter was equipped with a 2cm-long saddle coil with an operator-controlled tip signal adjustment unit to enable real-time MR-guidance.

For BVS implantation a non-metallic BVS delivery system (Abbott Vascular, Wetzlar, Germany) was used in combination with an MR-safe 0.014" guidewire (MaRVis Interventional GmbH, Frechen, Germany) which was doped with iron microparticles for MR visibility.

The MR-guided PCI was performed in 6 Göttingen minipigs on a clinical 3T MR system (Siemens PRISMA). A 10F sheath was placed in the right femoral artery for arterial access.

A whole-heart 3D navigator-gated FLASH sequence (fat saturation, T2 preparation, TE/TR: 1.6/3.5 ms, FA: 16°, FoV: 282x160, matrix: 176x64, TE_T2prep: 40 ms, R = 2) was used for localization of the coronary arteries. For real-time imaging a radial bSSFP sequence was used during the engagement of the LCA with the active guiding catheter (TE/TR: 1.4/2.8 ms, spokes: 105, FA: 40°, FoV: 275x7 mm³, matrix: 160x160, fat saturation).

After engagement of the LCA, contrast-enhanced MR angiography images were acquired during infusion of a 5 ml bolus (5% Gd-DTPA solution) through the guiding catheter. An ECG-triggered FLASH acquisition was used for imaging of the contrast enhancement in the myocardium (TE/TR: 1.1/2.2 ms, TŠR: 102 ms, FA: 8°, FoV: 225x300 mm³, matrix: 120x160, R = 2). Finally, a 18 mm long BVS with diameter of 3 mm was advanced via the active guiding catheter and the balloon was dilated using a 1% Gd-DTPA solution.

Imaging during the stent placement was performed with the real-time radial bSSFP sequence using an additional saturation pulse (TŠR = 170 ms).

Results: Intubation of the LCA with the 8F active guiding catheter was successful in 4 of 6 pigs. Figure 1 shows real-time images of a successful engagement of the LCA with the guiding catheter. The perfusion measurement depicts the myocardial area supplied by the LCA (Figure 2). The balloon dilation is shown in Figure 3b. Here, the BVS was implanted in the main stem. 3D imaging after BVS implantation shows the open scaffolded lumen (Fig. 3c). BVS implantation was successful in 3 of 6 pigs.

Conclusion: The feasibility of fully MR-guided PCI at 3T is demonstrated. In two pigs, engagement of the LCA was not possible as the catheter tip shape was incompatible with the anatomy of the pigs. Further work will thus include improvements in mechanical properties of the guiding catheters.

References:

Figure 1: Real-time images acquired during engagement of the LCA with the active guiding catheter which is seen as a hyperintense signal.

Figure 2: Selective perfusion measurement performed by injecting 5% Gd-DTPA solution through the guiding. Contrast enhancement depicts myocardial areas supplied by the LCA.

Figure 3: Real time images of the LCA (yellow arrow) acquired before (a) and during (b, with saturation recovery) dilation of the BVS balloon (blue arrow). The guiding catheter is visible via a signal void (green arrow) as the coil is switched off. c) shows a the LCA after BVS implantation. The BVS induces no imaging artifacts in the scaffolded artery segment (blue arrow). d) shows a photograph of the BVS in the explanted heart.

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MR-guided Percutaneous Sclerotherapy of Venous Malformations: Initial Clinical Experience Using a 3.0-Tesla MR System

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Purpose: Venous malformations (VM) are traditionally treated using ultrasound and fluoroscopy guided percutaneous sclerotherapy. However, certain lesions are particularly difficult to visualize and/or treat using these modalities. Magnetic resonance (MR) imaging has been used to safely and effectively treat VM that could not be treated with ultrasound and fluoroscopy. (1-3) We present here our experiences with targeting and treating VM using a 3.0-Tesla MR scanner.

Materials and Methods: Five patients with a VM in the neck (n = 2), chest (n = 1), and extremities (n = 2) were enrolled into this IRB approved study between 7/2014 and 2/2015. Each patient was selected for MR guidance for actual or predicted inability to find the lesion using ultrasound. Imaging was conducted with a 3.0T MR scanner (Skyra, Siemens Healthcare, Erlangen, Germany). After a planning sequence (3mm T2 TSE SPAIR), all lesions were targeted with 22 gauge 10 cm MR-compatible needles (Cook Medical, Bloomington, Indiana, USA) using MR guidance (3mm PD TSE). Once the needle tip was determined to be at target, confirmatory T2 TSE sequences were acquired. Patients were treated with gadolinium-doped 3% sodium tetradecyl sulfate (visualized with T1 TSE with and without subtraction). After treatment, confirmatory imaging was conducted (3mm T2 TSE SPAIR and/or 3mm 3D VIBE).

Results: Five patients were enrolled in this study with an age range of 19-54 years old. Three patients underwent MR-guided needle access of more than one component of the VM during the same procedure for a total of 10 targeted sites. All 10 targeted sites were successfully accessed and filled with sclerosant (100% technical success rate). Times (planning, targeting, intervention, and total procedure) were documented for each treatment. The average planning time (interval between the start of pre-intervention imaging and needle skin puncture) for all procedures was 0:27:55 (hours:minutes:seconds; σ = 0:17:25). The average targeting time (interval between needle skin puncture and lesion access) for all procedures was 0:13:38 (σ = 0:05:49). The average intervention time (interval between needle skin puncture and needle removal) for all procedures was 0:24:31 (σ = 0:09:09). The average total procedure time (interval between the start of pre-intervention imaging and the end of post-intervention imaging) for all procedures was 0:53:06 (σ = 0:23:40). There were no minor or major immediate or delayed complications.

Conclusion: A 3.0T MR system can be used for guidance when performing percutaneous sclerotherapy on VM that cannot be adequately visualized with ultrasound or 1.5T MR imaging. This small case series demonstrates that it is feasible to perform percutaneous embolization of VM using 3.0T MR guidance. The technical success rate and average total procedure time with 3.0T MR guidance are on par with our institutional experience with ultrasound and fluoroscopy guided procedures.

References
Figure 1: 54-year-old female undergoing initial treatment of a VM in the left paraspinal musculature using a 3.0T system. a: Pre-treatment axial T2 TSE with fat saturation demonstrating a small VM in the left paraspinal musculature. b: T1 TSE demonstrating needle at the target. c: T1 TSE confirming delivery of gadolinium-doped sotradecol within the VM. d: T1 TSE with subtraction confirming delivery of gadolinium-doped sotradecol within the VM.
Visualization of necrotic lesions from atrial fibrillation ablation with non-contrast-enhanced T1w MRI

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Background Atrial fibrillation (AF) is a common arrhythmia, and radiofrequency catheter ablation (RFCA) with pulmonary vein isolation (PVI) has become the standard therapy. Arrhythmic recurrence rate, however, remains high at 30-50%. Inability to identify necrotic lesions and gaps during the procedure may be a major factor for PV reconnection and AF recurrence. Recently, non-contrast-enhanced 3D T1-weighted (non-CE T1w) MRI with inversion recovery (IR), and long inversion time (TI), was shown to reliably identify acutely necrotic RFCA lesions in swine left ventricles. Our purpose was to determine whether non-CE T1w MRI can identify acute necrotic RFCA lesions and gaps in the thin walled left atrium (LA) and PV.

Methods RFCA was performed in 11 swine to achieve PVI. After confirming PVI with electrophysiological study (EPS), respiratory-navigated and ECG-Gated 3D MRI was performed. Typical imaging parameters were: voxel =1.1 mm³ with 2x interpolation in the slice direction, TI=700-800 ms (2RR triggering), flip=25°, TE=2.7 ms, FOV=300x220 mm, BW=200 Hz/pixel, matrix=272x200, requiring 15-18min. Early (<5 min post-injection) and Late (>15min post-injection) Gadolinium-Enhanced (EGE, LGE) imaging were also performed. Five swine were sacrificed after acute MRI (Group A). The other 6 swine underwent EPS, MRI, and sacrifice after 8 weeks (Group B). MRI-determined lesions and gap dimensions were compared with gross pathology.

Results EPS-confirmed acute PV isolation was achieved in all cases. Acute RFCA lesions in the LA and PV ostia were detected with non-CE T1w MRI (Figure). In Group A, the MRI-determined lesion widths correlated with those of gross pathology (r²=0.93, p<0.05), with a slight MRI underestimation of 0.9±0.3 mm. In Group B, 12 gaps (2.0±0.9 gaps/ PV) were detected acutely with non-CE T1w MRI, while only 3 were detected with EGE and none with LGE. EPS 8-weeks post-ablation revealed PV reconnection at 11 sites in 5 swine, with locations matching those of gaps seen acutely in non-CE T1w (92%).

Conclusions Non-CE T1w MRI acutely identifies RFCA necrotic lesions in swine LA and PV ostia, accurately detecting gaps associated with locations of chronic PV reconnection. The method provides valuable acute verification of RFCA treatment. It can be repeated intra-procedurally as needed since contrast agent is not administered.

Figure. A-F swine #1 results; A,B: Non-CE T1w MRI showed enhanced RFCA lesions (red arrows) in swine RSPV ostium. C: Volume rendering of T1w showed enhanced continuous lesions with one gap. D: Ablation points on navigation system did not show a gap. E,F: RFCA lesions and gap dimensions in T1w (E) were similar to those in pathology (F). G-I swine #2 results; A gap (red arrow) in anterior PV was detected in T1w (G) and EGE (H), but not in LGE (I).

Ao indicates aorta; LAA, left atrial appendage; RA, right atrium; RSPV, right superior PV.

Intramyocardial injections guided by active MRI-tracking for regenerative therapy

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Background or Purpose
Regenerative therapy for the treatment of heart failure is a promising prospect that could provide major benefit to millions of patients. It also poses a unique set of challenges with regards to not only the underlying biology of specific cell types, but also in terms of delivery and retention of therapies in the myocardium.

Late-gadolinium enhancement on cardiac MRI is considered the gold standard for assessment of myocardial infarction. However, MRI is rarely used to guide intramyocardial therapy. MRI has important advantages over the currently used delivery methods in terms of accuracy, reproducibility, independency of patent coronary arteries, and exposure to ionizing radiation.

Within the MIGRATE consortium we collaborated to develop an actively-tracked steerable MRI compatible injection catheter compatible with a new, MRI visible biomaterial. Here, we report on the feasibility of MR-guided delivery of biological therapies to the heart in four healthy pigs.

Methods
The injection catheter was adapted from an existing electrophysiology ablation catheter created by Imricor. It has active tracking capabilities with integrated receiver coils and a deflectable tip for accurate steering. The catheter was used in a 1.5T MRI equipped with the Philips iSuite iMRI platform. A supramolecular hydrogel, developed by the TU/e, was used for the injections. For this experiment the hydrogel was crosslinked with dotarem for MRI-visibility.

For active tracking a 3D-roadmap scan was acquired prior to the intervention. A 3D-shell of the endocardium was created in ITK-SNAP. During active tracking the interventional software platform displays the catheter location on the proper scan planes and renders a model of the catheter tip inside the 3D-shell. Passive visualization was performed using 2D balanced TFE sequences with a framerate of 2-5Hz.

Results
After induction of anesthesia the pigs were transferred to the MR-room. The catheter was introduced via the femoral artery. Under active tracking we could successfully pass the catheter retrogradely towards the left ventricle and through the aortic valve. Handling of the catheter under active tracking was intuitive and allowed us to inject at desired locations.

Ex-vivo MRI-scanning of the excised heart confirmed successful injections at several of the expected locations. However, not all injections could be identified. This could be caused by unsuccessful injections (potentially due to the novel nature of the technique) or by incomplete retention of the hydrogel.

Conclusions
iMRI-guidance of intramyocardial injections is feasible. The combination of active and passive tracking allows intuitive catheter handling as well as real-time confirmation of injection success. Adoption of interventional MRI for application of therapy could potentially be an important step forward to boost effectiveness of regenerative therapies.

This work was conducted with financial support of the NHS, ICIN- Netherlands Heart Foundation and partners of the MIGRATE consortium.
Status-quo and demands for MR-guided endomyocardial biopsies

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Background Minimal-invasive endomyocardial biopsies (EMB) play an important role in clinical diagnostics for heart diseases and to test for transplant rejection. In daily routine the procedure is guided under X-ray fluoroscopy or echocardiography, entailing several disadvantages like ionizing radiation, application of nephrotoxic contrast agents, and deficits in exact determination of the instruments’ spatial position. The high soft tissue contrast and discretionary slice positioning of Magnetic Resonance Imaging (MRI) outweigh the expense of developing new MR compatible instruments and routines. In general, visualization of instruments for interventional MRI can be divided into passive, semi-active, and active tracking methods [1]. While active tracking requires special set-ups, passive and semi-active methods can be used in any available MRI system and thus, are more flexible [1]. Until now, standard biopsy forceps are mostly metallic and given the length required MR Unsafe due to radio frequency heating [2]. Recently, basic feasibility of MR-guidance for EMB has been demonstrated [3]. Yet, only MR Conditional instruments for clinical use are available, such as core biopsy cannula (Somatex, Invivo) and guidewires (EPflex). Since the latter has been CE marked the objective of the joint project MR-Biopsy is the development and evaluation of a flexible MR Safe biopsy forceps to realize MR-guided EMB.

Methods At first, a design was realized that allows the production of the biopsy jaws made of non-magnetic, non-metallic, and non-conductive materials to fulfill the ASTM/ISO terminology of MR Safe. However, polymer or ceramic materials lack from adequate visibility in MRI. Thus, to investigate passive and semi-active tracking the instrument has been equipped with the respective markers and tested in different MRI systems (1.5 and 3 Tesla GE, Siemens and Philips). Standard and real time cardiac MRI sequences will be used to determine the best configuration for the desired application. For intensive ex-vivo analyses a detailed and realistic phantom of the vessel system from the femoral artery/vein access up to the heart has been modelled and manufactured. Therefore, segmented anonymous medical imaging data of patients serve as blueprint for 3D printing. To evaluate the forceps, a replaceable fresh porcine heart will be integrated into the phantom (Fig. 1). Later, in-vivo investigations will be carried out accordingly.

Results A first prototype has been produced from non-ferromagnetic polymers and composites. Special attention has been given to important specifics like sharpness of the applied material, low friction coefficient, and corrosion resistance. Additionally, the geometric properties of the biopctome design has been adapted for EMB via femoral access with usage of a guiding catheter. Compared to standard metallic forcipes the length of the jaw has been reduced by approximately 50% and the opening angle has been increased by 50%.

Conclusions To establish a novel MR Safe EMB forceps thorough investigations have been carried out and the first prototype has been realized. Further in-vitro studies are currently conducted to prove the applicability in terms of reproducible biopsy quality and reliable MR guidance. Another task is to implement a clinical workflow for MR-guided EMB, comprising optimized MR sequences, MR operation, intra-interventional communication, and patient safety.

References
Background. Magnetic Resonance Imaging (MRI) provides excellent soft tissue contrast while avoiding ionizing radiation issues. However, MRI-guided techniques are still limited by the lack of dedicated MR guidewires with appropriate mechanical properties. Conventional tools for X-ray-based fluoroscopy are made of ferromagnetic stainless steel or Nitinol, which are not suitable for the MRI environment. A new non-metallic, fiber-reinforced MR Safe guidewire portfolio has been used in several in-vivo MRI-guided radiological and cardiac interventions. In particular, the MR guidewires were tested during an extensive animal experiment for endovascular navigation and stent implantation using real-time MR imaging (1). The study demonstrated good results in terms of MR visualization and handling. In this study, the flexural rigidity of these MR guidewires (0.035” standard, 0.035” stiff, 0.014” micro) was measured and compared to standard commercially available guidewires for X-ray-based angiography.

Methods. The MR Safe guidewires portfolio (MaRVis Interventional GmbH, Frechen, Germany) was compared to the 0.035” standard, 0.035” stiff, and 0.018” Terumo Glidewire (no 0.014” Glidewire is available). The flexural rigidity was measured 10 times for each wire type. The results were compared to data from the literature for the standard 0.032” Terumo guidewire.

Results. The data calculated from the literature (2) for the standard 0.032” Terumo guidewire (mean flexural rigidity of 9.00E-05 Nm^2) is close to our measurement for the 0.035” Terumo, and confirms the validity of our measurements (Table 1). The flexural rigidity of the standard MR guidewire is of similar order of the corresponding metal wire. The metallic stiff wire is slightly stiffer, yet the clinicians who tested the wire in-vivo (1) confirmed that even if the MR guidewire felt less stiff, the difference in handling was negligible. Finally, the 0.018” metallic wire is stiffer than the 0.014” micro MR guidewire. However, having a larger diameter, the Terumo 0.018” wire was expected to have somewhat higher mechanical properties than the 0.014” MR guidewire.

Conclusions. Guidewires must have appropriate flexibility to allow for navigation in tortuous segments of the cardiovascular system. High stiffness may damage the vessel; floppy guidewires provide insufficient catheter support. The results showed that the MR guidewires present suitable flexural rigidity, comparable to the widely used Terumo Glidewire and match the requirements for use in MRI–guided endovascular interventions. However, further mechanical parameters, such as pushability, torquability, and tensile strength, should be investigated.

Table 1: Flexural rigidity of the Nitinol and MR guidewires

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<td>9.35E-07</td>
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References
Title: Intra-arterial delivery of bevacizumab for treatment of glioblastoma - first-in-human endovascular neurointerventions under real-time MRI guidance

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Background or Purpose Fluoroscopy, digital subtraction angiography (DSA) and 3D reconstructions of rotational angiograms are fundamental to practice interventional neuroradiological procedures. These X-ray based techniques accurately depict the intracranial vessels and allow for safe microcatheter navigation into distal intracranial arteries. Although its ability to visualize small vessels with high flow is enough to treat vascular malformations, when considering the slow parenchymal blood flow in brain tumors, its sensitivity is often not enough to document their supply and perfusion. MRI is a much more potent tool in visualizing tumors and brain tissue and is very sensitive in terms of flow detection even at very low speeds.

Methods We performed two procedures of intra-arterial drug delivery to recurrent glioblastoma under real-time MRI guidance. 39-year-old female with history of glioblastoma in the left parietal area treated with surgery, chemo- and radiotherapy in the fall of 2015, two years later presented with aggressive butterfly-type regrowth of the tumor in splenium of corpus callosum. Due to lack of therapeutic options and very fast growth of the tumor, we decided to treat her with intraarterial delivery of bevacizumab after BBB opening with hyper-osmotic mannitol. Digital subtraction X-ray angiography, failed to characterize precise tumor supply, showing faint to no distinct tumor blush with iodine contrast. We injected diluted gadolinium through microcatheter to visualize perfusion of the tumor and adjacent brain volumes under real-time MRI. During the first procedure we positioned microcatheter in right PCA, during second procedure (four months later) in the left PCA supplying largest regrowth area. Using various speeds of injection, we obtained significantly different tumor perfusion parameters. It enabled the modification of the subsequent drug infusion rate and improved biodistribution of therapeutic agent in the tumor, adding precision to intra-arterial drug delivery.

Results For the first time we were able to delineate in real-time MRI both brain tissue and tumor volume supplied by the microcatheter in the cerebral artery. We also demonstrated that a change in infusion speed deeply affects the brain territory supplied by the microcatheter, as well as the tumor. We assume that peak enhancement of tumor areas predicts peak concentrations of the subsequently administered drug. Importantly, the procedure was safe and no complications were observed.

Conclusions We have begun the translation of real-time MRI guidance of endovascular neurointerventions from bench to bedside. Intra-arterial infusion of bevacizumab after BBB disruption may provide symptom relief and initial efficacy in patients with recurrent glioblastoma. The application of drug under real-time MRI guidance added precision to the procedure and may further improve treatment outcomes of this deadly disease. Ongoing development in MRI infrastructure, software, and new MR-compatible devices will fuel the use of this MRI-guided approach and future applications will likely extend beyond neuro-oncology.
References


Towards the switching of an MRI-guidewire between configurations for imaging and active tracking via the photomechanical effect

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Background We propose a new concept for switching an endovascular imaging antenna on a single receiver channel between electrical configurations for imaging and tracking by utilizing the photomechanical effect. The imaging component of the probe consists of a loopless dipole antenna and a micro-coil is placed at the distal end of the antenna in order to actively track the tip. By utilizing a photomechanical liquid crystal elastomer (lce) or other material, at the tip of the probe and illuminating it with light through an optical fiber, the photomechanical material expands or contracts, which removes a conductor from the circuit. When all of the conductors are electrically connected, then the micro-coil at the tip of the probe is in electrical communication with the scanner and can be used for active tracking (Fig.1a). When the probe reaches the target vasculature for imaging, the actuation of the photomechanical material removes a conductor from the circuit, disengaging the micro-coil. The act of disengaging the micro-coil places the probe in an optimal, tuned imaging configuration (Fig.1b).

Methods We tested the imaging and tracking configurations by constructing a loopless dipole antenna and a related probe with a tracking micro-coil at the tip (Fig.2ag). Both probes were tuned/matched (S11<−20dB) and identical T2-weighted, FSE images on a 1.5T Philips scanner with 1x1x2mm³ voxels were acquired with each probe inserted into the center of a cucumber (Fig.2b). Multiple coronal and axial slices were captured to image the entire cucumber. Active tracking scans were run using I-suite to rapidly track the micro-coil at the tip.

Results Images using the tuned antenna are superior in SNR and have a larger, more uniform imaging coverage compared with the tracking probe. Tracking tests resulted in accurate calculation of the tracking coil for the tracking prototype.

Conclusion Imaging results support the need to disengage the micro-coil when using the antenna to image. In fact, the inferior imaging coverage was expected from the tracking probe since it is essentially a looped coil. Alternative to the single receiver channel probe described here, having an imaging and tracking probe with separate receiver channels is possible [1], but this inevitably introduces an additional micro-coaxial cable which adds significant dimension to the cross-sectional area. As shown in Fig.1cd, the proposed design has a total of 7 layers (3 dielectrics, 1 optical fiber (≈10µm), 3 conductors) and the minimal requirement for a probe with a tracking coil at the tip and a dipole antenna on separate receiver channels is 11 layers (6 insulators, 5 conductors). This design and concept will allow for an active tracking and imaging MRI-guidewire with a diameter between 0.01-0.014” for navigation to distant narrow vasculature, potentially for direct imaging of the thrombus in ischemic stroke, and venous and arterial (coronary) occlusions. Recent work with fast-action micro-lce’s shows that the size and response requirements of this probe can be met [2]. References [1] Kocaturk, Ozgur et al. "An Active Two Channel 0.035" Guidewire for Intervent. Cardiovasc. MRI.” Journal of magn. resounan. imag. : JMRI 30.2 (2009): 461–465. [2] Zeng, Hao, et al. "Light-Fueled Microscopic Walkers.” Advanced Materials 27.26 (2015).

Figure 1: Schematic of tracking (a) and imaging (b) configurations.blue = optical fiber, yellow= photomechanical material. Schematic cross-section (c) of (a-b) compared with probe (d) with antenna and tracking coil on separate receiver channels—assuming minimum number of layers of conductors and dielectrics.

Figure 2: Tracking (top) and imaging dipole antenna (bottom) prototypes (a). Axial slice through cucumber (b). Coronal (c,d) and axial (e,f) images of cucumber with tracking (c,e) and imaging (d,f) probes. Overview (g) of probe and cucumber showing the insertion depth of the probe. ND Poulin was funded by a grant from the Suzanne and Walter Scott Foundation.
Dedicated 3-Channel Surface Coil for Interventional Magnetic Resonance Imaging at 3T - First Evaluation

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Background

Interventional magnetic resonance imaging (MRI) at 3 Tesla is beneficial for a variety of procedures. In order to gain sufficient access to and maintain sterility of the interventional site, a flexible surface coil with a low profile and wide central aperture is desirable. We developed a dedicated 3T interventional MRI coil with 3 receiver channels and a wide central aperture, which we benchmarked against a 4-channel system surface coil.

Methods

We obtained institutional review board approval and informed consent from all participating subjects. All experiments were performed on a commercially available wide-bore 3T MRI system. We assessed signal-to-noise-ratios (SNR), geometry (g)-factors and instrument artifact size in a phantom and 100 subjects. The artifact size of a 20 gauge interventional needle was measured and compared at 4 different angulations relative to B0 using a high-bandwidth TSE pulse sequence. In 10 volunteers, SNR and CNR of various tissues were measured for various interventional TSE-based pulse sequences. Finally, the interventional MRI prototype coil was used in 100 subjects for a wide variety of interventional procedures. The interventional MRI prototype coil was benchmarked against an FDA-approved 4-channel system coil that had multiple small openings through which devices can be passed.

Results

The interventional MRI prototype coil produced similar SNR values and g-factors than the 4-channel system coil. There was no significant difference in artifacts, which were suitable for accurate and safe procedures. There was no visible loss of signal near the aperture of the interventional coil on interventional MR images. The interventional prototype coil improved access and performed error-free during a large variety of interventional MRI procedures (Figure 1).

Conclusions

We developed a dedicated coil for interventional MRI at 3 Tesla that has similar image performance characteristics than a diagnostic 4-channel system surface coil. The customary design with wide central aperture provides improved access to and ensures sterility of the interventional site.

References

Interventional Coil Design: Towards Disposable Coil
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Background or Purpose:
Commercial available coils are not optimal for interventional procedures due to their lack of flexibility and handling. Although Printed-Circuit-Boards (PCB) can be manufactured as flexible structure, lumped components are still required for Tuning/Matching and decoupling the probe. Soldered components reduce the flexibility of the PCB. Furthermore, they introduce susceptibility artefacts, which have to be encountered by thicker isolations increasing its cost. The following study presents a minimal coil design, which overcomes these limitations. This design can be seen as a first step towards disposable coils.

Methods:
The principal function blocks of a state-of-the art receive coil include the Matching/Tuning- and decoupling circuitry. Both are located directly on the loop, which contradicts the paradigm of a flexible and simple design. Introducing distributed capacitances by overlapping copper traces (Fig.1) allows the maximization of signal transfer from the coil, which replaces the Matching/Tuning circuit. This technique is well suited for flexible material as the resulting capacitance is scaled by its thickness. The “self-resonant” design cannot be detuned by inserting additional tank circuits anymore. Therefore, current suppression was applied to decouple the coil during transmit mode. The corresponding circuit is shown in Fig. 2. For the receive mode the PIN-diode is reverse biased and the coil is preamplifier decoupled, although it is just a one-channel design. During transmit the PIN-diode is forward biased. The resulting tank-circuit in combination with the cable length (approx. \( \lambda/2=80\text{cm} \)) suppresses the current in the loop.

A GRE-sequence with TE/TR=10/300ms was used to acquire MR images at a 3T scanner (Skyra, Siemens, Erlangen). The phantom consisted of a jelly filled puppet, with human like electrical parameters and geometric dimensions.

Results/Conclusion:
The implementation of the Flex Coil-Design is shown in Fig 3. (left) with the radius \( r=5\text{cm} \), trace width \( d=6\text{mm} \). Changing the degree of overlapping turned out to be a feasible method to tune and match the coil as shown in Fig 3. (middle). No \( B_1 \)-modulation was observed during the imaging, which demonstrates the functionality of the decoupling concept. We demonstrated an interventional coil design, which could lead to disposable receiver coils.

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Background or Purpose:
One of the major limitations during IMRI procedures is the lack of interaction with the scanner within the cabin. Physicians have to use MR-safe control panels, which are often unavailable, unintuitive or provide not enough input options. Alternatively, interaction tasks are delegated to an assistant outside the scanner cabin verbally or by hand signs. This workaround requires a well-rehearsed team high level of experience, which is very sensitive to team changes.

Methods:
Hardware: The whole system setup for the MR compatible gesture controller is depicted in Fig.1. The hardware concept involves a commercial available gesture controller (Leap Motion Inc., San Francisco, USA), and addresses two problems, which represent important limitations during interventional procedures:
- image quality degeneration: The outcome of each interventional procedure depends strongly on the available image quality. Therefore, radiated interferences are minimized by converting the USB-Dataflow to fiber optic cables.
- device’s functionality: During imaging, voltage spikes can be induced on the line, which causes the electronic to shut down. To avoid this a surge-filter (Würth Electronic, Niedernhall, Germany) and shielding of most components was implemented.

The degeneration of image quality was evaluated at a 3T-scanner (Skyra, Siemens, Erlangen) and a dedicated sequence, which acquires N=1500 noise spectra with a resolution of 61Hz/Px over a bandwidth of ±500kHz. The measurement was conducted for the scanner intern body coil and spine coil array.

Software: In cooperation with clinical expert’s certain commands were identified, which have to be available during an intervention. These included sequence selection, activation/deactivation, quality/time and image windowing, plane orientation (parallel/perpendicular) and Translation/Rotation. The implemented user interface is shown in Fig.2 and can control the scanner remotely (SRC, Siemens, Erlangen).

Results:
The results of the interferences evaluation are shown in Fig.3. The increase of noise for the body coil is approx. 8% but negligible for the spine array. Gestures are recognized very robust by a commercial controller. This enables the developer to implement two level entry confirmations f.ex. the user must navigate to the holding the gesture.

Conclusions:
We presented a fully MR compatible gesture controller with dedicated user interface to assist during interventional procedures. A two-level entry confirmation is increasing the reliability by avoiding false inputs. The system showed no image quality degeneration for surface coil arrays, which are normally used during interventions. We believe that control of MRI sequences and image planes using an in room MRI-safe device will save time, reduce communication errors and result in a safer, less stressful experience for the patient and the physician.

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Fig. 1 Hardware setup of the gesture controller. The communication protocol of the transceiver required a USB2.0/3.0 converter (both: (LINDY-Elektronik, Mannheim, Deutschland)

Fig. 2 User interface for interacting with the scanner by gestures.

Fig. 3
EasyJector – a lightweight, inexpensive, easy to use MRI injection system  
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**Purpose:**  
For better visualization and differentiation of target structures in MR imaging a contrast agent can be injected into the patient. Currently used injectors still have MRI compatibility and usability issues [1]. They are large, heavy and come with high purchase and running costs due to preparation afford and expensive consumables. Safety is critical in these systems since patient-to-patient contamination could not be excluded. We introduce a new concept for a portable, low cost, MRI-compatible and easy to use system for contrast and saline injection (EasyJector).

**Methods:**  
Based on clinical observations and consultations of surgeons and medical technical assistants (MTAs), the clinical needs were identified and specified. For the injector, a general concept was designed following a structured design process. The basic requirements for an MRI injector are determined by flow rate (~1-2 ml/s) and injection volume (~0.2 ml/Kg) [2]. A double cylinder design allows the use of prefilled cartridges for contrast and saline solution. These cartridges include a pressure reservoir to drive the injection with a constant flow rate. Thus, no additional motor is needed that leads to a unique MRI compatible, light weight and portable design.

To realize a MRI-compatible triggering mechanism, a new nitinol wire based switch combined with a wireless transmission was developed. Electronic components (power supply, control module) were reduced to a minimum with a focus on high MR compatibility. Beside the electronics, all parts of the injector are made for single use application.

A manual air removal during the preparation of the patient is implemented by a specific vent button. Despite the simple design, a “keep-vein-open” function (20 ml/h) is realized. The system was set up as a prototype. The flow rate, the reliability, energy consumption, usability and MRI-compatibility of the whole system were tested.

**Results:**  
The EasyJector provides an overall size of 140 x 80 x 50 mm and a filled system weight of 280g. This allows placement of the system directly on the patient’s arm leading to a reduced tube length (15 mm) and increased usability (see Fig.). The low weight and size of the injector does not restrict the patient’s movement at any time. The contrast agent can be injected with a constant flowrate of 1ml/s or 2ml/s powered by the pressure reservoir of the cartridge. The saline solution runs in parallel with a flowrate of 20ml/h for "keep-vein-open" function. The internal activation is acting through a nitinol wire that works reliably with a delay of 2.5 sec and can be performed more than 50 times with one battery pack according to previous tests. For remote control a tablet based application and wireless transmission is planned.

The small and light weight design comes with a highly improved workflow. Even patient preparation outside the MR cabin is possible. Preparation time per patient can be shortened to 3-5 min. A vent mechanism by a simple button allows reliable air removal of the hoses.

Tests of MRI compatibility proved safety for the patient and no influence on imaging.

**Conclusion:**  
The proposed injector design offers unique usability and cost effectiveness. The single use concept for all parts with patient contact guarantees a high safety level and avoids patient to patient contamination. The overall cost per injection is estimated to be in the order of <25% compared to standard machine injections.

**References:**  


**Keywords:** Injector; MRI; contrast agent; nitinol wire
MODULAR LOW-COST AND INTUITIVE SETUP FOR IN-BORE NEEDLE BASED MRI PROCEDURES

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Background. MRI interventions bring advantages over CT and US interventions as soft tissue contrast, anatomic detail, multiplanar capabilities, etc. [1]. Robotic teleoperation has been proposed as main improvement by research centers and companies to overcome iMRI obstacles [2]. Nevertheless, limitations like high acquisition price, manipulation complexity, special training required, sterilization and time inefficiency are still unsolved. In cooperation with radiologists from Otto-von-Guericke University Hospital (Magdeburg, Germany), we identified 3 iMRI problems: complex accessibility to the patient inside the MRI bore, multiple loss of needle alignment during the procedure and ergonomic difficulties for radiologists when manipulating the needle and coordinate the screen visualization simultaneously. We propose a low-cost and intuitive modular set-up conformed by multiple mechanical and electromechanical devices. The modular set-up aims to improve current free-hand techniques for in-bore MRI procedures in terms of comfort and efficiency.

Methods. As initial elements for the complete modular set-up a flexible holding arm (See Fig. 1a) and a disposable needle guide (See Fig. 1b) were prototyped and patented. The flexible arm is designed to fulfill complete MRI compatibility while holding different interventional instruments, e.g. biopsy needles, RF electrodes, etc. in certain positions adapting itself to the space limitation (MRI tunnel, patient and RF coils). The arm is composed by 3 links, 4 joint balls and a universal distal end for different tools adaptation. The components are fabricated with polymer Nylon 6 and elastomers for the locking mechanisms. The arm has a maximum length of 431 mm, a diameter of 53 mm, 6 DOF (degrees of freedom) and a weight of 725 g. The disposable needle guide offers 2 rotational DOF with respect to the needle entry point. The device enables rotations in a range of ± 40 ° in each axis and allows the user to read the adjusted angle from the scale. In addition, the needle guide allows the user to insert the needle longitudinally and laterally. Hence, the disposable needle guide can be placed before or after needle insertion and it maintains and guides the needle stably in any desired alignment. By using a deformable surface, the needle guide can be attached in any position on the patient’s skin. Both devices were evaluated in a MRI scanner (3T, Skyra, Siemens) and a human phantom positioned in supine and prone position. For both devices, defined alignments were stabilized and needles were inserted multiple times to ensure stability and evaluate the targeting precision.

Results. The holding arm reached successfully multiple positions in cranial, vertebral and ventricular cavity. Consequently, the holding arm evidenced potential assistance for needle alignment in periradicular therapy, ablation therapy and biopsies in rigid targets as spine cord, head, joints, arms and legs. The total configuration-time of the arm on the MRI table required less than a minute. In the case of organs affected by motion as liver, lungs, kidneys, stomach, etc. the disposable needle guide offers a better assistance since it moves together with the patient’s breathing motion. As a result, biopsies, drainage and RF ablation procedures are possible to be assisted in the ventral cavity. Both, holding arm and needle guide did not present any artifact nor undesired behaviors due to the magnetic field. Due to the fixed alignment in each device, the user is able to visualize needle movement on the screen comfortably.

Conclusions and outlook. Both the flexible holding arm and the needle guidance device improve significantly free-hand technic in iMRI. Their design is focused on simplicity which allows simple and low-cost manufacturing practices for their fabrication. Consequently, both devices can be introduced into medical market under significantly lower prices than existing products. The two devices illustrated, together with parallel devices under current development will enable real-time iMRI-Ultrasound fusion procedures to be performed [3].


Figure 1. First prototypes for modular setup in needle based procedures. A: Flexible holding arm; B: Disposable needle guide.
3D-printed, bendable grid marker for interventional MRI
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Background: The visualization of therapeutic instruments is fundamental for its application in interventional magnetic resonance imaging (iMRI) procedures. Depending on the choice of material, MR safe instruments usually are either only indirectly visible due to susceptibility artifacts or hardly visible at all. For the indication of the incision point for minimal invasive procedures (e.g. liver-, mamma- or prostate biopsy) there are different types of instrument alignment grids available on the market. During the procedure, those grids provide an estimation of the grid hole position, which is relevant for the incision point, by an indirect detection process using additional fiducial markers (e.g. gadolinium-capsules or in combination with Z-shaped-markers) that are attached on the grid [1, 2, 3]. With this process it is very hard to estimate the actual grid alignment and grid hole positions. Furthermore the additionally attached markers can block the access to relevant grid holes, which requires multiple iterations of a grid re-positioning at the interventional side [4]. We already presented multiple results about a fiducial marker shaped in a rotational-symmetric or Z-marker-structure which is fully additively manufactured to facilitate precise instrument tracking in iMRI. In the stereolithography fabrication process (SLA) we use only one UV-light sensitive polymer material (SLA-resin) to print a solid and completely enclosed marker body while the internal marker structure remains filled with the same but uncured and consequently liquid and MR-visible resin [5, 6, 7]. In this paper we present our first results about a bendable, printed and fully MRI-visible marker grid.

Methods: The grid marker-model has a total dimension of 100x100 mm² with a five by five hole matrix pattern and an effective grid hole size of 12x12 mm², which is accessible for the instrument; the MR-visible grid hole size was set at 16x16 mm² and the internal grid marker tunnels have a profile dimension of width x height = 2 x 4 mm². For the fabrication of the grid-marker we used the “FLFLGR02-Flexible” SLA-resin (Formlabs Inc.), which allows the additive fabrication of bendable models. After printing, the marker was washed in isopropanol and finally cured in its shape, which serves to print the proper characteristic 3D-structure (voxel size: 0.781 x 0.781 x 0.900 mm³), see Fig. 1 left.

Results: Depending on the desired configuration, the SLA-fabrication process allowed a fast and individual adjustment of the scale of the grid marker dimensions. Using hook-and-loop tapes, it was easy to place the grid marker on the phantom in a bent position, which is typically used for a liver biopsy. The internal marker structures, which are filled with the liquid “FLFLGR02-Flexible” SLA-resin, provided sufficient imaging quality and a full presentation of the complete grid matrix structure, see Fig. 1 right.

Conclusions: With this research we have shown that the additive SLA-process allows the fabrication of a bendable grid pattern in combination with sufficiently visible marker structures, which were integrated during the printing process. Consequently, the bendable grid marker can be taken out of the printer and directly used in the iMRI-application. As before with conventional fiducial markers, there are no subsequent processes necessary for filling and sealing the marker with MRI-visible liquid. This process shortens the fabrication time for precise fiducial markers dramatically in combination with cheap costs (marker material costs = 15 €). Compared to the conventionally used instrument positioning grids, the integration of the fiducial SLA-resin inside the grid marker profile and the full contact to the phantom surface, even on strongly curved surfaces, allows a full access to the interventional side and provides the most available precision for the determination of the incision point. These benefits have the potential to shorten the setup and alignment time for grid markers significantly. For future works multiple SLA-resins will be tested with the focus on higher tensile strengths. Furthermore the grid marker will be tested in combination with an instrument adapter in an interventional workflow.

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Circulation and Hemodynamics in Living Donation of Kidney Transplantation in Children - The CHILD-KiTC Study: MR Arterial Spin Labeling in pediatric KTx

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Background or Purpose In pediatric kidney transplantation with a living adult donor, donor-recipient size mismatch is hypothesized to cause loss of donor kidney mass and function over time through relative hypoperfusion of the adult donor kidney. Adult sized kidneys demand large physiological changes in the recipient in terms of blood flow and blood pressure. By noninvasively assessing flow and perfusion of the graft using MR Arterial Spin Labeling (ASL)[1, 2], before and after transplantation, we want to enhance knowledge and insight in hemodynamic response after pediatric kidney transplantation with a living adult donor.

Methods Twenty children with a maximum age of 15 and a maximum body weight of 40 kg will be included in this prospective clinical pilot study with a follow-up of 12 months. The study protocol has been approved by the ethics committee and the first patients are scheduled for the beginning of July 2018. Donor kidney perfusion will be measured the day before and immediately after the transplant, with recipients still under general anesthesia. Cardiac output will be measured with Transpulmonary Thermodilution (TPTD) and Esophageal Doppler (ED), aortic and renal artery flow will be assessed using intra-operative Doppler ultrasound. Renal graft perfusion will be measured with MR ASL at our hybrid operating theatre.

Results Results of hemodynamic measurements will show whether recipients will adapt to a supraphysiologic state. Changes in cardiac output, renal artery flow or graft perfusion will be quantified and correlated with clinical status, graft function and graft survival. Results will also show whether Doppler ultrasound and/or ASL MR proves to be a more reliable and less invasive alternative for the monitoring of donor kidney perfusion in children than current alternatives[2].

Conclusions Suboptimal renal graft perfusion due to inadequate hemodynamic adaptation increases the risk of loss of renal graft mass and function. By enhancing knowledge and insight in hemodynamic response after pediatric kidney transplantation with a living adult donor, our study helps optimize post transplantation monitoring and treatment protocols, while possibly providing clinicians with a reliable and non-invasive method of monitoring donor kidney perfusion in children.

References
Real-Time Closed-Loop Scan Control for Interactive MRI Guidance

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Background
Image-guided percutaneous ablations are widely practiced as an alternative to surgical resection in the liver, kidney, and other organs, especially for those who are not candidates for complete resection due to a poor physiologic condition. Intraprocedural MRI provides excellent soft-tissue contrast and ability to visualize thermal effect from ablation; hence it is considered an ideal imaging modality to guide and monitor ablations. Typically, those procedures require a repetitive in-scan-out/adjustment technique [1], where the patient is moved into and out of the gantry for imaging and probe placement, due to the lack of interactive and real-time imaging. However, this technique is cumbersome and can lead to prolonged procedure time. While active tracking has been developed to address this challenge [2], it would require specially-designed probes and MR pulse sequence to achieve real-time tracking. The goal of this project is to develop a real-time imaging for probe tracking by continuously aligning the scan plane with the probe detected in the previous images. In this preliminary study, we assess the feasibility of a new real-time interactive MRI interface that allows external software to remotely control the scanner over the network.

Methods
This study is performed using a 1.5 T MRI scanner (MAGNETOM Aera, Siemens, Germany). A proprietary API (Scanner Remote Control (SRC), Siemens, Germany) was used to establish a network communication between the MRI scanner and an external computer running medical image computing software, 3D Slicer (Version 4.9.0) [3] via Ethernet. The interface allows retrieving information, changing the state of the scanner, and transferring real-time images using a JSON based network protocol. A custom plug-in module for 3D Slicer that remotely controls the scanner was implemented using the Python language. The module calculates the slice positions and orientations of three orthogonal planes along and perpendicular to the needle detected on the previous images, and send them to the MRI scanner. To validate the mechanism, a phantom experiment was performed using a phantom made of gel wax. After placing the phantom in a head coil in the gantry, an 18-gauge biopsy needle as a mock ablation probe is inserted into the phantom. An initial multislice T2 image was acquired using a turbo spin echo sequence and loaded to the 3D Slicer, where the volume was re-sliced along the probe, and the new scan-plane was computed. The position and orientation of the new scan plane were then sent from the 3D Slicer to the MRI scanner via the interface. Then the scanner acquires 2-dimensional real-time images from the prescribed scan plane continuously using a real-time interactive sequence (BEAT_interactive, Siemens, Germany). To test whether the real-time MR images were acquired along the intended scan plane, the images were compared with the initial T2 image re-sliced at the prescribed imaging plane.

Results
The real-time MRI images matched well with the re-sliced initial T2 images. The images from the real-time MR scan matched well the actual scan-plane image. (Fig. 1).

Conclusion
We presented an MRI-closed-loop scan-plane control to an MRI scanner. The proposed system allows controlling the MRI from an external PC and updating the scan plane to the desired position. Further experiments will be required for the evaluation of latency for clinical use.

Acknowledgments
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References

Fig. 1. Re-sliced initial T2-weighted MRI at prescribed scan plane along a needle (left) and real-time MRI acquired at the corresponding scan plane (right).
1913 image-guided procedures have been completed in the Advanced Multimodality Image-Guided Operating (AMIGO) suite since 2011. MRI, PET/CT, angiography, and/or ultrasound are used alone or in combination by surgeons, interventional radiologists, and radiation oncologists to visualize the intra-operative state of targeted tissues. Navigation technology is used to guide surgical instruments to targets within the patients, using minimally invasive concepts. FDA approved, commercially available navigation systems are used extensively in AMIGO for MRI-guided procedures such as brain tumor resection, placement of electrodes for deep brain stimulation, and for laser ablation of brain tumors. For research, we combine these FDA approved systems with 3D Slicer, an open and extensible software platform (for use under IRB approval). We use 3D Slicer for research in MRI-guided breast conserving surgery, endocrine surgery, pelvic biopsy and brachytherapy, and soft tissue tumor ablation in the body and head and neck areas.

Numerous Deep Learning based methods from the Computer Vision and Machine Learning literature are directly applicable to image analysis in MRI-guided interventions. Deep convolutional networks can be used for the segmentation of targets such as tumors and surrounding structures of interest. This benefits surgical planning and visualization during intra-procedural navigation. In addition to leveraging existing methods, we are investigating novel algorithmic approaches using deep learning based solutions for passively tracking or segmenting instruments from intraoperatively acquired MRI. We have optimized a fully convolutional neural network architecture for automatic segmentation of biopsy and brachytherapy needles from several hundred T2-weighted MRI images from AMIGO procedures. The resultant accuracy is higher than alternative approaches and well within the clinically acceptable range for intervention, and we are continuing to explore extensions to other surgical instruments including ablation probes.

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Novel MR Imaging Techniques and Their Implications for iMRI

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Introduction In iMRI, imaging techniques are used that either provide good anatomical contrast to visualize tissue morphology and instruments, or functional imaging methods that are employed to quantify functional changes during the intervention. In contrast to conventional diagnostic MRI, during iMRI all these techniques underline a strict time limit: anatomical information must be presented in real-time when instruments are advanced to the target organ, and the results of a functional measurement should be available with only a short latency. With the advent of new MRI techniques the question arises which of these novel techniques has the potential to improve or even revolutionize IMRI procedures. As the novel imaging methods are often slow, because the optimal acquisition strategy for a given clinical problem is still under investigation, the potential advantages of the new techniques have to be weighed against the additional time needed for the acquisition. In this presentation, four new MRI techniques will be discussed that could improve MR-guided interventional procedures, and strategies to speed up imaging process will be presented to seamlessly embed these techniques into an intervention workflow.

4D Flow Quantification Dynamic ECG-gated phase contrast (PC) flow measurements can provide time-resolved information about the flow velocity vectors in complex vascular systems [1]. Based on the flow measurements, streamlines can be calculated, and functional information about flow vortices and wall shear stress can be extracted. This information is very valuable not only in a diagnostic context, but may also be used to directly assess the outcome of an interventional procedure. For example, the change in flow velocity patterns and values after placement of a vascular stent can be detected and quantified with 4D PC MRI. Currently, image acquisition times for 4D PC MRI are on the order of several minutes, which can be reduced if only smaller sections of the vasculature are studied.

MR Fingerprinting (MRF) The method of MRF aims at characterizing tissue MR properties via pseudo-random variations of the acquisition parameters and a comparison of the signal response with a database (dictionary) [2]. Thus, the relaxation times T1 and T2, the spin density, local off-resonance frequencies and RF inhomogeneities can be assessed in a single acquisition. MRF can be accelerated using rapid acquisition techniques such as spiral acquisitions. An interesting use of MRF in iMRI could be the measurement of temperature changes, as both T1 and off-resonance frequencies can be detected simultaneously [3], which are both dependent on the local temperature. Furthermore, MRF could provide more quantitative results about the change of tissue properties (e.g., after an embolization).

Chemical Exchange Saturation Transfer (CEST) MR spectroscopy provides information about biochemical processes in living tissue, but MRI is rarely used in clinical practice due to the low SNR and the long measurement times. With CEST, the spectroscopic information from the biological molecules is amplified via multiple proton exchange processes with the tissue water [4]. Thus, metabolic maps can be generated with a spatial resolution comparable to that of conventional MRI. CEST requires multiple acquisitions with different spectral offsets to acquire a so-called z-spectrum, in which the different molecules can be identified as characteristic asymmetries. In iMRI, CEST could be used to measure the delivery and uptake of specific molecules – for example, the cellular metabolism of glucose could be identified with rapid glucoCESTMRI acquisitions to identify metabolically active tumor regions [5] during an intervention.

X-nuclear MRI MRI and MRS with nuclei other than 1H has a long tradition in fundamental research, but clinical use of these so-called X-nuclei is limited due to the need for special RF hardware, ultra-short TE acquisition techniques and low SNR caused by the low natural abundance. However, X-nuclear MRI has the potential to measure cellular vitality with 23Na-MRI, the oxygen metabolism via dynamic 17O-MRI [7], or the cellular energy balance through 31P MRS [8]. Thus, X-nuclear MRI could provide valuable information during an intervention. The low SNR could be overcome by integrating local X-nuclear RF coils into the devices so that local measurements in the interventional target regions can be performed, or by injecting isotope-enriched substances to increase the spin density of the X nuclei.

Magnetic Resonance Imaging (MRI) provides exquisite soft tissue contrast due to a wide array of physical and physiological contrast mechanisms. However, the underlying tissue properties affecting the images are rarely mapped quantitatively, due to inefficiencies in the mapping experiment, and difficulties with issues such as accuracy, precision, and availability of normative and clinical data. MR Fingerprinting (MRF) is a platform technology for quantitative tissue property mapping by MRI (1,2), and was developed in response to some of these issues. Initial applications of MRF were in relaxation time measurement, though multiple other extensions into mapping other properties of interest are now emerging. In this talk, I will briefly discuss the MRF relaxometry experiment, initial clinical applications with a particular focus on prostate, and potential areas of impact/interest for the MR-guided intervention community.


Navigated MRI-guided liver biopsies in a closed-bore scanner?

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Purpose: The aim of this work was to show how virtual navigation supports biopsies in a standard, closed-bore diagnostic MRI-scanner environment.

Background: MRI allows visualizing lesions that cannot be reliably detected with computed tomography or ultrasound. MR imaging-enhanced fluoroscopic real-time guidance is highly favourable to effectively place the needle especially in motion affected organs like the liver. The major limiting factor of using closed-bore MRI scanners to perform this technique is the reduced access when the patient is in the magnet. The use of dynamic MR-sequences as fluoroscopy for instrument guidance is not feasible in most cases. Even wide-bore scanners with a bore size of 70 cm often do not allow for comfortable MR fluoroscopy and scanners with magnet lengths as short as 125 cm have been discontinued by the vendors.

On the other hand, diagnostic high-field MRI systems with powerful imaging capabilities are widely available. As manipulation of the instrument inside the scanner under MR fluoroscopy is not feasible other solutions have been reported. In a simple but potentially time-consuming or even harmful method, the interventional radiologist (IR) defines the cutaneous access point and needle orientation and then approaches the lesion by iteratively controlling and readjusting the needle position inside and outside of the magnet, respectively (1).

Methods: An add-on navigation system outside of the magnet represents a more refined solution. A fast automated registration helps to provide a smooth workflow and accurate targeting. The combination of diagnostic image quality and high frame rates provides good hand-eye coordination to navigate and insert the instrument outside of the bore (2). If the target organ is not motion affected, the trajectory can be defined by navigation and then fixed in a dedicated needle holder. In moving organs, a different strategy has to be performed. The biopsy device is inserted outside of the bore after dedicated breath-hold training. This ensures comparable depth of breath-holds between imaging and puncture procedure. A highly flexible, sterilizable instrument holder stabilizes the needle at the patient’s skin to avoid dislocation while allowing a certain movement to prevent organ injury. At any time, the patient can be moved into the scanner for control imaging. Currently the application was integrated more deeply in a new 1.5T MRI-environment which spares time-consuming preparation and setup in comparison to the former mobile system.

Results: Targeting accuracy, procedure time and user experience were evaluated in 240 experimental MRI-guided biopsies in a non-moving phantom. 24 users with different experience in image-guided procedures (experienced IRs, residents and students) had a 92% success rate to reach a target of 8mm diameter in a 20cm phantom. Interestingly residents had the same success rates as experienced IRs. The mean procedure time for 10 successive biopsies of different targets was 4.5min (3).

The clinical effectiveness of the systems in motion-affected organs was evaluated in 55 liver biopsies in 52 patients. 54 procedures were completed successfully. The workflow and duration of the whole procedure was accurately recorded. No major and four minor complications occurred. Mean tumour size was 23±14 mm and the skin-to-target length ranged from 22 to 177 mm. In 39 cases, access path was double oblique. Sensitivity, specificity and diagnostic accuracy were 88 %, 100%, and 92 %, respectively.

The mean procedure time was 51±12 min, whereas the puncture itself lasted 16±6 min. On average, four control scans were taken (4).

Conclusions: In conclusion, biopsies in both static and motion-affected targets can be performed reliably in a closed-bore MRI scanner with the help of a dedicated navigation device. Even in poorly visible and difficult to access liver lesions biopsies are performed safely with high diagnostic accuracy. The system can be easily implemented in the clinical routine workflow.

References:

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Passive Needle Tracking with Deep Convolutional Neural Nets for MR-Guided Percutaneous Interventions

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Purpose. During percutaneous interventions knowledge of needle position and orientation is crucial to get effective diagnostic (e.g. biopsies) or therapeutic results (e.g. thermal ablation). Automated needle tracking approaches are anticipated to reduce the duration of percutaneous interventions, due to the reduction of manual slice positioning steps. Passive tracking methods have the advantage that no additional hardware is needed. In the past, conventional image processing methods have been employed for this task. Recently, deep convolutional neural nets (CNN) were used in image processing with excellent results. This work investigates the capability of a deep learning algorithm to detect needles in porcine in-vivo images.

Methods. The CNN was trained on image data acquired during MR-guided swine studies (10 animals). All images were acquired in an IRB approved study (cf. [2]). The bSSFP image data (BEAT IRTTT, Siemens Healthineers, Erlangen) contains different needle paths, slice orientations, and matrix sizes. A total of 1979 images containing a needle artifact have been manually annotated (non-clinician) and split into training and validation sets by study to minimize similarity of training and validation images (1634/345). During training, augmentation (rotation, zoom, translation) was randomly applied on every image to create well distributed artifact positions and sizes. The algorithm was implemented with Tensorflow and trained on an NVIDIA Tesla (V100-SXM2-16GB) for 250 epochs (8 h). An Encoder-Decoder model similar to UNet was designed. The collapsing arm was five blocks deep with each block containing two convolutional layers (3x3-kernel, ReLU) followed by a batch norm and a 2x2-max pooling. The number of filters is successively doubled after each pooling. The input is symmetrically padded such that the valid padding during convolution is compensated and the output image has the same size as the input. In the decoding part, the transposed convolution is followed by concatenation of activation maps from the encoding part and two convolutional layers. As loss function a sigmoid-cross-entropy with pixel wise Gaussian weighting by distance to the needle was used (optimizer: adaptive gradient descent).

Results. Model complexity and the hyper parameters dropout rate, learning rate, number of epochs, loss weight scale and L2 kernel regularizing scale have been chosen by comparing the inference on the validation dataset. In Figure 1 the inference of representative images from the validation set thresholded at 0.5, 0.6 and 0.7 is shown. On a test subset thresholded at 0.6 and filtered by TP score >0.1 (319 images with acceptable performance) the segmented area corresponding to the needle was extracted. The Euclidian distance [mm] to the annotated tip position (Median=4.4, Q₁₆=5.24, Q₃₄=16.9) and angular difference [°] to the label (Median=0.2, Q₁₆=1.1, Q₃₄=6.8) was derived.

Conclusions. The initial results show that CNNs can be employed to successfully detect a needle in interventional in-vivo MR images. Images in which needles are clearly separated from tissue are segmented precisely (Fig. 1a), but the algorithm needs to be improved on images that contain banding artifacts of the same size as the needle (Fig. 1b). The results show that the algorithm could benefit from additional information like pulse sequence parameters to learn the orientation dependent artifact appearance and an AI based position extraction. In a next step, the algorithm will be trained on larger number of datasets and human in-vivo image data. The method is a promising approach to create a robust and general method for tracking needles in MR-guided interventions.

References
MR-projection imaging with perspective distortion as in X-ray fluoroscopy for interventional X/MR-hybrid applications

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Purpose
Hybrid X/MR-devices are promising for interventional applications (e.g. intravasculature) exploiting the high frame-rate of X-ray imaging and the contrast variety of MRI [1]. Standard cone-beam fluoroscopy exhibits perspective distortion due to the projection onto the detector. In contrast, MRI data are sampled point-wise with a high flexibility in k-space. Synthesis of both modalities might be achievable through X-ray-like MR projections. Here, we demonstrate initial experiments yielding MR-fan-beam views without the need of time consuming 3D acquisition.

Methods
Principle: According to the Fourier-slice theorem, fan-beam views can be obtained from k-space projections covering the fan-angle of the X-ray system [2]. Using this idea, we are able to synthesize fan-beam projections from multiple parallel MR projections spanning the respective angles.

Measurements: 2D MR projections were acquired with a gradient-echo sequence by omitting slice selection in view direction. The projection angle was swept from -6° to 6° in steps of 0.1°. 2D/3D acquisitions were performed with a volunteer and a head phantom at 1.5T (Aera, Siemens Healthineers, Erlangen) within 3.8 s / 14:20 min at 1 mm resolution and TE/TR/flip-angle = (3/6/9/12) ms / 15 ms / 8°.

Analysis: Measured 2D-projections and resampled fan-beam views were compared to a ground truth obtained through parallel/fan-beam forward projection of the 3D image data, respectively.

Results
2D MR projections approach the ground truth for short TE<3 ms, where the projections should ideally match the line integral of the relaxation-weighted proton density (Figure 1). Signal voids occur due to dephasing with increasing TE. Perspective distortion as seen in fan-beam X-ray can be generated from MR projections (Figure 2). Only a small number of angular views is sufficient (error below 10% with 3 projections).

Conclusions
We demonstrate an acquisition and reconstruction scheme for MR data enabling straightforward transfer to X-ray data. This enables image fusion of both modalities during an intervention without time-consuming and error-prone transformations. In future, the implementation of dedicated magnetization preparations can tailor the image contrast to the application at hand.

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Purpose 3D online motion assessment and quantification with excellent soft-tissue contrast during irradiation is one of the major benefits of MR-guided radiation therapy (RT) compared to conventional RT. Conventional real-time pulse sequences work with fixed temporal resolution. Recently, a method for real-time imaging with dynamic temporal resolution was proposed to improve image quality in breathing phases with little motion and high temporal resolution in breathing phases with fast motion [1]. However, this approach was restricted to single 2D slices. Thus, only 2D motion capture was feasible. In this work, we introduce a pulse sequence for 3D online motion quantification that allows for dynamic temporal resolution. The new CROSSBARS sequence (Crushed Rephased Orthogonal Slice Selection with Balanced golden Angle Radial Sampling) combines the CROSS approach [2] with a radial bSSFP sequence [3,4] for multi-slice acquisition in MR-guided RT for online 3D motion capture.

Methods CROSSBARS acquires two slices, which are perpendicular to each other, by alternately measuring radial spokes in the first and second slice. Within each slice, the spokes are rotated by the golden angle (Fig. 1). Within the pulse sequence diagram (Fig. 2), all gradients are fully balanced to achieve a very high signal-to-noise ratio. An experiment at 1.5 T (MAGNETOM Symphony fit, Siemens Healthineers, Erlangen, Germany) was performed with a healthy volunteer (Fig. 3).

Results Both slices intersect at the dark vertical line with little signal. Within each TR, one spoke for each slice was measured, resulting in two spokes per 16.0 ms.

Conclusions The new pulse sequence enables interleaved imaging of two orthogonal slices with balanced gradients and TE = TR/2 for a high signal-to-noise ratio at low field (e.g., Viewray MRIdian 0.35 T). Even though TR is long for bSSFP, possible banding artifacts are mitigated on MR-guided RT devices with low B₀ field. The radial acquisition scheme enables a variable temporal resolution in real-time MRI [1], where a reduced temporal resolution increases the image quality in case of little motion, while a high temporal resolution ensures images without blurring during fast motion.

References
Purpose: We aim at developing an endo-vaginal forward-looking RF coil, inserted up to below the cervix that improves imaging signal-to-noise ratio (SNR), relative to the scanner’s spine and body-array coils, by 4-8 times along the forward direction, at locations 30-40 mm superior to the patient’s cervix, providing high-resolution gynecological imaging in shorter scan times. The cervix and posterior-endometrium are areas where advanced in-operable cervical-cancers, which are candidates for radiation therapy [1], are found. The coil supports completing multi-parametric (T2, DWI, DCE, UTE, BOLD) imaging, utilized for improved live-tumor localization, in clinically-acceptable acquisition times, a difficult task using the surface coils alone. Forward-looking (“flashlight”) coils, are difficult to develop within the constraints of thin (<25 mm) body orifices (the vagina).

Methods: The coil was constructed utilizing the image magnetic-field concept, wherein metallic surfaces force magnetic fields to project along desired directions [2]. A cone-shaped plastic former (Fig 1) with an inner lumen, had a 1-mm thick metallic cone placed inside it. A 2-mm thickness dielectric region was deposited outside the plastic cone, and solenoidal windings were wound on its outside. The coil winding density was higher on the left (Forward) direction relative to the right (Backwards) direction, concentrating the magnetic field in the Forward direction, with the internal metal reducing the Backwards and inner-lumen field. Phase coherence was maintained with two series caps placed along the coil. A 12-cm coaxial cable connected the coil to 1.5 T (63.8 MHz) tuning, matching, and decoupling circuit at the proximal end of the coil’s shaft (Fig 2). Finite-element electromagnetic simulations (CST, GE) evaluated the magnetic-field around the coil. Phantom experiments were performed with the coil surrounded by saline solution, mimicking the genitourinary environment, validating the simulated magnetic-field profile. Fast Spin echo (FSE) images were obtained in a 1.5T Siemens MR scanner. The endo-vaginal coil SNR was calculated, relative to the scanner’s spine array, measuring its forward-looking SNR gain. A swine experiment was performed to evaluate in-vivo performance. The coil was inserted into the vagina up to the cervix. High-resolution 2D and 3D FSE images (resolution=0.47×0.47×3.00 mm³) were acquired in the coronal plane.

Results: Network analyzer tests showed a Q-factor of 58 at the resonance frequency. Figure 3 shows that the coil’s EM-simulated magnetic field is focused towards the forward direction and extends for 30-40 mm. Phantom Images acquired with the endo-vaginal coil (Fig 4A) were in good correlation with the simulated magnetic field profile. Measured SNR values along the forward direction of the endo-vaginal coil were 4-8 times higher relative to the surface coil over a 30-40 mm region. In-vivo swine images acquired with the endo-vaginal coil demonstrated strong hyper-intensity above the vaginal canal (Fig 4B).

Conclusions: We demonstrated a forward-looking endo-vaginal coil that provided 4-8 times SNR enhancement at distances of 30-40 mm above the coil. A 2nd sideways-looking channel for vaginal-wall imaging will be added.

Title: Real-Time Imaging with HoloLens Visualization and Interactive Slice Selection for Interventional Guidance

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Background In previous work, we have shown that through-time non-Cartesian GRAPPA can be used to generate images in preset imaging locations with high temporal resolution and in real-time, making it an attractive tool for guiding interventional procedures. However, when performing a procedure with MRI guidance, the interventionalist may wish to change the imaging plane often and quickly. Because through-time GRAPPA requires a unique GRAPPA weight set for each slice position/orientation, it is necessary to collect calibration data and compute weights each time a new slice is selected. Such a calibration process would be inconvenient if performed in the middle of an interventional procedure. Here, we show that it is possible to pre-select multiple imaging positions and calculate their GRAPPA weights at the beginning of a session. The interventionalist can then switch among these slices during the session without needing to re-calibrate, enabling a rapid transition from one slice to the next. This feature is integrated into a real-time imaging and visualization system, specifically using the Microsoft HoloLens, which offers the interventionalist a view of the imaging slices in an intuitive manner.

Methods Data were acquired with a variable-density spiral trajectory on healthy volunteers on a 3T clinical scanner (Skyra, Siemens). 40 frames of fully-sampled calibration data were collected for 12 imaging slices in the heart. GRAPPA weights for each slice were calculated and saved to the reconstruction computer. The calibration data acquisition time for 12 slices is 90.8s, and the GRAPPA weights calculation takes ~5min. Accelerated data were then collected at R = 4 (12/48 spiral arms) and reconstructed using a parallelized implementation of through-time spiral GRAPPA in the Gadgetron framework. The user selected a subset of the 12 slices to image in a selection menu on the user interface of the host computer. The following imaging parameters were used: FOV = 300x300mm²; matrix = 128x128; in-plane resolution = 2.34x2.34mm²; slice thickness = 5mm; flip angle = 15°; TR/TE = 3.94/0.92ms; bandwidth = 500Hz/pixel; 26 coils. Reconstructed images were exported to a rendering framework for display as holograms in the HoloLens framework. An initial accelerated scan was performed at each of the 12 slices to initialize the rendering framework with slice position/orientations. Thereafter, the user was able to select any combination of the 12 available slices to image.

Results/Discussion Sample images at each of the 12 pre-selected slices are shown in Fig.1. Their relative positions are shown in Fig.2a. Three different subsets of 3 or 5 slices each were then imaged (Fig.2b-g). The acquisition time/slice is 47.28ms. The frame rate for 3 slices is 7.05fps, and 4.23fps for 5 slices. The number of slices acquired should therefore balance desired coverage and temporal resolution. The rendering system is a useful way to keep track of the available slices. A user wearing a headset views the renderings as 3D holograms and can click on individual slices to see the slice number before selecting it on the host computer. Future work will include real-time feedback from the hologram to the scanner to allow the user to select slices to image directly from the hologram. For the scan and GRAPPA reconstruction parameters used here, the weight set for each slice requires 135.36MB of memory, and the accelerated and reconstructed data require 2.5MB each. On the 8GB graphics card used here for reconstruction, ~40 slices could be pre-calibrated. However, one limitation of this method is that if the patient moves during the scan, calibration must be repeated, which becomes more time-consuming as more slices are pre-selected. Options to speed up this process, such as use of a weight-sharing technique to reduce the total number of weights required, are currently being explored.

Conclusion We have demonstrated the option to save weights for a large number (12) of pre-selected slices or common views for a procedure, allowing the user to take advantage of the high temporal resolution and real-time reconstruction compatibility of through-time spiral GRAPPA without needing to pause during a procedure to calculate GRAPPA weights.


Fig.1 Sample images at each pre-selected slice. One 2-chamber (1), one 4-chamber (12), and a stack of 10 short-axis slices (2-11) were chosen. The numbers correspond to the slice subsets shown in Fig.2.

Fig.2 Image renderings of the 12 pre-selected slices (a), and different subsets of the available slices (b-g). Renderings in each column belong to the same group, and show different views of the rendering.
3-Tesla MR-guided Diagnostic and Therapeutic Scalene Injections for Neurogenic Thoracic Outlet Syndrome

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Abstract

Purpose Surgical management of neurogenic thoracic outlet syndrome is controversial due to the lack of predictors of success. The selective use of computed tomography-guided nerve blocks has shown some benefit in predicting surgical success [1]. Interventional magnetic resonance imaging (MR)-guided nerve blocks at 3-Tesla field strength carry a high degree of validity because targets, needle tip, and distribution of injectants are visualized with high accuracy [2]. We sought to examine the use of 3-Tesla MR-guided anterior scalene nerve blocks in predicting the success of transaxillary decompression and botulinum toxin (Botox) injections.

Methods Following internal review board approval and informed consent, 226 consecutive patients (average age: 38; age range: 15–66 years) undergoing MR-guided diagnostic intramuscular anterior scalene anesthetic injection with a 3T wide-bore MRI system were prospectively included. Technical success of the MR-guided injections was defined as complete intramuscular injection of the local anesthetic without extra-muscular spread. A diagnostic response was considered “positive” if the injection led to resolution of or greater 50% of symptom improvement; and “negative” if there was no improvement or worsening of symptoms. Patients’ course, including subsequent surgical decompression and Botox injection into the inter-scalene muscle, were recorded. Positive predictive value of diagnostic blocks for resolution of symptoms after transaxillary decompression was the primary outcome variable.

Results 225/226 (>99%) diagnostic injections were technically successful, with one patient having extramuscular spread. Of technically successful injections, 200/225 (89%) were positive, and 11/225 (5%) were negative. 61/200 (31%) patients with positive blocks subsequently underwent surgical decompression, all of whom had significant improvement of symptoms. 91/200 (46%) patients with positive scalene blocks subsequently received intramuscular scalene Botox injections. Among them, 32/91 (35%) underwent subsequent decompression, of whom 31/32 (97%) had long-term symptom improvement. 1/25 (4%) patients with a negative diagnostic block underwent surgery, which was followed by no improvement of symptoms. The positive predictive value for diagnostic blocks was 0.99 based on 92/93 total patients with positive blocks undergoing decompression surgery and subsequent significant improvement of symptoms.

Conclusions 3-Tesla MR-guided diagnostic intramuscular scalene injections have a high technical success rate and high positive predictive value for successful transaxillary decompression surgery in patients with neurogenic thoracic outlet syndrome.

References


The Effect of MR-guided Botox Injections into the Piriformis Muscle for the Treatment of Deep Gluteal Syndrome

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Abstract

Purpose Piriformis injections are commonly used in the evaluation and treatment of patients presenting with deep gluteal syndrome [1]. In combination with magnetic resonance imaging (MRI)-guided injection of local anesthetics and long-acting steroids into the infra-piriformis foramen, intramuscular piriformis injections of botulinum toxin (Botox) are used therapeutically in an attempt to reduce the piriformis muscle volume and increase the space of the infra-piriformis foramen [2]. However, the effect of Botox on the piriformis muscle bulk is not well understood. Therefore, the purpose of our study was to assess the effect of therapeutic Botox injections on the piriformis muscle volume.

Methods Following institutional review board approval, a prospective cohort that underwent combined high-resolution MRI-guided intramuscular piriformis injection with Botox and infra-piriformis foramen injection with local anesthetic and long-acting steroids was searched for patients with follow-up MRI. Our search derived 12 patients (average age: 45; range: 18 to 71) who underwent MRI follow-up at an interval of 2-12 months. Outcome variables included the maximum axial thickness of the center of the treated piriformis muscle at baseline and follow-up. The normal contralateral piriformis muscle served as control. Statistical tests included two-tailed Wilcoxon signed-rank test for comparison of measurements and Spearman’s correlation coefficient for evaluation of an association between muscle bulk and time between injection and follow-up. P-values of less than 0.05 were considered statistically significant.

Results MR-guided Botox injections into the piriformis muscle resulted in significant reduction in the axial thickness of the piriformis muscle (mean thickness = -32%, range = -2% to -50%, p < .0001). There was no significant difference in piriformis muscle thickness for the untreated side after Botox injection (p = 0.8). There was no correlation between muscle thickness and the time to MRI follow-up (r < 0.1, p < 0.05).

Conclusions We demonstrate the effectiveness of MR-guided intramuscular piriformis injections with Botox for muscle volume reduction therapy. The piriformis muscle volume loss subsequently leads to an increase in the size of the infra-piriformis foramen, which is implicated as a site of nerve compression in deep gluteal syndrome.

References


Integration of Interventional MRI Guidance Improves Efficiency and Quality of MR Arthrography of the Shoulder

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Abstract

Purpose Shoulder MRI arthrography is often performed as a combination of ultrasound or fluoroscopy-guided joint injections and subsequent MRI (1). However, the coordination of rooms, teams, and transportation can be time consuming or unavailable at outpatient sites, in which case MR-guided MR arthrography may be advantageous. Therefore, we evaluated the performance of single-session MR-guided MR arthrography at 3-Tesla.

Methods Following IRB approval and informed consent, 154 consecutive patients (average age, 36; age range, 13-77 years) undergoing MR-guided shoulder MR arthrography with a 3T wide-bore MRI system were prospectively included. Patients underwent MRI, MR-guided glenohumeral injection, and MR arthrogram as a single-session procedure. The injections were performed by fellow or attending physicians. Outcome variables included a.) rates of technical success, defined as intra-articular injections with adequate joint distention, b.) qualitative analysis of extra-articular leakage of contrast, c.) lengths of time for the entire procedure and MR-guided arthrography, d.) major complications, e.) and patient experience obtained through a postprocedural questionnaire. Time efficiency was measured by comparing to the procedural times of 50 recent MR arthrography procedures performed under conventional fluoroscopic guidance at the same institution using unpaired t-test and a significance level of p < 0.05.

Results MR-guided shoulder arthrography was technically successful in 152/154 (99%) patients, whereas in 2/154 patients the procedure was prematurely terminated due to patient discomfort and inability to achieve intra-articular puncture. 10/152 (7%) procedures had mild extra-articular contrast leakage. There were no major complications. The procedure was well tolerated, with low rates of moderate nausea (3%), moderate pain (7%), and no higher-grade claustrophobia, flashes, or heat sensations. MR-guided MR arthrography required an average total of 87 (range, 53-140) min including MRI [39 (16-59) min], MR-guided injection [28 (9-77) min], and MRA [16 (4-27) min]. In comparison, fluoroscopy-guided MR-arthrography required an average total time of 104 (51-158) min (p < 0.001) and did not produce a separate diagnostic MRI.

Conclusions 3-Tesla MR-guided MR arthrography of the shoulder is clinically feasible and affords high technical accuracy, as well as a favorable safety profile and efficiency, which may supersede fluoroscopy-guided MR arthrography. Single-session MR-guided MR arthrography can eliminate coordination of and delays between fluoroscopy-guided injection and MRI of traditional MR arthrography.

References

MRI-monitored Anterior Cervical Discectomy and Fusion (ACDF) Surgery: Observation of Intraprocedural Nerve Decompression at Several Procedure Phases

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Background Anterior Cervical Discectomy and Fusion (ACDF) is a surgical procedure in which a herniated or degenerative disc in the neck is removed to alleviate pain and weakness in the arm/hand due to spinal cord compression1. A series of MRI-monitored surgeries was planned to understand the mechanics of nerve decompression in response to ACDF surgical stages and potentially modify the procedure to reduce risk of complications associated with resection close to the cord2. Intra-operative MRI has been shown to be viable during spine surgery3-6.

Methods The patient was placed head-first supine on the diagnostic table of a 3T MRI scanner (IMRIS, Minnetonka, MN) with the neck in hyper extension. General anesthesia was administered. The spine coil was utilized for posterior coverage. A body array was sterilely draped and added prior to imaging for anterior coverage. Since no spine attachment was available for MRI-conditional high-speed drills, a Sonopet ultrasonic aspirator with Payner tip (Stryker, Kalamazoo, MI) was used for disc and osteophyte removal. The ferromagnetic foot-pedal was affixed to a granite base to mitigate risk of magnetic attraction. An electrosurgical unit (Force Triad, Medtronic, Minneapolis, MN), required for cutting skin and muscle, was activated by a switch on its MRI-compatible handpiece. All consoles were placed outside the 5-Gauss line. A carbon fiber distractor and retractor were produced by Life Instruments (Braintree, MA). However, a titanium retractor was used for this first procedure (V. Mueller). It was removed prior to imaging. Imaging was performed at four phases to visualize the status of cord decompression: (I) Baseline, to localize the target disc, (II) Following vertical distraction of neighboring vertebrae and removal of the disc, (III) Following removal of osteophytes lining the spinal foramen, (IV) Following removal of the posterior longitudinal ligament (PLL). Next, a bone graft was inserted in-place of the disc and a plate was screwed to the two adjoining vertebrae for immobilization and facilitation of subsequent spinal fusion.

Results Feasibility of efficient (15 min/phase) MRI-monitored ACDF was shown in a patient. Cord compression is observed in phases I and II, with decompression visible in phases III and IV (Fig. 1). Minimal artifact due to the metal distractor pins was observed. 3D Wide-band Steady State Free Precession (WB-SSFP) neurography7 was also acquired to test high-resolution nerve visualization.

![Image of MRI images showing nerve decompression](image_url)

Figure 1: 2D FSE images (I) Baseline (II) Disc removal (III) Osteophyte removal (IV) PLL removal. Arrows show a layer of CSF returning around the spinal cord at phase III.

Conclusions Spinal decompression was immediately visible on images during the ACDF procedure, demonstrating the utility of intra-procedural imaging. If decompression is repeatedly achieved prior to PLL removal, PLL removal may be omitted in the future, possibly reducing complications.

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Percutaneous Ablations in High Field Strength MRI: 8 Year Experience

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In the early stages of interventional MRI, it was believed that open configuration magnets were required to be able to perform percutaneous procedures since narrow gantry sizes of diagnostic scanners were prohibitively small (1,2). Despite initial enthusiasm and few advantages such as direct access to the patient, limitations of these low field strength magnets became evident such as low image quality and speed, limited pulse sequence options as well as having to be dedicated to interventional use alone. With the introduction of wide-bore magnets, percutaneous procedures have become possible using high field strength magnets. Although typically the patient has to be brought in and out of the gantry during applicator placements, this has brought all the advantages of being able to use the most up-to-date diagnostic quality MR imaging hardware and sequences.

Since 2010, we have performed 420 percutaneous tumor ablation procedures in a 3T wide-bore MRI (Siemens Verio, Erlangen, Germany) including 411 cryoablations and 9 microwave ablations in the kidney, liver, adrenal, bone/soft tissue, and prostate. The MR imaging coils and pulse sequences were specific to the organ system, tumor type, location and patient positioning. Most commonly used MRI coils were spine coil elements with body matrix coil or loop coil. Most commonly used pulse sequences were half-Fourier T2WI (HASTE) and spoiled gradient echo T1WI (VIBE). Specific indication pulse sequences were occasionally utilized such as T1 or T2WI (TSE) with or without respiratory gating.

Now that high quality cutting edge imaging is possible during percutaneous ablations, this lends itself to new areas of research such as computerized monitoring methods (3), small-foot-print motorized MRI compatible needle guidance devices (4), and MR thermometry for cryoablation (5).

References:

Background  Osteosarcoma (OSA) occurs in both children/young adults and dogs with an annual incidence of 4501 and 25,000 cases, respectively, making dogs a useful comparative oncology model for the development of OSA treatments.2 OSA metastasizes in about 30-40% of children making the cancer incurable, and there has been little progress in developing new treatments for metastatic OSA in the past 30 years.3 Canine OSA has many striking similarities with respect to genetics and tumor biology, with metastatic spread more likely to occur than in pediatric OSA.4 Cryotherapy is used to treat a variety of cancers including breast, prostate, kidney, and lung cancers. In addition to directly killing cells in tumors, there is anecdotal evidence that cryotherapy of a primary tumor can activate the patient’s own immune system, i.e., immunotherapy, to eradicate tumor cells far from the site of where the primary tumor was frozen. Using Magnetic Resonance Imaging (MRI), one can precisely determine the extent of tumor tissue that is frozen by cryotherapy to accurately kill tumor cells without exposure to ionizing radiation. In this study, we aim to demonstrate the feasibility of performing MRI-guided cryotherapy in dogs with naturally occurring OSA and study the native immune response.

Methods All canine studies were approved by the institutional animal care and use committee. Dogs of either sex and any breed with radiographic criteria and histopathology suggestive of appendicular OSA were recruited from referring veterinarians to the Center for Image-Guided Animal Therapy at Johns Hopkins University. Informed consent was obtained from all dog owners. Complete blood counts, blood chemistries, and chest films were acquired to assess anesthetic risk. After placement of an IV catheter, the dogs were anesthetized and placed on isoflurane anesthesia and mechanical ventilation. A chest cone beam CT (DynaCT Body preset, Axiom Artis Zee, Siemens) was acquired to assess the presence of pulmonary metastases. Using a transfer table, the dogs were moved to a 1.5T wide-bore MRI scanner (Espree, Siemens) for imaging of the affected limb. After obtaining scout images, proton density (PD) images (5800 ms TR; 26 ms TE; 4 NSA; 18 ETL; 151 Hz/pixel BW; 4 mm slice thickness; 448x436 matrix; and 270 mm FOV) were acquired in the axial and sagittal planes for treatment planning. Five contiguous axial images were then planned for the cryoablation needle path with the skin entry point marked by MR-visible fiducials. A single loop coil was centered on the planned skin entry point. The skin was then steriley prepared and draped, and a local anesthetic block was performed. Using an MR-conditional 4mm sertated drill, co-axial trocar sheath, and blunt ejector (In Vivo), the trocar-sheath was advanced into the osseous lesion using intermittent metal-artifact reducing, TSE MRI axial images (1940 ms TR; 23 ms TE; 1 NSA; 24 ETL, 5 mm slice thickness, 280x280 FOV; 384x384 image matrix, and 407 Hz/pixel BW). Once the near cortex of the tumor was penetrated, the sheath was locked and the stylet was replaced with the bone drill to obtain biopsy specimens. After the biopsy specimens were obtained, an MR-compatible cryoablation needle (IceSeed, Galil) was placed and two 10-minute freeze/5-minute thaw cycles were performed using an MR-compatible cryoablation system (Galil) while the TSE MRI was repeated to document the extent of the ice ball. The cryoablation needle and sheath were then removed and PD MRI images in the axial and sagittal planes were repeated prior to recovery of the dog. After cryotherapy, all dogs received non-steroidal analgesics and oral antibiotics until amputation at approximately two weeks post-cryoablation. Histopathology was performed on the amputated limb and peripheral blood was collected at amputation to assess the tumor infiltrating lymphocyte response.

Results  Two dogs have been enrolled without evidence of pulmonary metastases and completed cryotherapy and amputation. MR-guided bone biopsies and cryoablation were successfully completed in both animals. Histopathology from MR-guided biopsy confirmed osteosarcoma in one dog and altered the diagnosis to chondrosarcoma (CS) in the second dog. The OSA tumor (~3.7x6.2 cm) was in the distal radius whereas the CS (~4.2x3.7cm) was confined to the proximal tibia. Neither tumor could be totally ablated with two freeze/thaw cycles with a single needle. The extent of cryoablation after amputation was highly correlated to the visualized iceball during MR-guided cryoablation in both tumors (Fig 1). A larger inflammatory response was seen in OSA versus CS tumor to cryoablation.

Conclusions  MR-guided biopsy/cryoablation can be successfully performed with accurate monitoring of the tumor dimensions in the bone to avoid critical vascular and neurological structures. The variable inflammatory response to cryotherapy may reflect the different tumor types and will require further investigation to determine whether cryotherapy can be used to invoke an immunotherapeutic response to the tumor antigens.


12th Interventional MRI Symposium  63  October, 2018 Boston, MA
**Background or Purpose** Arteriovenous malformations are classically treated using strategies which access the malformation intravascularly with injection of a sclerosant material. While this is effective, there is a risk of non-targeted embolization and/or complications related to the intense inflammatory reaction from the local sclerosant. This is especially dangerous in the hands and the feet where the small spaces can lead to compartment syndrome or superficial necrosis and the complex anatomy increases the risk of neurovascular injury. As an alternative, using MR-guidance, we have utilized cryoablation as a novel treatment of pedal arteriovenous malformations. This study examines the feasibility and safety of this procedure.

**Methods** A retrospective review was performed of the 479 MR-guided procedures performed between January 2011 and May 2018. Patients who had cryoablation performed on pedal arteriovenous malformations were selected to be included in this review. Their medical records were evaluated for technical success, procedure related complications and evidence of recurrence at follow-up including imaging confirmed recurrence or recurrence of clinical symptoms. Complications were classified using the SIR classification system for complications by outcome.1

**Results** Of the 417 total procedures, 62 patients with arteriovenous malformations were treated with either laser or cryoablation. 3 of 62 patients had pedal arteriovenous malformations treated with cryoablation and were included in this review. The patients were between 11-40 years old who all had plantar surface venous malformations which interfered with activity. Cryoablation was performed using ultrasound to guide cryoprobe placement and MRI to verify needle placement and monitor iceball formation during the ablation cycles. 2-3 IceRod cryoprobes were used for treatment. 3 freeze-thaw cycles were performed. Technical success was 100%. Symptomatic relief was achieved in all three patients with a significant reduction in pain to levels allowing desired activity which had been previously limited (i.e. working, hiking, and gymnastics). No complications were identified during or immediately after the procedures. Two patients had a new paresthesia following the procedure; one resolved 2-3 months following treatment and the other has not at the most recent follow up of approximately 0.5 months (SIR A).

**Conclusions** MR-guided cryoablation of pedal arteriovenous malformations is a safe and effective treatment strategy to control arteriovenous malformations in sensitive and complicated anatomical regions. Further evaluation with long term clinical and imaging follow up is needed to better understand the long term efficacy and durability of this technique. References:

Evaluation of 2D simultaneous multi-slice EPI at 1.5T for MR-thermometry in presence of motion.

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\textbf{Purpose}: Respiration-induced motion of abdominal organs poses significant challenges to measure accurate MR temperature maps \cite{1} using the proton resonance frequency shift technique. Simultaneous multi-slice (SMS) echo-planar imaging (EPI) using parallel image reconstruction may be exploited to increase volume coverage or reduce acquisition duration of temperature mapping. Nevertheless, the use of SMS-EPI imaging combined with in-plane acceleration results in a reduction of image signal-to-noise ratio (SNR) \cite{2} and has not been validated in free breathing acquisition in mobile organ. In this work, we have investigated the benefits of SMS acquisitions for monitoring radiofrequency ablation (RFA) in a mobile gel and in liver in volunteer without ablation. The performance of the sequence was evaluated in terms of potential false-positive heating at multiband (MB) factors of 1, 2, and 3 and temporal standard deviation of temperature $\sigma(T)$.

\textbf{Methods}: \textbf{Acquisition in gel}: To simulate a respiratory motion, an agar gel phantom was positioned on a motor-driven platform to generate a horizontal oscillating translation (10 mm amplitude and 0.21 Hz frequency). 12 slices were acquired using an interleaved pattern in a coronal orientation (motion included into the imaging plane) every 1.2 s, over a total duration of 3 minutes, on a 1.5 T clinical imaging system (MAGNETOM Aera, Siemens Healthcare, Erlangen, Germany) using a prototype 2D single-shot gradient echo blipped-CAIPI SMS echo planar imaging. Three different MB factors (1, 2 and 3) were combined with in-plane parallel imaging (GRAPPA 2 with 50% oversampling in the phase encoding direction). Sequence parameters were: $TE=26$ ms, FOV$=180\times180$ mm, spatial resolution $1.6\times1.6\times3$ mm\(^3\) voxel size, FA $= 90^\circ$, 6/8 partial Fourier and pixel bandwidth $= 1565$ Hz/pixel. The spine coil and two flexible coils surrounded the gel, allowing the activation of 24 receiver channels. \textbf{RF ablation device}: RF energy was delivered at 15 W during 30 s using two MR-compatible RF electrodes inserted into the gel and connected to a programmable RF generator (IGT, Pessac France). \textbf{Acquisition in volunteer}: images were acquired with the same protocol in coronal orientation with the spine coil and the body coil with the addition of saturation slabs surrounding the imaging plane. \textbf{Thermometry}: in-plane motion compensation, susceptibility correction, and spatial-temporal drift correction was implemented as previously described \cite{3}. Each slices of the reference frame was also automatically aligned in the slice direction using additional rigid registration to avoid misalignment between adjacent slices.

\textbf{Results}: In the gel study, the temporal resolution for acquiring the 12 slices was 1179 ms, 594 ms and 398 ms for MB=1, 2 and 3, respectively. A temperature rise of 25°C was reached for each acquisition with a resulting heated region of 8x3 voxels at the end of energy delivery. No false-positive temperature spots due to potential signal leakage between simultaneously excited slices were observed under the tested conditions (Figure 1). The temperature distribution in the $(x,z)$ and $(y,z)$ planes indicate that spatial homogeneity of the heating was preserved whatever the acceleration factor. Figure 2 display representative magnitude images acquired in the gel. Significant motion occur between the acquisition of the slices at MB $= 1$ resulting in visible relative motion between slice in the $(y,z)$ plan (red arrows). Increasing SMS factor improved through-plane geometry (green arrows).

\textbf{Conclusions}: This study presents the first evaluation of MR-thermometry using SMS-EPI acquisition in presence of motion. While increasing the SMS factor to 3 induced some aliasing artifacts, it reduced the displacement between adjacent slices and thus allowed to reconstruct a 3D volume ($180\times180\times37$ mm\(^3\)) more precisely, with acceptable temperature uncertainty ($<2^\circ$C). Pseudo-volumetric temperature imaging could thus be performed without compromises on acquisition time and resulting temperature images showed similar patterns independent of the SMS acceleration factor (up to 3). Such a strategy is expected to increase procedure safety by monitoring larger volumes more rapidly for MR guided therapeutics on mobile organs. \textbf{References}: 1. Rempp H. et al. MAGMA. 2008. 2. Borman P.T. et al. MRI. Phys Med Biol. 2016. 3. Ozenne V. et al. Magn Reson Med. 2016.

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Motion Correction for PRF-based Thermometry during Tumor Ablation

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Background or Purpose: Magnetic resonance imaging (MRI) has the unique ability to measure temperature distributions non-invasively in-vivo. Thus, the thermal dose, a key variable for a successful minimal-invasive ablation of cancerous tissue, can be monitored in real-time. However, MR-thermometry for temperature measurement is prone to motion artefacts. Known motion correction (MoCo) techniques for thermometry range from conventional methods (respiratory gating, navigator echoes) towards reference-less and multi-baseline approaches. We present a novel method for motion-corrected thermometry during radiofrequency (RF) or microwave ablation (MWA) that is potentially more accurate and simpler. The method is based on an optically tracked marker, which is attached at the distal end of the rigid RF or MWA needle and thus moves continuously with the local motion pattern of the organ during ablation. The local six degrees of freedom (6DOF) motion information, which is provided by the tracking camera, can be exploited to prospectively correct the thermometry slice through real-time adjustment of gradient and RF-pulses. We implemented and evaluated this method in moving ex-vivo pig liver tissue using the optical Moiré Phase Tracking (MPT) system during MWA.

Methods: The liver tissue together with the inserted MWA needle was periodically moved within a 3T wide-bore MRI scanner using an in-house built drive unit. A MRI-compatible camera continuously recorded 6DOF of the MP marker attached to the MWA needle. The tracking data were processed by an in-house written gradient echo sequence (GRE) to prospectively adjust each k-space line in real-time. 2D thermometry images were acquired every 6s with the modified GRE sequence (TE=4.65ms, TR=20ms, 18°, 1.9mmx1.9mmx4mm, tAq=1.3s, 40 repetitions). The MWA generator was automatically paused during the image acquisition to improve image quality. Magnetic field drift was corrected using external oil references. The accuracy of MR-thermometry was examined with a fiber optical temperature sensor, placed at an approximate distance of 1.5cm to the MWA needle. Temperature maps without motion (Ref), with motion and without correction (MoCooff) as well as with motion and with correction (MoCoon) were acquired.

Results: The difference between MR-thermometry and the optical temperature sensor was significantly reduced from 7.51°C ± 4.76°C to 1.32°C ± 0.81°C using prospective motion correction (t(76)=8.02, α=0.05, p<0.01). However, there was still a significant difference compared to the reference (0.92°C ± 0.90°C), where no motion was present (t(76)=2.01, α=0.05, p=0.0478). Fig.1 visualizes the MR-thermometry together with the temperature sensor for the three different cases.

Fig. 1 Temperature profile of the temperature sensor (black) and the MRI measurement (red) without motion (top), with motion and without correction (middle) as well as with motion and with correction (bottom).

Conclusions: Prospective motion correction using MPT significantly improved the temperature accuracy compared to the uncorrected case. The significant difference to the reference may be explained by motion-related local inhomogeneities of the main magnetic field causing phase variations. If optical tracking is used to guide the positioning of the ablation needle, the method can easily be integrated into the work flow.


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Purpose
Proton resonance frequency shift (PRFS)-based MR thermometry captures the temperature change (ΔT) that occurs due to the temperature-induced frequency change in underlying tissue during thermal therapy by subtracting pre-treatment baseline phase images from intra-treatment phase images. During thermal therapy it is important to visualize ΔT accurately, precisely, and in real-time without image and measurement artifacts due to e.g. distortion, coil combination errors, field drift, and off-resonance effects. In this work, a prototype PRFS-based thermometry system is presented that comprises: a selection of sequences ranging from GRE to multi-shot and single-shot EPI; 2D/3D acquisition strategies; efficient k-space reordering schemes and acceleration techniques (GRAPPA/CAIPIRINHA); B₀ drift monitoring; coil combination techniques; such as adaptive coil combination and phase difference combination method; 16-bit (2¹⁶ data points) dynamic range of ΔT and fly-back readout trajectory to minimize potential off-resonance effects due to ΔT or fat-water. The system is well-suited for continuously monitoring the ΔT during MR-guided thermal procedures such as LITT, RF ablation and HIFU.

Methods:
The PRFS-based ΔT prototype was implemented within a GRE/EPI-based sequence having above features. An interleaved B₀ drift module using an ROI placed outside of the anticipated heating zone but within the receive coil sensitivity was incorporated. All experiments were performed on a 3T scanner (MAGNETOM Prisma, Siemens Healthcare, Erlangen, Germany). An in-vivo brain scan was performed (after IRB approval informed consent) using a 20-channel head coil, and an ex-vivo heating experiment was performed using HIFU sonications (256-element phased array transducer, 1-MHz, Imasonic Inc., & IGT, Pessac, France) in a gelatin phantom using an in-house-built 5-channel coil array. In both the phantom and in-vivo the following protocols were compared: 1) 2D GRE (TR(ms)/TE(ms)/(ETL)=23/10/1), 2) 2D segmented-EPI (39/19/7), 3) 2D single-shot EPI (160/73/125), 4) 3D GRE (10/5.5/1), 5) 3D segmented-EPI without flyback (25/18/5), and 6) 3D segmented-EPI with flyback (23/13/5). All scans had a 240x240 mm FOV with 0.94x1.88 mm resolution, 2D protocols acquired 1 slice and 3D protocols 10-12 slices. All reconstructed ΔT maps were corrected for field drift. Results: Left figure panel shows ΔT overlaid on magnitude images from the phantom experiment, and right figure panel show magnitude and temperature standard deviation (SD) through time (measure of precision) images from the volunteer study. GRE approaches experience the least amount of image distortions, and segmented EPI approaches also demonstrate an acceptable level of distortions. Best precision is seen in single-shot EPI (but with bad distortions), and segmented EPI demonstrates a good balance between small distortions and high precision. The B₀ drift was observed on the scanner over a 7 minutes acquisition of a 3D segmented EPI scan; which led to corresponding effect on ΔT, resulting in an approximately 2°C temperature drift. Conclusion: In this study, we demonstrated a versatile system for temperature mapping that was evaluated in-vivo (without heating) and during an MR-guided HIFU phantom study (with heating). 2D/3D segmented EPI approaches demonstrate a good trade-off between good image quality and ΔT. References: [1] Ishihara Y, et al. MRM 1995;34:814–23 [2] Parker DL, et al MRM 2014;72:563–569.
Background or Purpose: Due to its excellent soft tissue contrast, its possibility of arbitrary slice positioning and its real-time capability, Magnetic Resonance Imaging (MRI) is a unique modality to treat oncologic diseases within minimal-invasive ablation. MR-thermometry allows real-time control of thermal ablation\textsuperscript{1,2}. However, the MRI scanner is strongly sensitive towards external electronic devices such as RF or microwave ablation systems. These systems potentially introduce radio-frequency noise, decreasing the signal to noise ratio in an MRI image and thus rendering thermometry unreliable. We present a modified microwave ablation (MWA) system interfaced and synchronized with the MRI scanner to allow simultaneous imaging and ablation.

Methods: The MWA system was automatically deactivated during image acquisition. Therefore, a modified gradient-echo sequence (GRE) produced an optical trigger signal (duration 100ms) at the beginning and at the end of the image acquisition to control the duty cycle of the MWA generator. The resulting modified (triggered) MWA generator was compared to an unmodified (untriggered) MWA system by ablating ex-vivo pig livers. During each ablation, a 2D thermometry image was acquired every 6s with the GRE sequence (TE=4.65ms, TR=20ms, $18^\circ$, 1.9mmx1.9mmx4mm, $t_{Acq}=1.3s$, 40 repetitions). The accuracy of MR-thermometry was examined with a fiber optical temperature sensor, placed at an approximate distance of 1.5cm to the MWA needle. The SNR was measured using the magnitude images of the GRE sequence.

Results: With the triggered MWA system the difference between the optical temperature sensor and the MR-thermometry measurement was significantly reduced from 2.30°C±2.21°C to 0.92°C±0.90°C ($t_{(76)}=-3.61$, $\alpha=0.05$, $p<0.01$, see Fig. 1). Fig. 2 presents one example magnitude image with the untriggered and triggered MWA system, respectively. The noise reduction with the triggered MWA system is clearly visible. This is also reflected by an increase of the SNR from 11.11±6.95 to 44.43±5.64.

Conclusions: Deactivating the MWA system during image acquisition resulted in a significant image quality improvement and thus more accurate MR-thermometry. The ablation duty cycle is reduced and lower energy deposition may prolong the ablation time. For clinical use, this effect has to be examined in more detail in the future.


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Initial Results of Image-Guided Percutaneous Ablation as Third-Line Treatment for Symptomatic Venous Malformations

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Purpose The purpose of this study was to determine the feasibility, safety and early effectiveness of MR guided percutaneous cryoablation as third-line treatment for symptomatic venous malformations (VM).

Methods Retrospectively a review was performed of all patients who underwent percutaneous MR guided cryoablation as a third line therapy for symptomatic venous malformations during the period from 11/6/2015 till recent. US and MRI guided needle placement and MRI monitored cryoablation was performed. Patients were treated under general anesthesia. Procedures were performed in a 3-T MR system (Magnetom Skyra, Siemens, Erlangen, Germany). Clinical follow-up started after one month and was assessed with subjective criteria.

Results Six symptomatic VM patients with three torso and three lower extremity VM with moderate to severe pain were treated with US or MR guided cryoablation. The median maximal diameter of the VM was 4,55 cm and the median of the iceball was 4,15 cm.

At an mean follow-up of 10 months, all patients reported symptomatic pain relief. 2 patients were re-treated due to persistent moderate pain. One patient was totally pain free. There were no minor or major complications.

Conclusion MR guided percutaneous cryoablation is a feasible, safe and effective third-line treatment for symptomatic venous malformations.

Figure 1 – MRI-guided cryoablation in a 21-y.o patient with symptomatic fibro adipose vascular anomaly (FAVA) of the lower leg. A) Pre-ablation gadolinium-enhanced axial T1-weighted SPGR shows an enhancing intramuscular lesion in the right m. soleus (arrow). B) Sagittal T2-weighted TIRM shows abnormal T2 signal within the vascular anomaly (arrow). C) Intra-procedural axial and D) sagittal T1-weighted VIBE images show placement of two cryoneedles (arrows). Two freeze-thaw cycles are applied under continuous T1-weighted VIBE imaging; E) Axial T1-weighted VIBE image shows the final frozen area (arrow). F) Immediate post-ablation sagittal T2-weighted TIRM shows signal drop-out due to the ice-ball (arrow) with no remaining abnormal T2 hyperintensities.
Clinical workflow for MRI guided microwave ablation and thermometry in the liver

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Background or Purpose: Despite many advantages, interventional MRI (iMRI) is still limited to specialized clinical centers due to access, workflow limitations and robust software solutions for thermometry (1-5). Therefore, in order to make interventional MRI more time efficient, workflow, guidance support and interventional tools are essential. Our goal was to evaluate setup and techniques that will help to facilitate MRI guided thermal ablation in a standard wide closed bore MR magnet.

Methods:
With the patient in general anesthesia, baseline imaging is performed to visualize target lesions. The fingertipping method was used to define and mark the skin entry point. After skin prepping sterile covering and local anesthesia, a 4 channel flex coil covered with surgical foil was positioned. Insertion of the microwave antenna (Medwaves AveCure) was performed under real-time MR imaging guidance. After reaching the final destination, the position was verified with a 3D-GE sequence and the lesion was ablated while thermometry images were acquired. After the ablation, the antenna was pulled back and a postcontrast 3D-dataset was acquired to determine the ablation zone. If necessary, the antenna was repositioned and the ablation was repeated. Time for preparation, puncture and ablation were measured in ten consecutive patients. The non-enhancing area was segmented and compared to the temperature map by using the Dice Similarity Coefficient (DSC).

Results:
Preparation time ranged from 30 to 42 minutes. Interactive imaging control facilitated swift positioning of the microwave antenna into the desired location (see Fig. 1). Once the needle was inserted, targeting ranged from 85 to 621 seconds when using the BEAT_IRTFT sequence. Thermometry images acquired during the ablation revealed a hot spot increasing in size and temperature during energy application. The post-contrast control scans visualize coverage of the lesion and correlate well with thermometry. In cases of incomplete coverage, the control data set can be used for repositioning of the antenna.

Conclusions: Using the workflow described here, MR guided tumor ablations in a wide closed bore MR magnet are clinically feasible and can be performed within a reasonable time frame. MR-thermometry correlates well with postcontrast MR-images.

References:

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MR Guided Cryoablation of Symptomatic Abdominal Wall Endometriosis: Safety and Feasibility  
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Background or Purpose: Abdominal wall endometriosis (AWE) is frequently painful necessitating  
chronic opioid use and is seen in up to 1% of patients who undergo caesarean section [1].  Traditional  
treatment includes hormonal therapy and wide surgical excision.  Percutaneous thermal ablation has  
emerged as a minimally invasive alternative to traditional therapy and early studies document feasibility,  
safety, and a prompt clinical response with decreased pain [2, 3].  The purpose of this study was to  
assess the safety and feasibility of MR guided cryoablation of AWE.

Methods: MR ablation is performed on a dedicated 1.5 Tesla Philips Ingenia interventional MRI machine.  
Patients are brought to a dedicated interventional MRI anteroom and placed under general anesthesia.  
After safe induction of general anesthesia, transfer to the MR table is completed after a thorough MR  
safety check.  Cryoablation is performed using a combination of ultrasound and MRI guidance per  
operator preference.  A MRI compatible version of the Galil Visual Ice cryoablation system is utilized for  
treatment (Galil Medical, Arden Hills, MN).  Two or three freeze-thaw cycles are performed at the  
performing Interventional Radiologists discretion with timing of each cycle based on ice ball coverage of  
The index lesion with the goal to achieve margins just beyond the tumor for nonmalignant lesions.  
Dynamic contrast enhanced MRI is obtained after treatment to assess treatment adequacy.  Follow up  
imaging is obtained in conjunction with the primary oncology/clinical team but in general is obtained three  
months after ablation.  Two patients who underwent treatment of three AWE deposits were included for  
analisis.

Results: MR ablation was technically successful in treatment of all three AWE deposits.  Follow up  
imaging at three months demonstrated no residual AWE with expected post treatment change.  Both  
patients experienced substantial pain relief with no ongoing narcotic use.

Conclusions: MR ablation may represent a feasible and safe alternative to traditional therapy in patients  
with symptomatic AWE with significant improvement in pain.

References

2. Cornelis, F., et al., Percutaneous cryoablation of symptomatic abdominal scar endometrioma:  
Background or Purpose: Percutaneous thermal ablation has emerged as a promising alternative to surgical resection in select patients unable or unwilling to undergo definitive surgical resection for primary breast malignancies [1-3]. A 94 year old female with a biopsy proven grade II invasive mammary carcinoma (ER positive, PR negative, HER2 negative) of the upper outer left breast presented for consideration of MR guided cryoablation. She had previously met with the Breast Cancer clinic and surgical teams and declined aggressive treatment.

Methods: The patient elected to undergo MR guided cryoablation of the left breast malignancy. MR ablation is performed on a dedicated 1.5 Tesla Philips Ingenia interventional MRI machine. Patients are brought to a dedicated interventional MRI anteroom and placed under general anesthesia. After safe induction of general anesthesia, transfer to the MR table is completed. Cryoablation is performed using a combination of ultrasound and MRI guidance per operator preference. A MRI compatible version of the Galil Visual Ice cryoablation system is utilized for treatment (Galil Medical, Arden Hills, MN). Two or three freeze-thaw cycles are performed at the performing Interventional Radiologists discretion with timing of each cycle based on ice ball coverage of the index lesion with the goal to achieve margins of 0.5-1 cm. Dynamic contrast enhanced MRI is obtained after treatment to assess treatment adequacy. Follow up imaging is obtained in conjunction with the primary oncology/clinical team but in general is obtained three months after ablation.

Results: Complete ablation of the patient’s invasive mammary carcinoma was obtained at the completion of the procedure. Three month follow up imaging demonstrated no residual viable tumor at the treatment site with expected post ablation changes. The overlying skin was preserved with no injury.

Conclusions: MR ablation may represent a feasible and safe alternative to surgical resection in patients who are unwilling or unable to undergo surgical resection of breast malignancies.

References

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Background or Purpose

Gynecological malignancies are initially treated with resection but unfortunately if there is local recurrence, radical surgery, including pelvic exenteration is often employed. Radical surgery carries a significant rate of postsurgical morbidity and mortality. Alternatively, thermal ablative techniques have been applied as a minimally invasive approach to treat local disease. Using MR guidance, we utilized cryoablation as a novel treatment of local gynecologic pelvic recurrences. This study examines the feasibility and safety of this procedure.

Methods

A retrospective review was performed of the 417 MR guided procedures performed between January 2011 and January 2018. Patients who had local pelvic recurrences of gynecologic malignancies were included in this review. Their medical records were evaluated for technical success, procedure related complications and evidence of recurrence at follow-up including imaging confirmed recurrence or repeat biopsy. Complications were classified using the SIR classification system for complications by outcome.

Results

Five patients underwent six MR guided cryoablations for pelvic recurrent disease. The primary tumor types included endometrial adenocarcinoma, squamous cell carcinoma of the vagina, and urethroendometrial stromal sarcoma. Technical success was 100%. The average time to recurrence was 204.8 days following ablation. Only two complications were noted which included post procedural nausea (A) and one episode of bladder leak after breakdown of the bladder wall into the ablation zone (D). The bladder leak was treated first with bilateral percutaneous nephrostomy tubes but the patient ultimately underwent anterior pelvic exenteration due to its persistence and the patient's inability to tolerate the nephrostomy tubes.

Conclusions

MR guided cryoablation of focal pelvic gynecologic recurrences is a safe and feasible minimally invasive treatment option which can be used to control local tumor progression with high technical success while avoiding or delaying the need for radical pelvic surgery.
Improving MR-thermometry during MR-guided microwave ablations

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Purpose: Proton resonance frequency shift (PRFS) thermometry is a well-established technique to map temperature changes with MRI. The accuracy of PRFS is directly related to image SNR¹, ², which is reduced with active microwave ablation during image acquisition. PRFS and PRFS-based thermal dose computation³ rely on alignment of an initial reference image with each subsequently acquired image frame, which can be a challenge with respiratory motion. The purpose of this study was to modify microwave system hardware and patient image acquisition protocol to reduce image noise, RF interference, and inaccuracy of PRFS thermometry caused by respiratory motion during MR-guided microwave ablations.

Methods: A phantom experiment using an active microwave system (Medwaves AveCure) with a microwave antenna submerged in saline was conducted on a 1.5T MRI scanner using thermometry image SNR to establish an optimal combination of the numbers of ferrite RF chokes added to the RF power and temperature sensor wires connecting the antenna to the microwave generator. The effects of adding RF chokes on PRFS thermometry were subsequently studied in multiple microwave ablations in porcine tissue phantom. The modified microwave system was subsequently employed in its optimal configuration for clinical procedures. To reduce errors in PRFS thermometry caused by misregistration of images due to patient respiratory motion, image acquisition for temperature monitoring was manually synchronized with the prescribed respiratory cycle of the patient’s ventilation system during the ablation procedure. Temperature maps during which image acquisition was synchronized with the patient’s respiration were compared to those during which acquisition fell out of synchronization.

Results: The images acquired in a porcine phantom with the modified microwave system (i.e. added RF chokes) were substantially improved relative to images acquired with the unmodified system, see figure below. Specifically, both image noise and RF interference artifacts were reduced to levels at which accurate PRFS temperature mapping was possible. Synchronizing acquisition of PRFS thermometry images with the patient’s respiratory cycle reduced misregistration between the images acquired during the ablation and the reference image acquired prior to ablation. The respiratory motion artifact remained present in MR thermal maps obtained from images acquired at times out of sync with patient respiration.

Conclusions: RF-interference reducing modifications to microwave ablation system combined with adjustments to MR acquisition protocol of the PRFS thermometry were successful in achieving clinically usable thermal maps for monitoring clinical MR-guided microwave ablation procedures.

References:
Improved MR thermometry during Microwave ablation by correcting for electromagnetic interference
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Background Microwave ablation (MWA) is a minimally invasive treatment for localized diseases (1-3). MRI is advantageous for guiding MWA due to its excellent soft tissue contrast for localizing tumorous tissues, guiding microwave antennae placement and assessing treatment. The feasibility of monitoring MWA using MR thermometry has also been demonstrated; however, its clinical application is often hindered by the electromagnetic interference (EMI) from the microwave generator (MWG). Here we present an approach to correct for EMI in MR thermometry images. Improved temperature maps and thermal damage maps were demonstrated after EMI correction in our clinical MWA patient studies.

Methods MR-guided MWA in the liver were performed with the patient under anesthesia with a MRI-configured AveCure system (MedWaves Inc., San Diego, CA) on a 1.5T scanner. A 2D FLASH sequence was used for MR thermometry. To minimize respiratory motion artifacts, scanning was synchronized with the patient’s respiratory cycle with a 3s acquisition time during expiration.

For EMI correction, k-space data were analyzed based on the average signal $S_{avg}$ from 20 or so points in the periphery zone where the signal fell to near noise level on each phase encoding line. A line was considered as contaminated if difference of $S_{avg}$ between the corresponding lines in the current and the baseline frames exceeded an empirical threshold. The contaminated k-space lines were then replaced using the most recent uncontaminated data at the same k-space locations. EMI-corrected images were reconstructed from the resultant k-space data. The reference-based proton resonance frequency shift (PRFS) method was applied to obtain temperature maps and thermal damage maps using the cumulative equivalent minutes at 43 °C ($CEM_{43}$) metric (4,5).

Results Fig. 1a shows the original k-space data from three consecutive frames during a liver MWA procedure with various degree of EMI contamination. Fig. 2b and 2c show the corresponding k-space data after removal of contaminated data and after correction, respectively. The magnitude images (Fig. 2d-e) and thermal maps (Fig. 2f-g) show the effectiveness of the algorithm. The treatment zone is much better defined in the corrected thermal damage map (Fig. 2i). As the nearest uncorrupted data available were mostly 1-2 frames away from the current frame, the error in MR thermometry introduced by the correction method is expected to be small. This was confirmed in a tissue sample experiment.

Fig 1. EMI correction for a liver MWA. (a-c) original, EMI corrupted data removed and corrected k-space data from 3 consecutive frames. (d-e) original and EMI-corrected magnitude images. (f-g) original and EMI-corrected temperature maps. (h-i) original and EMI-corrected thermal damage maps.

Conclusions Significantly improved MR thermometry has been demonstrated with the proposed EMI correction method. This method can potentially be implemented to obtain real-time thermometry for monitoring clinical microwave ablation procedure.

Title: Percutaneous MRI-Guided Hepatic Tumor Cryoablation: Experience and Long-term Outcomes

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Purpose: The goal of this study is to assess the technical efficacy and long-term outcomes, including local recurrence, systemic progression and overall survival, of MRI-guided hepatic tumor cryoablation procedures performed at a single center between 1998 and 2014.

Methods: A total of 105 patients meeting the following inclusion criteria were studied: 1) age>18 years; 2) pathology-proven hepatic malignancy; 3) and MRI-guided hepatic cryoablation performed at Brigham and Women's Hospital between October 1998 and August 2014. Percutaneous ablation procedures were performed with MRI-guidance by a board-certified radiologist using either a 0.5T GE Signa SP MRI scanner or a 3T wide bore Siemens Magneton Verio MRI scanner. The standard cryoablation protocol was performed using the SeedNet Cryoablation system (Galil Medical, Inc) and consisted of predominantly two 15-minute freeze applications separated by a 10-minute thaw period. Technical efficacy was assessed at 3 months post-procedure. Multivariable logistic regression was used to assess for factors independently associated with technical efficacy. Local recurrence, systemic disease progression and overall survival post-procedure were assessed using Kaplan-Meier survival analysis (1). Cox regression analysis was used to assess the clinical and technical factors independently associated with patient outcomes, with P<0.05 considered to be statistically significant on Wald’s test. Procedure-associated complications were graded based on the common terminology criteria for adverse events (CTCAE) (2).

Results: A total of 105 patients met inclusion criteria (56% female, age range 29 to 88 with mean of 61.7). Average tumor diameter was 2.4 ± 0.9 cm. 14.3% of tumors were primary hepatic malignancies with the remaining consisting of metastatic hepatic lesions. Technical efficacy was 76.5% at 3 months post-procedure. Smaller tumor size was independently associated with technical efficacy (OR=0.42; P=0.016). Long-term local tumor progression occurred in 30% of tumors (17.5% of tumors if tumor size < 4cm; 62% if tumor size > 4cm), all occurring within 36 months post-procedure. Larger tumor size was an independent predictor of local tumor progression on Cox regression analysis (HR=1.98, P<0.001). Systemic disease progression was noted in 90% of patients at 10 years post-procedure with mean time to systemic progression of 11±0.9 months. Survival analysis revealed a survivor function of 0.12 at 10 years post-procedure with mean survival time of 39±6.1 months. Adverse events of grade 3 or higher were observed in 15.2% of cases, with all patients recovering and no procedural-related deaths reported.

Conclusions: Percutaneous MRI-guided hepatic cryoablation procedures are associated with high technical efficacy, favorable outcomes and acceptable adverse event rates. MRI-guided liver tumor cryoablation is a reasonable treatment alternative when heat-based ablation technologies are considered problematic or when MRI monitoring of ablation is paramount such as in tumors near critical structures.

References:
Thiel embalmed cadaver study of shoulder and hip arthrography with a patient-mounted MRI compatible robot

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Abstract: We have developed a patient-mounted MRI-compatible robot with four degrees of freedom for needle guidance in pediatric interventional procedures. Our clinical goal is to move arthrography from a two-step procedure (fluoroscopy followed by MRI) to a solely interventional MRI procedure. In this abstract we describe a recent study using Thiel embalmed cadavers to demonstrate the concept for the shoulder and hip.

Background or Purpose: Arthrography is the evaluation of joint condition using imaging such as computed tomography (CT) and magnetic resonance imaging (MRI). Among American children ages 5-14, there is, on average, over one sports-related injury during this period, often involving shoulders, hips, and wrists. MRI arthrography is the modality of choice for evaluation of the labrum, articular cartilage, and other internal structures of the joint in children. Currently, this test requires two separate stages, an intra-articular contrast injection typically guided by fluoroscopy, followed by an MRI. The current inability to leverage the imaging capabilities of the MRI itself and the manual nature of needle placement lead to increased cost, anxiety, and in some cases prolonged sedation time, especially for the youngest and most anxious patients. Our long-term goal is to enable radiation free procedures in children using MRI, as well as to take advantage of the exquisite soft tissue imaging characteristics of MRI for interventions.

Methods: The body-mounted robot used for this study provides 4 degrees-of-freedom for positioning and orienting the needle guide to a prescribed needle trajectory; it is manufactured from materials compatible with the MRI environment and does not affect the image quality. The robot is registered to the scanner coordinate system using fiducial markers attached to the robot base and then based on the prescribed target and skin entry points, it aligns the needle guide to the planned trajectory. The robot has shown targeting accuracy of 2.08 mm in MRI phantom studies [1].

![Image of robot and needle placement](image_url)

Figure 1: (a) Robot mounted on right shoulder of cadaver specimen with circular coil placed around mounting ring, (b) Injection of saline at hip joint after targeting and needle placement with robot assistance and (c) Needle confirmation MR image showing the needle trajectory, where the needle tip is successfully inserted in the shoulder joint space.

Thiel embalmed cadavers from the University of Dundee Anatomy Department were used for this study. Thiel embalmed cadavers [2] offer significant advantages over traditional formalin embalmed and fresh cadavers including improved tissue flexibility, texture and tone, low infection risk and odor. Thiel cadavers retain vascular patency resulting in cadavers that can be perfused and imaged in multiple imaging modalities, resulting in an anatomically realistic pre-clinical model [3]. Imaging was performed with a 1.5T GE Signa HDx scanner (GE, Milwaukee, USA) using a SCH DuoFLEX phased array coil (24cm paddle combined (4CH) with an interventional loop coil (1CH) at the Institute for Medical Science and Technology. A mounting ring was strapped on the shoulder and hip with the square paddle underneath the cadaver and the loop coil around the mounting ring (Fig. 1(a-b)). 3D-volume Fast Spin Echo (3D CUBE) images were acquired for registration of the robot with the image space, planning needle insertion trajectory and needle placement confirmation post insertion (Fig. 1(c)).

Results: On one female and one male cadaver, a total of 13 targeting attempts were made, 10 in the shoulder and 3 in the hip. For both, the shoulder and the hip, the robot was registered to the scanner coordinate system only for the first attempt and then the same registration was used for the remaining attempts. All attempts were successful with an average procedure time of 20 minutes. However, for the first targeting attempt, the total time was more than 1 hour as it involved the complete clinical workflow including robot attachment, registration to the scanner coordinate system, learning curve for the robot assisted trajectory planning and contrast agent injection. For the remaining 9 targeting attempts, the average time was 12 minutes. In future studies we want to optimize the clinical workflow to reduce the total procedure time to less than 1 hour.

Conclusions: The Thiel embalmed cadaver is an excellent real human anatomy model for technology evaluation and provides useful data that will be important before we move to clinical studies. The study showed the feasibility of using the robotic device but identified issues that must be resolved before moving to clinical trial, particularly in terms of robot mounting.

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Design of a Novel Mechanism for Robotic Needle Guide for MRI-guided Prostate Biopsy
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Abstract

Background or Purpose: Prostate cancer is estimated to be second most common form of cancer among men in the US with 29,430 related deaths and 164,690 new cases in 2018 [1]. Men with symptoms of prostate cancer are recommended to undergo core needle biopsy based on Prostate-Specific Antigen (PSA) level. Currently, Transrectal Ultrasound (TRUS) guided biopsy is clinically most prevalent even though MRI guided targeted biopsy has proven to be better. MRI provides excellent soft tissue contrast and higher detection rate compared to TRUS. To enhance needle placement accuracy, MRI compatible needle guide robots [2-4] have been introduced but complex and bulky designs have prevented widespread clinical translation of such systems. This motivated us to design a compact, 4 degrees-of-freedom (DOF) robotic mechanism for MRI-guided targeted prostate biopsy.

Methods: The design requirements for the new MRI guided robotic mechanism are identified: (i) the mechanism should be compact enough to fit between-leg space while the patient is lying in lithotomy position inside the 60 cm bore; (ii) it should provide targeting with needle angulation range of ±15 degrees to allow a physician to access the prostate along the safest trajectory; and (iii) it should be built using non-magnetic materials with combination of polymers and non-ferrous metals to have safe operation and minimize image artifacts. Accordingly, we designed a robot consisting of a 4-DOF mechanism with belt drive and motors for power transmission. The mechanism consists of two sub-mechanisms, a set of two double discs, and each providing planar motion for a ball-joint. When the needle is inserted through the two ball joints that are constrained to move along a profile slot on the discs, their planar movements provide 4 DOF positioning of the needle tip.

Results: A novel mechanism for robotic prostate biopsy was designed consisting of four discs. A belt drive composing of MLX timing belts and pulleys with pitch of 1/8” transfers power from motors to the mechanism’s discs. The overall size is 100 width by 170 mm height and 30 mm thickness. The kinematics of the mechanism was analyzed in which the equations correlating the needle tip position with the disc rotations were derived. A path-planning algorithm was implemented to compute the required rotations of the discs to move from one target to another. Finally, a prototype of the mechanism was fabricated. Most of the parts were 3D printed. The standard parts (i.e. timing belts and pulleys) were obtained off-the-shelf. Each 2-DOF sub-mechanism provided a required in-plane positioning for the ball-joint. By connecting the two ball-joints with a needle guide, the independent rotation of the discs could control 4-DOF needle guide. Insertion depths were kinematically computed for manual operation.

Conclusions: The emergence of MRI guided robotic needle guide systems for prostate biopsy promise higher accuracy and precision. Unlike existing systems in the literature that are bulky and complex, our system utilizes a novel mechanism which is significantly compact and simple. In our design, a stack of four discs with size of perineum area provides 4-DOF manipulation. The overall robot dimensions are close to the existing manual template for prostate biopsy [5].

References
Integration of a MR-compatible robotic arm for PET/MRI guided focused ultrasound treatment

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Background MR-guided focused ultrasound (MRgFUS) works in a non-invasive way without radiation leading to acceptance of FUS as an interventional method for ablation of benign tumors like fibroids [1], local treatment of prostate cancer [2], palliative pain reduction of bone metastasis and cure essential tremor [3]. Additionally, MRgFUS was used in experimental settings to support drug delivery, opening of the blood-brain barrier, immunomodulation and supports conventional procedures like chemotherapy and irradiation. Currently, existing FUS systems at the market exhibit transducers integrated into the patient table or allow only treatment of a specific organ. Hence, a robotic arm positioning the FUS system according to the treatment planning should be more versatile.

Methods To enable flexible positioning of a FUS transducer a MR-compatible robotic arm system (InnoMotion by InnoMedic GmbH) [4] was integrated into a Biograph mMR PET/MRI system (Siemens Healthineers). Therefore, the C-arm holding the robotic arm was modified to fit onto the patient table. A 3D-printer (Makerbot Z18) was used to manufacture the necessary adaption and fixation parts.

To integrate the system into the existing clinical infrastructure, the hardware, which contains the planning software of the robotic arm, was virtualized using Oracle VirtualBox. This virtual machine was placed on the Linux server which is attached to the PET/MRI system for post-processing, storage and distribution of data. In this way, image data can be transferred easily and efficiently to the planning software which acts as a DICOM receiver.

Results The robotic arm system was successfully modified to fit into the Biograph mMR PET/MRI system. A concept for integrating the robotic arm system into the clinical IT infrastructure was developed and implemented.

Conclusions Positron Emission Tomography (PET) combined with Magnetic Resonance Imaging (MRI) represents a unique method for monitoring interventional procedures like biopsies and MRgFUS ablation. Due to the early stage of these combined therapies, MR-capable robotic systems are hardly available. Therefore, clinical experience and standardization with this integration of systems is lacking. The presented technical setup opens the field to start gaining clinical experience. Evaluation and validation studies will be conducted to assess the potential of using this robotic system for MRI-guided FUS interventions.

References
Remote Controlled Manipulator in combination with Automated Real-time Needle-guide Tracking for fast MR-guided Transrectal Prostate Biopsy: a Phantom Study

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Background: Various strategies have been developed to make in-bore MR-guided biopsies less time-consuming, e.g. robot-assistance and the use of an automatic, real-time needle-guide tracking sequence. The use of a real-time tracking sequence shows a promising reduction in procedure time. However, reaching into the magnet to hold the needle-guide during tracking can be imprecise and impractical, and robot-assistance might be employed to solve this issue.

Purpose: To assess the feasibility of a remote-controlled manipulator (RCM) in combination with an automatic real-time needle-guide tracking sequence for fast in-bore magnetic resonance (MR)-guided transrectal prostate biopsies.

Methods: A phantom study was conducted on a 3-T clinical MRI system (Magnetom Skyra, Siemens, Erlangen, Germany). Three MR-guided biopsy settings were tested: I. manual procedure, II. robot-assisted procedure and III. robot-assisted procedure combined with real-time needle-guide tracking (Fig. 1). In the manual procedure an adjustable MR-compatible biopsy device (DynaTrim; Invivo, Schwerin, Germany) was used to direct the needle-guide at a biopsy target. In the robot-assisted procedure an MR-compatible RCM (Soteria Medical BV, Arnhem, the Netherlands) was used, which could be directed at a biopsy target using integrated planning software. For the third procedure the RCM was combined with a phase-only cross correlation (POCC) algorithm-based automatic needle-guide tracking sequence to facilitate targeting under real-time image feedback (Fig. 2). In each setting, 25 fiducials embedded in agar gel were targeted. Correct targeting was confirmed with short balanced steady-state free precession (bSSFP) imaging. Total procedure times and targeting accuracy were determined. The procedure time was defined as the time from acquisition of the first targeting image to the confirmation image with the biopsy needle in situ. Targeting accuracy was determined by measuring the targeting error, biopsy error and target displacement: the targeting error was defined as the shortest distance from the needle trajectory to the initial target location, the biopsy error was the shortest distance from the needle to the transformed target location after needle insertion and the target displacement was the distance and angle between the original and transformed target location.

Results: Total procedure time with the manual procedure, robot-assisted procedure and robot-assisted procedure combined with real-time tracking, were respectively 10:49±1:45 min, 6:33±0:46 min and 5:47±0:54 min (Fig. 3). All fiducials were successfully targeted and hit on subsequent biopsy.

Conclusion: This study demonstrated the feasibility of MR-guided biopsy by using an RCM in combination with a real-time tracking sequence. Combining robot-assistance with real-time tracking resulted in 46% reduction in procedure time per target compared to the manual procedure. Updated results on the targeting accuracy will be presented when available.

References
Preclinical Evaluation of an Integrated Robotic System for MRI-Guided Shoulder Arthrography

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Purpose: Shoulder arthrography is a procedure to evaluate joint injury, which is often performed under fluoroscopy guidance for contrast agent injection, resulting in exposure to radiation. Additionally, for diagnostic imaging, the patient is required to be moved from fluoroscopy to MRI suite making the procedure longer. Performing the contrast agent injection under MRI guidance using an MRI compatible robotic assistant could improve needle placement accuracy and would eliminate exposure to radiation and patient movement between the fluoroscopy and MRI suite. In this paper we present a shoulder mounted, MRI compatible robot capable of precisely positioning and orienting the needle guide. Results from experiments performed on gelatin phantoms are presented. The results shown here build on our previous works [1-2].

Methods: An MRI compatible robot that provides 4 degrees of freedom for needle guide position and orientation is used for location targeting in the MR images. As shown in Fig. 1(a), the robot motion is divided in two stages, positioning of the insertion point and orientation of the needle at the insertion point. The base rotation and translation joints provide redundancy and result in two unique solutions for a desired insertion point. This allows us to minimize the required robot motion which is desired for a body mounted system to reduce patient discomfort. There are 4 fiducial markers mounted on the robot base for registering it to the MRI scanner coordinate system. We demonstrate accuracy evaluation while following the proposed clinical workflow including robot initialization, registration to MR coordinate system [3], needle trajectory planning, and needle placement and confirmation. Experiments were performed in gelatin phantoms aligning the needle guide trajectory to a desired target defined from the planning image set.

Results: Experiment were performed in 1.5 Tesla Siemens scanner using a gelatin phantom to evaluate the robot targeting accuracy. For each needle insertion, the system is able to successfully register the robot to MR scanner coordinate system using the inbuilt scanner table/body coil and align the needle guide trajectory to desired path defined using the planning image-set. Results show an average in-plane targeting error of 2.08 mm and average orientation errors of 1.48 degrees, errors along the needle insertion and rotation are not considered as they are performed manually.

Conclusions: We present an MRI-compatible robotic device for precise needle insertion to a desired target for contrast agent injection for shoulder arthrography. The proposed system is able to precisely target the desired target locations. In future work we plan to perform experiments in a more anthropomorphic phantom and in a cadaver study. We also plan to improve the rigidity of the system to prepare it for clinical trials.

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References:
Actively-tracked metallic rigid and flexible devices for MR-guided soft-tissue and vascular interventions

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Purpose: Long (>1200mm) and thin (<3mm) metallic-construct or metallic-reinforced devices have preferred mechanical properties and are therefore widely employed in interventional applications. Metallic devices are difficult to positionally locate (“track”) in the MRI scanner using active, MRI-based techniques, due to changes that metallic devices induce in both the static and radio-frequency (RF) magnetic fields used in MRI. Additionally, when the metallic-device length exceeds ¼ of the effective (~8 times shorter) RF wavelength in the body, there is substantial risk that the device, and the cables running through it, can heat surrounding tissues. As a result, use of metallic devices (needles, catheters, guidewires) in the MRI was until recently restricted to short metals (typically <300 mm), which were tracked with passive (susceptibility-based) methods, requiring long acquisition times (>0.5 frames per sec), at reduced spatial precision (~3x3x3mm³), and not supporting simultaneous multi-device tracking. Conversely, to actively-track longer (>500mm) devices, the devices’ metal backbones were substituted with polymer, reducing mechanical (pushability, torquability) performance or requiring larger footprints for equivalent performance. Additionally, space-occupying heat-amelioration methods were added to each cable inside the active devices.

Our goal is to develop metallic interventional devices that can be safely used and actively tracked. In phase 1, we developed the RF and MR-Tracking (MRT) tools required to actively-track metallic devices, and employed them in short (low heating risk) rigid devices [1]. In phase 2, we developed miniature RF tools to prevent heating of long metallic devices, and used them in long (>100 cm) and mechanically complex actively-tracked flexible devices.

Methods: For phase 1: Metallic devices placed in MRI’s static magnetic field distort the field in their vicinity, which perturbs the linearity of MRT. We therefore developed outward-looking MRT micro-coils that receive signals outside the perturbed region. Secondly, in the body metallic devices interact inductively with neighboring metal devices and with surface coils, affecting (broadening and deflecting) the MRT signal, preventing localization. We added phase-field-dithering to the MRT sequence to reduce this distortion, enabling accurately tracking multiple metallic devices. We then constructed active brachytherapy stylets and used them in 20 patients at BWH (3T) and JHU (1.5 T), placing 4-20 High Dose Rate catheters/patient [2]. We measured placement accuracy and procedure time, relative to passively-tracked placement. For phase 2: Long (>wavelength/4) metallic devices, when radiated by RF from the scanner’s body coil, create induced currents on the metal surfaces, which in turn create large electric fields around the devices, that can heat surrounding tissues. Active devices include internal wires and cables that transmit signals from sensors (micro-coils, ECG electrodes) on the devices’ tip and shaft, that similarly receive induced (common-mode) currents. In addition to the heating risk, induced currents on the wires/cables add to the sensor-transmitted signals. In MRT, when the signal does not originate entirely from the tracked micro-coils, localizing the micro-coils can be difficult. To remove these induced currents, we developed the miniature floating resonant RF trap (MBalun) [3]. MBalun employs similar principles to rigid concentric-tube Baluns that are found on the cables of commercial MRI coils, with design changes resulting from the smaller footprint (1 vs 25 mm diameter) and greater-flexibility requirements. We used the devices’ long metallic (braid or tube) backbone as MBalun’s inner tube, and a multiple-winding large-pitch solenoid as the outer tube, with thin film capacitors resonating the devices. MBaluns were placed on the device shafts at ~15 cm increments, using the magnetic field produced by the induced currents to capture and attenuate them. We designed MBaluns using electromagnetic simulation (Figure 2), and built two active devices; an MRI-compatible 1mm-diameter cardiac guidewire with 8 MBaluns and an MRI-compatible 3mm-diameter braided electrophysiology catheter with 9 MBaluns. We tested heating in phantoms, and navigation in animal models.

Results: Phase 1 Brachytherapy MRT stylets were used clinically, providing tracking rates of 13-16 fps, at an accuracy of 0.6x0.6x0.6mm² [2]. Clinicians placed MRT stylets closer (mean:28 mm) to desired locations than possible with passive tracking. Active MRI-guidance was performed at ULS speeds, with vastly higher precision. Phase 2 MBaluns [3] provided effective (~15dB/MBalun) common-mode attenuation, removing heating risks. MRT navigation of guidewires/braided catheters was performed in swine hearts with excellent visibility of the micro-coils.

Conclusions: Both short and long metallic interventional devices can be safely, accurately and rapidly actively tracked utilizing revised MRT coils and sequences, with MBalun heat-mitigation. The door is open for space-efficient soft-tissue (percutaneous) and vascular devices with mechanical performance similar to non-MRI-safe equivalents.


Figure 1: (Below) Tracked metallic Brachy stylet with two-MRT coils. Time history (Right) showing two stylets (Green, Blue) actively navigated into a tumor (Brown) from locations achieved with passive tracking, which were not in the tumor.

Figure 2: (Left) MBalun design (Upper) and attenuation of voltage on wire (Lower). (Middle) active metallic guidewire with 2 MRT coils and metallic-braided EP catheter with 4 MRT coils (Right) navigated into swine hearts. Yellow arrows show MRT coils. Red arrows point to dark shaft, indicating lack of elevated flip angles in metallic shafts.
Percutaneous interventions play fundamental roles in both diagnosis and treatment of prostate cancer (PCa). Nearly one million prostate biopsies are performed annually in the United States, where tissues are sampled from the prostate either systematically or targetedly by using a biopsy needle for pathological examination. The confirmed lesions may then be treated percutaneously using brachytherapy or some form of thermal ablation (i.e. laser, cryoablation) using needle-shape probes depending on their grade, clinical indications, and patient preference. For those procedures, the demand for accurate placement of needles or probes is higher than ever, as clinicians are now capable of pinpointing a small lesion due to the widespread use of multiparametric magnetic resonance imaging (MRI). While needles and probes are often inserted into the lesion under ultrasound-guidance or MR-ultrasound fusion guidance, direct MR guidance can potentially improve the clinical outcome by making the procedures truly closed-loop with its abilities to localize the needle tip relative to the lesion and monitor the treatment effect in real-time by means of thermal imaging. This talk will focus on our recent work on enabling technologies for closed-loop needle placement in the prostate under MRI guidance. In particular, the talk will discuss our collaborative projects on MR-compatible needle guide robot, interactive MR imaging, and modeling of needle deflection based on patient-specific anatomical model.
Assistance techniques for percutaneous MRI interventions
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**Purpose**  Clinicians are usually confronted with a number of technical and procedural challenges when it comes to interventions in an MRI environment. This presentation will give a brief overview of clinical assistance techniques for percutaneous interventions in different body regions and try to identify some trends in recent research studies and MRI development.

**Methods and Discussion**  Percutaneous interventions can be guided by either ultrasound, X-ray, CT or MR imaging with each modality having well-known strengths and weaknesses. A common indication for MRI is given when other techniques fail to properly identify suspicious regions or nearby structures. Given that MRI provides near real-time feedback on the distribution of temperatures and estimated damage, it should also be highly considered for any type of thermal therapy.

Interventional techniques [1,2] widely benefit from ongoing progress in the diagnostic field, ranging from powerful system hardware and high-density coil arrays to advanced acceleration techniques and pulse sequences with special sampling or image reconstruction algorithms. The main obstacles are that in-room procedures call for special MRI tools and safety measures, access to the imaging region is difficult, signal generation takes time, and system architecture follows diagnostic needs, not interventional ones.

MRI tools from needles to special coils with proper opening are available but choices are limited. Some imaging and guidance devices are routinely used for special brain, breast or prostate procedures. Research systems naturally explore a broader range of applications and body regions. Navigational aids are prominent for both in-bore and out-of-bore procedures, usually registered or tracked by special markers. Various systems are enhanced by robotic functions to improve overall workflow and reliability [3].

Current prototype design might draw some profit from affordable computer hardware, a growing number of software frameworks for medical image processing or novel manufacturing options like 3D printing or deposition. Despite many technical opportunities, it should be stressed that an early involvement of clinical experts is highly recommended.

Another positive trend can be seen in the growing number of wide-bore MRI systems which not only provide additional in-bore space for patients and devices but should also foster the adaptation of concepts and devices between different scanner makes and models. MRI manufacturers have also recently put some effort into automating parts of the diagnostic workflow, a factor that is even more relevant for MRI interventions.

So far, interventional components, such as holders, manipulators, tracking or control devices, typically need to be added to a diagnostic system resulting in extra setup and removal steps. Some recent MRI systems feature tablet-like control interfaces and devices for in-bore patient monitoring or scan control (e.g., respiration sensor or tracking camera), which may eventually find an interventional use as well. Development could also be streamlined if manufacturers find a way to share both software and hardware interfaces with third-party developers.

**Conclusions**  Assistance techniques are not essential for MRI interventions but often provide the means for refined targeting, better control and improved performance, especially for complex access paths or less experienced interventionalists. It remains to be seen for which applications and to what extent they will lead to substantially shorter procedure times or lower costs. Persistent challenges are the seamless integration of concepts into the MRI environment as well their clinical translation.

**References**

MRI-Compatible Robot for Pain Injections in Adults and Children: Concept and First Results
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Abstract. Our research team is developing a body-mounted MRI-compatible robot for perineural injections used to treat pain in adult and pediatric patients. The robot is intended to enable needle tip and target visualization under MRI in real-time through an integrated imaging coil, built-in fiducials for image registration, and active needle insertion/rotation. MRI provides unmatched soft tissue visualization of the targeted nerves and delivery of the locally injected medications without contrast and is therefore an ideal imaging modality for these procedures.

Background or Purpose. Chronic pain management is an important clinical problem in both adult and pediatric patients. Studies indicate that approximately 35% of the US population in adults and 20% to 35% of children worldwide suffer from chronic pain [1], [2]. We aim to enable MRI-guided interventions for pain management to gain the following benefits: 1) exquisite image quality and visualization of peripheral nerves and surrounding tissue; 2) elimination of radiation exposure for both the patient and clinical staff, which is particularly important in the pediatric environment; 3) develop a new streamlined MRI workflow using a body-mounted robot [3] to enable the procedure to be done in the MRI room within one hour; and 4) create a platform technology for needle guidance under MRI that can be applied to other interventions including precision biopsy and thermal tissue ablation in future work.

Methods. The proposed workflow will allow needle placement inside the bore of the scanner without moving the patient in and out as follows:
1. The patient is brought into the MRI suite and positioned on the table. If anesthesia is required, the anesthesia lines are placed.
2. The robot is placed on the region of interest and secured using a mounting ring and straps.
3. MRI images are obtained using the table coil(s) and the coil integrated with the robot. Imaging includes T1/T2 weighted and contrast enhanced sequences that visualize both anatomy and fiducial markers integrated into the robot.
4. The MRI DICOM image data set is sent to the planning workstation. The radiologist selects the target point and entry point and the software simulates the needle trajectory.
5. The robot coordinates are registered to the image coordinates using fiducials and paired-point registration
6. The robot is commanded to move and orient the needle-guide. The interventional radiologist will then use a joystick to drive the needle to the target. The needle position can be viewed continuously using a real-time MRI sequence.
7. Once the needle is placed, the radiologist injects contrast or medication.
8. Diagnostic images are obtained using the table coil and robot-integrated coil.

Figure 1: (a) New modular robot design by Johns Hopkins LCSR consisting of a 4 degree-of-freedom (DOF) positioning and orienting stage and a 2-DOF needle driver which is remotely actuated by flexible transmission cables through motors located at table end. (b) Laser cut prototype of four degree of freedom positioning and orientation stage and (c) Single loop coil developed at Cincinnati Children’s shown between two conventional coils straddling a ham phantom in a Philips 1.5T Ingenia MRI system. This coil will provide a base for the robot.

Results. Initial results from the project are shown in Figures 1(a-c). Fig. 1(a) shows the modular robotics design from the Johns Hopkins LCSR group. Fig. 1(b) shows the prototype of the orientation stage. Fig. 1(c) shows a single loop coil from Cincinnati Children’s that will fit under the robot mounting ring.

Conclusions. We have started developing a modular robotic system for precise injection of nerve roots under MRI imaging. In the next step we plan to continue to develop the system components and complete cadaver studies.

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References
MRI-based Quantitative Oxygen Sensing for Guiding Radiation Levels in High Dose Rate Brachytherapy
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Abstract
Hypoxia is a hallmark of solid tumors and has been linked to chemo- and radiotherapy-resistance and a generally poor prognosis for patients. This can be overcome by boosting the radiation dose. Clinicians lack a viable method of quantitatively measuring tumor oxygen content to enable dose escalation. We present the use of a silicone-based sensor to quantitatively measure oxygen using a clinical MRI.

Background
Hypoxia is a hallmark of solid tumors and has been linked to chemo- and radiotherapy-resistance and a generally poor prognosis for patients. This has been observed in cervical, prostate, and head and neck cancers. A compelling treatment approach is the delivery of an increased radiation dose to hypoxic tumor sub-volumes. High dose-rate (HDR) brachytherapy is the most effective option to achieve dose escalation in hypoxic regions of the tumor without exposing healthy tissue and organs to unsafe radiation levels. Tumor oxygen levels are not currently considered during the treatment and dose planning process. Attempts to overcome hypoxia have been of limited clinical utility due to the lack of an appropriate oxygen measurement technique to quantitatively map tumor hypoxia. We report on the development of an oxygen-sensitive silicone polymer for quantitative and longitudinal monitoring of in vivo tissue oxygen levels. The T1 relaxation time of the polymer correlates with the tissue oxygen content, allowing measurement of tumor hypoxia using MRI.

Methods
The work presented here is in support of an early feasibility trial in ten patients. The trial will take place during MR-guided catheter placement for HDR brachytherapy of gynecological cancer. Early feasibility trials are used to guide the further development of a technology before finalizing the device design. This trial will involve the temporary (<5 hours) placement of the silicone oxygen sensor (1.5 mm diameter and x 7 mm long cylindrical) and the measurement of the tumor oxygen level. The sensor will be placed within 3.5 cm of an endorectal coil during clinical use. The oxygen sensor is a proprietary silicone polymer produced from a combination of a liquid silicone oil and a silicone elastomer. These sensors are produced using implant grade medical silicones. Synthesized sensors are measured in a 3T MRI scanner (Siemens Verio). T1 relaxation measurements are conducted using an inversion recovery turbo spin echo sequence. Sensor performance related to resolution and equilibration rate were evaluated using an MRI compatible environmental chamber that controls oxygen concentration. The endorectal coil is used to further enhance the SNR of the measurement beyond what is possible with the spine coil alone.

Results
Nine sensors were measured in a phantom at discrete distances from the coil, mimicking the in vivo use conditions (Figure 1 (L)). The T1 relaxation time of the sensor was measured under conditions of 0% and 21% oxygen. The relaxation time under these conditions were statistically significant (Figure 1 (R) p<0.001). This is sufficient for use in this clinical trial.

Conclusions
Silicone-based oxygen sensors are a viable method of quantifying tumor oxygen content. MRI has become the preferred method of imaging patients undergoing HDR-brachytherapy allowing the sensor to integrate well with the existing clinical practice. Sensor resolution can be further enhanced when the requirement of using materials already intended for implantable use is removed (new materials can be validated for implantable use). Use of a lower viscosity silicone oil will increase the resolution of the sensor. Pairing of these sensors with HDR-brachytherapy will provide clinicians with the information and means necessary to deliver elevated doses of radiation therapy to hypoxic tumor sub-volumes and improve treatment outcomes.

References

Figure 1 (L) MRI scan of 9 oxygen sensors (3 per tube). The figure shown is at a single slice captured during the inversion recovery pulse sequence. (R) The T1 relaxation time of the sensor under 0% and 21% oxygen environments. The measured relaxation time is statistically significant (p<0.001).
Towards Haptic Transparency in MRI-Guided Needle Biopsies: A 3-DOF Macro-Mini Manipulator

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Background or Purpose: Inability to access patients within a MRI machine is a major roadblock in achieving real-time MRI-guided interventions [1]. MRI compatibility requirements prohibit conventional electromechanical solutions. Some specialized robotic devices have been proposed; however, these do not provide physicians with haptic feedback and rely on imaging. In minimally invasive procedures, haptic cues are valuable. For example, changes in tissue stiffness help physicians locate tumors and identify tissue boundaries [2]. To address this need, we are building a MRI compatible system that consists of a macro teleoperator with three degrees-of-freedom (DOF) for manipulating a biopsy needle inside a MRI bore. To this, we add a mini manipulator designed specifically for precise rendering of contact forces from a biopsy needle. The combination allows remote manipulation of a needle inside the MRI bore with haptic transparency (a sense of touch at the input) for MRI guided biopsy.

Methods: The macro teleoperator uses high stiffness, low friction hydraulic lines [3] to transmit motions and forces between the input and output (Fig 1). Each end of the teleoperator consists of a hybrid parallel-serial 3-DOF mechanism with two rotational DOF in series with a translation DOF. This provides a spherical workspace. In a biopsy procedure, the center of rotation is placed near the entry point on the skin. The teleoperator is constructed from MRI compatible materials (plastics, glass, ceramics, and small amounts of non-ferrous metals). Position accuracy between the input and output was tested for the rotational DOF using an OptiTrack camera system. Tracking markers were mounted on each end of the device and overhead cameras recorded the motion while the input was manipulated. The OptiTrack has sub-mm accuracy and data were acquired at 125Hz. The force sensitive mini manipulator consists of a second hydraulic system made with precision ground glass pistons with no seals or diaphragms [4]. Force measurements were conducted using a Mark-10 M4-50 force gauge and a Jennings JSR-100 scale.

Results: The average Euclidean error between the input and output of the macro teleoperator was ~3mm. Fig 2 shows sample data points gathered with the OptiTrack system overlaid on a spherical fit which depicts the full workspace. The error between the spherical fit and the theoretical (designed) radius was ~1.5mm. Experiments on the mini manipulator reveal that a user can resolve forces as low as ~0.01N at an insertion velocity of ~2mm/s.

Conclusions: Our preliminary work demonstrates a promising hybrid technology for achieving precise teleoperation with haptic feedback in an MRI environment. The proof-of-concept prototypes will be refined to develop a system for performing a remotely-guided transperineal prostate biopsy with real-time MRI. The prototypes are constructed from MRI compatible materials. The next step is to conduct experiments in phantom tissue in the MRI, to evaluate the advantages of haptic transparency in image-guided procedures.

3-DOF MR-Conditional Haptic Transmission System for Bilateral Teleoperation
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Background
Magnetic resonance imaging (MRI) is used for soft tissue pathology diagnosis and assistance with targeted lesion procedures. However, limited physician access to patients in the MR scanner bore requires iterative positioning where the patient is physically inaccessible for surgical intervention. The MR images are used to guide the physician in precisely locating the area for targeted solutions. There is a time lag between the imaging and the surgical procedure leads to subtle inaccuracies. There is a pressing need to combine detection and biopsy into a single procedure. As a solution we present a real-time teleoperation device for needle biopsy.

Methods
The device is made of non-ferromagnetic materials using a rolling-diaphragm hydrostatic transmission in a purely passive mode. The device has a 1:1 kinematic mapping. This overcomes the difficulties imposed by the lag time in existing practice. This master-slave device uses a new low friction hydrostatic actuator based on antagonistic pairs of rolling diaphragms. The system is counterweighted on the master side. The 3-DOF slave side is connected to its mirror image on the master side through the hydrostatic transmission. The geometry of the device is a pantograph plus one DOF for yaw. The maneuverability provided by the design maximizes the working volume, giving the clinician flexibility of approach to affected tissue. There is a passive 2-DOF swivel which holds a biopsy needle, at the end effector. Template grid needle plates on each side of the device assure needle alignment. Phantom tissue is on the slave side to test the device. The operator is able to change the angle and stroke of the needle on the slave side by manipulating the master side. The working fluid is sealed and has common air pre-load; this ensures that the transmission is backdrivable and bidirectional. Hydraulic swivels were added to reduce friction and increase haptic transparency.

Results
As expected the hydrostatic transmission system reproduces the input motions generated at the master side to the corresponding output motions at the slave side. Our device is a 3 DOF master-slave haptic mechanism that uses rolling diaphragms, non-ferrous materials to ensure MR-compatibility and a 2-DOF unactuated swivel to provide needle manipulability. The system reliably transmits changes in force. During operational testing using an agar phantom tissue, operators were able to detect different viscosity within materials embedded in the phantom. The compliance of the system results from the following: the diaphragms as they roll: air bubbles in the waterline: and some of the structural components like 3D printed parts, which are not perfectly stiff. The device can transmit forces and motions repeatedly. The manipulator has been instrumented with optical encoders and fluid pressure sensors to quantify performance.

Conclusions
This telepresence system will be an ideal tool to expand scientific understanding of the impact that transmission transparency provides for MR-guided interventions. The device will enable a clinician to perform remote needle biopsies directly while a patient still inside an MRI machine. This work was funded in part by NSF CHS grant 1617122.

References
MR Safe Robot for Long Bone Biopsy: System Concept and Phantom/Cadaver Studies

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Abstract: Our team has developed a table-mounted MR safe robot to facilitate accurate MRI-guided bone biopsy and enable a new clinical workflow paradigm aimed at minimizing radiation exposure by avoiding CT-guided biopsy. In this abstract we describe the system and our phantom and cadaver studies for long bone biopsy in the leg.

Background or Purpose: Accurate and rapid diagnosis of suspicious bone lesions in children is essential to clinical management. Pediatric patients typically present with symptoms of pain/tenderness or reluctance to use the affected limb. If clinical suspicion for malignancy or infection is high, an MRI is performed due to its superior soft tissue contrast, and visualization of the bone marrow and joint spaces. If MRI shows a suspicious mass involving the bone cortex or marrow, a biopsy is performed for tissue diagnosis prior to treatment. Currently, either an open surgical biopsy is performed in the operating room by an orthopedic surgeon or an image-guided needle biopsy is performed in the CT scanner by an interventional radiologist. In either case, the biopsy is performed in a separate location and sometimes under a separate anesthesia session after the diagnostic MRI. In this current clinical workflow, there can be significant time delay in obtaining a definitive tissue diagnosis, delaying treatment and increasing patient / caregiver anxiety. The MRI safe robot we developed will allow the biopsy to be performed in the MRI suite, following diagnostic imaging, thereby reducing trauma and radiation exposure to the patient and providing accurate lesion sampling while shortening the time to final diagnosis.

Methods: The Hopkins URobotics Laboratory designed and built a completely new MRI compatible robot that presents no artifact under MRI as it contains no metal or electric components [1]. Novel features include the use of the pneumatic stepper motors and a non-collinear parallelogram mechanism that provides high stiffness. The new robot design and construction, a complete set of MRI Safe testing experiments according to the standards required by the FDA, and a comprehensive set of phantom MRI-guided targeting experiments are described in [1]. The manipulator consists of a novel 2 degrees of freedom (DoF) Remote Center of Motion (RCM) module, an actuation module, a passive arm with 3 degrees of adjustment (DoA), and a mount for the MRI table. The position of the robot can be adjusted with 4-DoA, sliding the base on the table channels and adjusting the positions of the arm.

Results: We evaluated the accuracy of the system in phantom study in a 1.5T Siemens Aera scanner at Children’s National. A custom-built table mount (purple/blue frame in figure) was anchored to the mounting slots in the Siemens table and the robot was attached. A long bone phantom was created by placing a femur phantom model (Sawbones, Pacific Research Laboratories) in a gelatin mixture inside a long cylindrical tube. A small opening was cut at the top of the tube to allow access for targeting experiments. Small holes were drilled in the bone along this opening as targets. Four holes were used for this study and each hole was targeted twice. A workflow analysis showed the average time for each targeting attempt was 32 minutes, including robot setup time. The average 3D targeting error was 1.39 mm with a standard deviation of 0.40 mm. All of the targets were successfully reached [2]. In a second study, a cadaver leg was procured from an anatomy supply house (Science Cares Inc.) and mounted on the MRI table along with the robot. All required hospital precautions for infection control were followed and study personnel wore protective equipment. A total of 10 MRI-guided, robotically assisted, targeted bone biopsies were performed, 5 in the femur and 5 in the tibia. A hand held battery-powered bone biopsy drill was used to facilitate drilling the bone. Since the drill was not MR Safe, it was tethered to the wall of the room as shown in the figure. After the study, a high resolution CT scan was obtained to demonstrate the missing bone cores at all of the biopsy sites. All of the targets were successfully reached with an average targeting accuracy of 1.43 mm and a maximum error of 2.38 mm. A workflow analysis showed the average time for each targeting attempt was 35 minutes, including robot setup time [3].

Conclusions: The MRI safe robot was able to facilitate accurate bone biopsy in phantom and cadaver studies. The cadaver study showed the need for an MR safe drill which will be part of future work.

Funding Sources: This research was funded by the NIH grant R01CA172244, Pneumatic Robot for MRI-Guided Long Bone Biopsy. The MR Safe robot technology developments were supported in part by awards RC1EB010936 from the National Institute of Biomedical Imaging and Bioengineering, and W81XWH0810221 from the Department of Defense.

Augmented Reality-Guided Soft Tissue Sarcoma Resection
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Purpose: Soft tissue sarcomas (STS) are rare and heterogeneous malignant mesenchymal neoplasms. For most STS lesions, margin-negative resection is the only potentially curative therapy, often with pre- or postoperative radiation therapy (RT) and/or chemotherapy. Inadequate surgery results in disease recurrence and lower survival. We explored the feasibility and utility of an augmented reality (AR)-enabled head-mounted display (HMD) to precisely delineate the extent of a STS prior to surgery.

Methods: A novel AR application was developed on the device, Microsoft HoloLens, to augment the vision of the surgeon by allowing 3-dimensional (3D) radiographic models to be overlaid precisely on the patient. Diagnostic MRI of the patient prior to undergoing preoperative RT was obtained from PACS and loaded into the open-source image-processing and navigation software 3D Slicer. The STS was manually segmented from the post-contrast MRI by delineating the regions of enhancement on the MRI (corresponding to the STS), and a 3D surface model was generated and imported into the Unity game development environment. The Unity app also included functionality to change the opacity of the model, rotate and translate the anatomical models in space using the visual reticule and a Bluetooth-enabled wireless pointer. The Unity app was then deployed on the Microsoft HoloLens for guiding the STS resection.

Results: The HoloLens app was tested on a patient with an upper arm myxofibrosarcoma. Pre-RT MRI (Figure 1(a)) was loaded in 3D Slicer to ensure that the extent of resection matched the extent of the STS on pre-RT MRI. The MRI scan parameters were: Philips MR 1.5T scanner, 2D, TR=599.8, TE=15, Number of averages=3, matrix=248x198, slice thickness=1 mm, pixel size=0.375x0.375mm. Figure 1(b) shows the segmented model of the upper arm (brown), sarcoma (green) and the critical vessels (red). The surgeon first marked out the anticipated margins of resection based on measurements from the pre-RT MRI. The 3D surface models were aligned with the patient using the pointer device interfaced to the HoloLens (Figure 1(c),(d),(f)). The HoloLens app allowed the models to be rotated and translated in 6-degrees of freedom (DOF) and be overlaid precisely on the patient (Figure 1(f)). Natural anatomical landmarks such as the elbow and the skin surface were used to align the models on the patient. Once the surgeon confirmed the position of the sarcoma models on the patient the outline of the sarcoma was delineated on the patient (Figure 1(g)). The AR-guided extent of surgery was somewhat larger than the margins of resection anticipated based on applying measurements from the MRI imaging. Margins on the resected specimen were widely negative.

Conclusion: We developed a novel HoloLens application to enable AR-guided surgery for STS. We have thus explored the possible benefits of advanced AR-guided interventions to better guide resection and reduce the rate of local recurrence.

Figure 1. (a) Contrast MRI of the patient with myxofibrosarcoma, (b) segmented models of the arm, sarcoma and critical vessels, (c) User visualizing the models and placing the model on the patient, (d) Anatomic models placed in space, (e) patient arm, (f) models being aligned on the arm using the visual reticule (red circle) and wireless pointer, (g) surgeon outlining the sarcoma on the arm.
Integration and Clinical Use of a Premium Cart-based Ultrasound Scanner System inside Interventional MRI Suite – a Case Study

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Purpose: Real-time ultrasound (US) imaging provides valuable guidance for placement of treatment applicators. However, it is challenging to integrate US systems into an MRI suite due to safety and image quality concerns. This study aims to test the use of a cart-based Philips EPIQ 7 US system inside an interventional MRI (iMRI) suite hosting a 1.5T Philips Ingenia MRI scanner and to safely deploy it during clinical cases.

Methods: Relevant US transducers were identified according to specific imaging guidance tasks such as liver, breast, prostate and superficial imaging, MR safety tests were performed on each transducer and the US system using a standard approach¹. Both US and MR image quality were investigated to determine the impact by the other modality³. An external 40” NordicNeuroLab (NNL) LCD monitor was tested for US image display to meet the needs of various viewing positions. A Clear Guide MR-US image fusion system was also safety-tested for potential use during procedures. Thorough sonographer training in the MRI environment was conducted, and a safety checklist was developed.

Results: Two safe use locations in front and the back of the MR scanner were determined for the US system and labeled on the floor. At these locations US imaging was found to not be affected by the MR environment. The US scanner was appropriately labeled² and tethered at either location. US system battery was taken out to eliminate any potential fire hazard and the DVI output to NNL display was adjusted to achieve best image appearance. During active MRI scanning, the US scanner was put into the sleep mode, which resulted in minimal and clinically irrelevant effect on MR image signal noise ratio. The sonographers supporting ablation procedures went through iMRI-dedicated safety training, and passed a “live” safety evaluation. The established safety checklist was attached to the US system.

Conclusions: The Philips EPIQ7 US system has been successfully integrated into a 1.5T iMRI suite and utilized clinically. MR safety testing results and clinical use scenarios are specific to this US and MRI system.

Figure 1: Clinical use of the EPIQ 7 US system in location at the front of the MR scanner during cryoablation of a breast lesion. Kevlar tether is indicated with the yellow arrow.

References:
MR guided prostate cancer Detection Diagnosis and therapy: Added Value and Added Science

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Abstract
The healthcare costs of prostate cancer (PCa) care were $11.85 billion in 2012, this is expected to increase by 42% by 2020. The standard of care in clinical practice today to detect and diagnose prostate cancer remains a physical exam and measurement of the serum prostate specific antigen (PSA). If either are abnormal the patient will be advised to get a biopsy. The typical biopsy remains a “blinded” non-targeted sampling of the gland under ultrasound guidance (US)- the so-called TRUS or transrectal US biopsy. This approach has led to major over diagnosis and over treatment of men world-wide and more so in USA. Five individual technical and clinical MRI advances have converged to result in the current new added-science and added-value approach to prostate cancer diagnosis. The initial MR guided prostate interventions pioneered at BWH and beyond clearly established MR’s role for both a guidance and monitoring. Followed by advances in Prostate MR with DWI and now PIRADS, the accuracy and ability to detect Gleason pattern 4 disease has held to worldwide acceptance of MRI. The role of MR in pre-biopsy assessment is now gaining traction globally. The recent PROMIS and PRECISION trial results exemplify this combined approach.

Background MR imaging of the prostate has been performed in clinical practice for over 30 years. MR guided interventions have been an option in clinical practice for over 20 years. Over the past 30 years multiple advances have converged to change this paradigm and lead to a new exciting approach rapidly being adopted and deployed world-wide.

Methods This talk will summarize the technology development and outline lessons learnt in each of the 5 areas listed. Over the past 20 years multiple trials and investigations have been performed to 1) Improve prostate MR techniques, 2) Increase the clinical applications or problems which can be solved by standardized MRI, 3) Interventional MR systems have been introduced and new approaches to prostate interventions have been tested, validated and clinically applied, 4) multiple new prostate biopsy approaches using MR guidance have been tested, validated and clinically applied and cost-effectiveness studies of the new/approaches have been performed.

Results Changing clinical practice is complex multi-factorial process. The MR techniques which have evolved were fundamental to each aspect of this process. Interestingly the clinical focus changed and evolved as the techniques improved. MR techniques: Early work began in the late 1980’s with small single center studies of small populations of men with normal and diseased prostates. Multi-center trials for the evaluation of MR technology as applied to pre-operative staging and MR spectroscopy began in the 1990’s with several major ones (NCI funded RDOG and ACRIN). Since then many others have been performed in multi-center-multi-vendor settings. The major advances have been 1) introduction of diffusion imaging and 2) overall hardware improvements with rapid scanning, increased SNR and 3) standardization by way of PIRADS v1 and V2. Clinical applications: Prostate MR is now used to detect clinically significant disease foci, used to monitor change of such lesions in active surveillance, pre-treatment staging and post therapy responses. MR interventions are routinely performed in-bore: Biopsy and focal or whole gland therapies. Major exciting results have demonstrated the added value and practice changing role of MR prior to prostate biopsy. MR Thermometry is used in MR guided cryotherapy, MRgFUS and MR guided laser therapy. Other interventions occur out of bore using either “fusion” or cognitive approaches. This has led to multiple new commercially available devices. Others have focused upon the next big challenge- development of techniques, tools and devices for image guided focal therapy- also multiple devices and techniques in development and some early data/results from the first multi-center pivotal trial in the US will be shared. Cost-effectiveness data is also available from several centers and one study by Dunne et al presented at RSNA 2017 will be reviewed. This was a model-based approach using a decision-analytic Markov model. It computed the costs and impact of 2 approaches- one TRUS guided biopsy and the other mpMRI followed by MRTB with a 10-year time.
horizon. It concluded that adoption of MRTB in clinical practice produces health benefits for patients at reduced costs for the healthcare system.

Conclusions Summary: Five individual technical and clinical advances have converged to result in the current new added-science and added-value approach to prostate cancer diagnosis. The recent PRECISION trial (7) results exemplify this combined approach.

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MR guided Focused Ultrasound for Native Prostate Cancer

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In 2018, the American Cancer Society (ACS) estimates that 164,690 new cases of prostate cancer will be diagnosed and 29,430 will die due to the prostate cancer in the United States.¹,² Many men with prostate cancer are often managed with aggressive therapy including radiotherapy or surgery. No matter how expertly done, these therapies carry significant risk and morbidity to the patient’s quality of life.³ Furthermore, screening programs using prostatic specific antigen (PSA) and transrectal ultrasound (TRUS) guided systematic biopsy have identified increasing numbers of low risk, low grade “localized” prostate cancer. Although active debate continues on the suitability of focal or regional therapy for low or intermediate risk prostate cancer patients, many patients are pushing for focal therapy due to decreased morbidity.⁴

Treatment of the prostate with focused ultrasound ablation is not new although the MRI guided version of procedure has not, as of yet, been approved by FDA in the United States. HIFU achieves cellular death by rising the cellular temperature >60°C causing cellular necrosis. HIFU ablation technique does not require placement of a needle probe in a targeted prostate tumor via the rectum or skin (perineum) to deliver thermal energy and destroy cancerous tissue. This treatment modality has been performed with transrectal ultrasound (US) imaging guidance with success in Europe for many years.⁵,⁶ The major limitation of US imaging guidance for prostate ablation is that ultrasound cannot precisely visualize the focus of cancer nor visualize the heating effect of the FUS. With MR localization of the cancer and thermal imaging of the heat within the prostate, focused ultrasound can be performed with more targeted treatment zones resulting in improved treatment margins and decreased morbidity. Currently, there are two MRI-integrated systems using transrectal (Exablate, InSightec, Haifa, Israel) or transurethral (Profound Medical Inc., Toronto, Canada) transmission routes for treatment of prostate lesions with focused ultrasound technology. Each system is fully integrated with the MRI console with temperature feedback control to adjust power, frequency, and rotation rate. Both systems are currently being used in patient trials assessing safety and efficacy for evidence to get FDA approval.

References:
Prostate cancer is the most frequent non-cutaneous malignancy in the western male population, with almost 200,000 newly diagnosed patients in the United States in 2008 (1). Due to widespread use of the prostate-specific antigen (PSA) test and the lowered PSA threshold for biopsy, the number of newly diagnosed prostate cancers strongly increased in the last 20 years (2).

At present, treatment choice for prostate cancer patients at low or intermediate risk of disease progression lies between active surveillance (AS) and radical therapies, such as radical prostatectomy or radiotherapy. For these patients, radical treatments have a comparable effectiveness, with a risk of specific death of less than 1% in 15 years. However, none is devised of consequences on the quality of life and can induce significant morbidities such as incontinence and impotence (3-5). On the other hand, active surveillance has established limitations. It is a source of anxiety and imposes, according to the current terms of use, clinical (rectal examination), biological (PSA) and yearly repeat biopsies reassessments that represent a burden for the patient and increase the risk of infection. Lastly, the presumed low risk of progression defined by systematic biopsies is underestimated in about 30% of cases, particularly when the tumor originates in the anterior part of the prostate. Thus, more than one third of men exit the protocol at mid-term and ask for a radical treatment.

For this reason, innovative ablation techniques such as cryosurgery, high intensity focused ultrasound, photodynamic therapy and laser ablation therapy have emerged and are increasingly applied in clinical practice. In this presentation, patient selection, treatment planning, monitoring and technical implications of MRI guided prostate interventions will be discussed.

References
In-Bore Freehand Transgluteal MRI-Guided Focal Laser Ablation of Localized Prostate Cancer: Feasibility and Initial Experience

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Background and purpose: Multiparametric MRI has enabled the visualization and subsequent targeting of prostatic cancerous lesions for focal ablation. Transrectal and transperineal approaches are currently utilized to guide the placement of laser fibers during the ablation procedure. However, some patients may have posteriorly located lesions in close proximity to the rectal wall that may be damaged during the ablation or have limited access through the rectum or perineum due to rectal or perineal lesions or even absence of rectum. We are sharing our initial experience using freehand in-bore MRI guided transgluteal approach to guide focal laser ablation (MRG-TG) of prostate cancers.

Patients and methods: We searched our 24-subject in-bore MRI-guided prostate cancer laser ablation database for patients who had ablation procedure using transgluteal approach from 2013-2018. Subjects with gland-confined low or intermediate-risk disease (Gleason score ≤7, Grade Groups [GG] 1-3) were offered focal ablation after they declined alternative standard-of-care therapies. MRG-TG was performed based on a posterior lesion location with proximity to rectum or limited/contraindicated rectal access. 10 consecutive subjects were finally included in this analysis. All patient had antibiotics and Foley’s catheter inserted before the procedure. All procedures were performed using a 1.5 T MR scanner (Magnetom Espree, Siemens, Germany) in the prone position under general anesthesia. Pre-ablation scans were obtained (high-resolution T2WIs, DWI, VIBE). Triplane TrueFISP sequence was used to provide real-time MR-fluoroscopy needle guidance to the target using an in-room interactive RF-shielded monitor. A 14 G coaxial guiding needle was used to approach the target. When the needle position was deemed satisfactory, a laser fiber (980 nm diode laser system-Visualase®, Medtronic, USA) was then introduced through the guiding needle and its location was further confirmed on TSE-T2WIs with oblique planes oriented parallel to the fiber. In cases where the lesion was in close proximity to the rectum, hydro-dissection was performed using another 14 G MR-compatible puncture needle situated in the perirectal space with slow infusion of up to 1000 cc of normal saline to separate the rectal wall from the lesion. The ablation procedure was monitored using interactive temperature maps. Patients were followed up at 3-week, 3-month, 6-month and 12± month time points for complications, recurrence (using PSA and MRI), sexual function (Sexual Health Inventory for Men (SHIM)) and urinary function (International Prostate Symptom Score (I-PSS)).

Results: Median patient age was 69.5 years (range: 54-75), median PSA was 7.7ng/ml (range: 1.9-28.7), median procedure duration (from start of preprocedural imaging till the last post ablation scans) was 235 minutes (range: 170-270). Median interactive free-hand laser fiber placement time under MRI fluoroscopy (calculated from the needle puncture time to the last scan confirming a satisfactory placement) was 9 minutes (range: 4-17). Most cases had ablation with a 1.5-acive tip laser fiber (9/10, 90%). Gleason scores were 3+3=6/GG1 (2/10 subjects, 20%), 3+4=7/GG2 (7/10 subjects, 70%) and 4+3=7 /GG3 (1/10 subject, 10%). Median total laser energy deposited in tissues was 8118 Joules (range: 4200 – 19062). 8 subjects had focal laser ablation as a treatment for primary disease and 2 subjects had focal laser ablation as a salvage treatment for recurrent disease. 7/10 subjects had saline infusion for hydro-dissection. No major complications were observed. 11 lesions were ablated with median volume of 1 cc (range: 0.6-5.7) and median ablation overlaps of 2 (range: 1-7). Median laser power used was 24 Watts (range: 12-27) and median total duration of laser application was 362 seconds (range: 119-813). Median maximum follow up durations was 7 months (range: 1-28). Two subjects (20%) had recurrent disease observed after the 12+ -month follow up time point. No significant changes in erectile or urinary function were observed.

Conclusion: Transgluteal in-bore MRI-guided laser ablation of localized prostate cancer is feasible with no observed morbidity. It may offer an alternative route for patients with contraindications or limitation to other approaches. However, intermediate and long-term treatment efficacy needs to be better evaluated on a larger cohort of subjects.
Real-time Needle-guide Alignment during 3-T in-bore MR-guided Prostate Biopsy using an In-room Tablet Device: Initial clinical experience

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Purpose To assess the feasibility of real-time needle-guide alignment on an in-room tablet device during transrectal 3-T in-bore magnetic resonance (MR)-guided prostate biopsy.

Methods Twenty patients with one cancer suspicious region (CSR) with PI-RADS v2 score ≥4 on diagnostic multi-parametric MRI were prospectively enrolled in this IRB-approved study. An MRI safety assessment was performed to establish the safe operating conditions of the tablet device (iPad 2, Apple, California, USA) in the MR-suite. Hereafter, the tablet device was installed in the MR-suite and connected to a stand-alone computer outside the scanner room via a remote desktop application (VNC Viewer, RealVNC, Cambridge, UK) (Fig. 1a). Biopsy procedures were performed on a 3-T clinical MR system (Magnetom Skyra, Siemens, Erlangen, Germany) by one prostate interventionalist. After CSR-reidentification, two orthogonal scan planes of an MR-fluoroscopy sequence (~3 imgs/s) were aligned to intersect both the biopsy target point and the pivoting point of the transrectal needle-guide (Invivo, Scherwin, Germany) using planning software (Interactive Frond End, Siemens, Erlangen, Germany) (Fig. 1b). Targeting of the CSR was then performed by manipulating the needle-guide into both scan planes under MR-fluoroscopy feedback visualized on the tablet device in the scanner room (Fig. 1c). Technical feasibility and single-step targeting success were assessed. Complications and biopsy procedure times were also recorded. A reference cohort (n=20) that underwent standard in-bore MR-guided biopsy for same indications was retrieved from our institutional database as initial reference. Statistical analysis was performed to evaluate biopsy times between groups.

Results Needle-guide alignment on the in-room tablet device was technically successful in all patients and allowed sampling of each CSR (median size 14 mm, range: 4-45) after a single alignment step in all but one patient (19/20 lesions; 95%). Biopsy cores contained cancer in 18/20 patients. There were no per-procedural or post-biopsy complications. Using the tablet device, mean time to first biopsy was 50% (5.8±1.0 min. vs. 11.6±5.0 min; P<.001) and mean total procedure time 29% (23.7±4.1 min. vs. 33.4±6.9 min; P<.001) (Fig. 2) reduced compared to the reference cohort.

Conclusions Real-time needle-guide alignment with use of an in-room tablet device was feasible and safe during transrectal 3-T in-bore MR-guided prostate biopsy. Our initial clinical experience indicates potential for procedure time reduction compared to the standard biopsy procedure.


![Fig.1](image) – a) Setup of the tablet device in the MR-room. b) IFE planning module where the biopsy target (pink) and needle guide pivoting point (green) were set. The software then calculates the planned trajectory through these points (yellow path), representing the desired needle guide trajectory to target the cancer suspicious region. c) Real-time alignment of the needle-guide is performed under MR-fluoroscopy feedback displayed on the tablet device.

![Fig.2](image) – Total procedure times for biopsy with use of the in-room tablet device and the routine biopsy procedure, with means indicated. * = P<.001.
Preliminary experience with a remote-controlled manipulator for transrectal in-bore biopsies of the prostate

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Purpose To evaluate the procedural and clinical performance of a remote-controlled manipulator for transrectal in-bore biopsies of the prostate at 1.5 T.

Methods This preliminary prospective study included the first 15 consecutive patients that underwent robotic (Soteria Medical, Arnhem, Netherlands) in-bore biopsies of the prostate in a wide-bore 1.5-T MRI (Magnetom Aera, Siemens Healthcare, Erlangen, Germany). The device [1,2] was quickly registered by automatic detection of the MR-visible needle guide in any image set. Robotic positioning was controlled with short (acquisition times around 10 s) balanced SSFP sequences in two independent planes roughly along the guide (oblique sagittal and oblique axial, 7-9 slices each). Biopsies were performed by two radiologists with 4 years of prior experience using a fully automatic (150 or 175 mm long) 18G biopsy gun (Invivo, Gainsville, FL, USA). Analysis involved pre-biopsy MRI findings (PIRADS v2), procedure times (between planning and final control MRI), periprocedural complications and histopathologic results of the samples.

Results The mean age (range) was 67 (54–80) years and mean PSA level was 11.1 (0.7–21.5) ng/dl. Twelve patients (80%) had undergone prior biopsies under transrectal ultrasound guidance. Prebiopsy MRI reports involved 12 cases with a single suspicious finding (2x PIRADS 3, 5x "P4" and 5x "P5") and 3 cases with two ones (2x "P3" and 1x "P5"). A sample case is illustrated in Fig. 1. Histopathologic examination revealed prostate cancer in 7 cases (47%). One patient developed urosepsis which was successfully treated with antibiotics. Procedure times ranged between 26 and 85 min (mean 45 min).

Conclusions Transrectal in-bore prostate biopsies could be successfully performed with a robotic manipulator at a field strength of 1.5 T. Our results suggest an improved comfort for the patient (no table motion required for adjustments) and the operator (automated workflow and control).

OBJECTIVE: To evaluate the intermediate-term effectiveness of MRI-guided salvage cryoablation in the treatment of recurrent prostate cancer after radical prostatectomy with 24 month follow-up.

MATERIALS AND METHODS: From retrospective review of recurrent prostate cancer patients with localized disease in the prostate bed treated with MR guided cryoablation from 2011 to 2014, 28 patients (mean age 66 years old) were treated with 2 lost to follow-up after treatment. Fifteen patients had prior radical prostatectomy followed by radiation with local prostate bed recurrence prior to cryoablation. Four patients had prior radiation therapy but no surgery prior to cryoablation, with one lost to follow-up after treatment. Nine patients had radical prostatectomy with recurrence and no radiation prior to cryoablation, with one lost to follow-up after treatment.

RESULTS: Overall, 26 patients were treated with salvage MRI guided cryoablation with 2 year follow-up. At 1 year followup, 16 of 26 (61%) showed no evidence of biochemical recurrence (PSA>0.2ng/mL), and at 2 years, 15 of 26 (57%) showed no evidence of biochemical recurrence. Four patients had repeat MR guided cryoablation, two in year 1 and two in year 2. One patient went on to chemohormonal therapy and one patient had radiation therapy.

CONCLUSION: In this very difficult patient subgroup, MRI guided salvage cryoablation of biopsy proven, locally recurrent prostate cancer in patients who failed standard therapies is feasible and offers a valuable additional alternative to patients who are running out of therapeutic options.
Optimization of Cryoprobe Placement for Prostate Focal Cryoablation
Pedro Moreira, Kemal Tuncali, Clare Tempany, Junichi Tokuda
Department of Radiology, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA

**Background:** Prostate cancer (PCa) is the second most common cancer in men worldwide and the fifth cause of cancer death in men [1]. However, more than half of men diagnosed with PCa have small localized cancers and may not need radical treatments [2]. The concern of overtreatment has led to the exploration of focal PCa treatments, which only destroy the diseased portion of the prostate while preserving healthy tissue. Among the several available options, cryoablation offers unique features, including the visibility of thermal effect on CT, MRI, and ultrasound, and its applicability to salvage treatment after radiotherapy failure. In the current practice, physicians rely solely on his/her own experience to define locations of the cryo-probes aiming to achieve maximal target volume coverage. However, this empirical approach does not always produce an optimal probe placement plan and may lead to an unsatisfactory clinical outcome due to insufficient ablation volume, damage to critical structures, and/or use of an excessive number of probes. Furthermore, even if the plan is optimal, probe placement error can also cause in an unintended ablation zone resulting in an unsatisfactory outcome. In this abstract, we propose a new focal cryoablation planner that optimizes locations of the cryo-probes based on the given geometry of the target volume and a geometric model of the iceball. In particular, our method takes account of potential probe placement errors to provide a plan that is robust to placement errors.

**Methods:** A geometric model of the tumor is obtained by manually segmenting the tumor on a T2-weighted MR image acquired at the beginning of the procedure. The segmented tumor is then dilated by a given safety margin (typically 5 mm) to define the target volume. The urethral warmer catheter is also modeled as an obstacle for the probe placement. We model the placement error as a zero-mean Gaussian noise with 1.5mm standard deviation on three degrees-of-freedom for each probe. During the MRI-guided cryoablation, the probes are inserted parallel to the magnetic field using the grid-based approach similar to in-bore prostate biopsies [4]. The planner consists in an optimization algorithm to find the location that minimize a cost function given by: $J = \frac{1}{N} \sum \text{DSC} + k \cdot \text{PTC}$, where DSC is the dice similarity coefficient, PTC is the percentage of target volume covered by the iceball, and $J$ is the empirical probability of achieving at least 95% of target volume covered in N trials. The iceball was considered an ellipsoid with dimensions derived from the experimental results presented by Shah et al. [5]. The algorithm uses a numerical solution based on the Nelder-Mead approach. We performed a preliminary evaluation of the planner using the retrospective data of four prostate focal cryoablation. The parameters k and N were experimentally tuned to 5 and 100, respectively. The output of the planner was compared to the probe placement achieved during the procedure performed by an experimented interventional radiologist with more than 20 years of practice.

**Results:** In three cases, the planner and the radiologist “agreed” on the number of probes to be used. In one case the radiologist used one probe, while our planner suggested that two probes would increase the probability of success. However, it is worth mention that this result is highly influenced by the value of k, and a different choice would change the planner output. The planner took an average of 7 minutes to find a solution with an average probability of success of 93%. The average disagreement between the planned probe location and the placement achieved during the procedure was 5.7mm with 2.4mm standard deviation. One representative result is presented in Figure 1.

**Conclusions:** We presented a preliminary evaluation of a focal cryoablation planner using the geometry of the iceball and an optimization algorithm. The trade-off between probability of complete ablation of the target zone and amount of healthy tissue ablated is defined by the gain value k, and will have to be decided case-by-case by the physician. Our preliminary results suggest that the use of computational planning for such procedures may help the planning process, especially for cases with large tumors. However, more research is required to evaluate the planner using a more extensive dataset. Currently, one limitation of our approach is that our planner is not able to take into account the synergetic effect of two or more probe and the heat-sink effect from the urethral catheter.

**References**


12th Interventional MRI Symposium 101 October, 2018 Boston, MA
Developing and evaluating logistic regression models for predicting needle deviation during transperineal prostate biopsies

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**Background:** Prostate cancer is the fifth leading cause of death from cancer in men and is the second most common cancer in men globally \([1]\). Prostate biopsies can be obtained either transrectally, transgluteally, or transperineally. Benefits of transperineal prostate biopsies include a lower risk of sepsis compared to transrectal prostate biopsies, and easier access to the anterior and apical regions of the prostate. During transperineal prostate biopsies, the physician plans the needle insertion path as a straight line from the point of insertion to the target. However, the biopsy needle tends to deviate from this planned path as it interacts with anatomical structures, resulting in the needle tip missing the suspected cancerous tissue. We created logistic regression models that account for interactions with anatomical structures in order to predict the needle deviation, and implemented them in a 3D Slicer module that will assist the physician in finding an optimal insertion.

**Methods:** Logistic regression is a statistical method used in machine learning which analyzes a dataset containing one or more independent variables to predict an outcome. The outcome is measured with a binary variable. The independent variables are quantitative metrics describing mechanisms of tissue needle interaction in our application. The outcome is needle placement error defined as the probability to miss the pre-defined target by less than 5.76 mm in the horizontal and vertical direction. Source data for both the metrics describing mechanisms of tissue needle interaction and needle placement errors were obtained from images collected during MRI-guided transperineal prostate biopsies using an MRI-compatible robot \([2]\). The logistic regression model used to classify insertions with less than 5.76 mm placement error was defined as:

\[
\text{logit}(p_S) = \alpha + \beta_1L_1 + \beta_2L_2 + \beta_3L_3 + \beta_4L_4 + \beta_5L_5 + \beta_6L_6 + \beta_7L_7 + \beta_8L_8
\]

where \(p_S\) is the probability of the needle deviating <5.76 mm from the target and successfully hitting the target region, which is within the range reported in literature \([3]\), \(\alpha\) is the bevel angle of the biopsy needle, \(L_i\) (\(i = 1\ to \ 5\)) is respectively the length of insertion inside the prostate, pelvic diaphragm, bulbomembranosus, ischiocavernosus and inside unsegmented tissue. \(L_i\) is the length of the entire insertion, \(L_c\) is the radius of curvature of the needle, and \(L_d\) is the deviation of the needle as it pierces the perineum. In addition, we defined the logistic regressions used to classify insertions by horizontal and vertical direction of error as:

\[
\text{logit}(p_x) = \alpha + \beta_1L_1 + \beta_2L_2 + \beta_3L_3
\]

where \(p_x\) (\(x = \text{left}\)) is respectively the probability of the needle deviating to the right and the probability of the needle deviating to the top of the target. The metrics and needle placement errors were collected from 175 insertions performed in 26 patients (50-80yo, average 64yo) after the anatomical structures and needle path were reconstructed for each patient. The logistic regression models were calculated using a training dataset with 116 insertions and a testing dataset with 59 insertions. The logistic regression models were used to create a 3D Slicer module (Figure 2) that accounts for interactions with anatomical structures to return the probability for an insertion to miss the target by less than 5.76 mm in the horizontal and vertical direction.

**Results:** \(\text{logit}(p_S)\) correctly classified 64.4% of the test insertions and the Chi-square test returned \(p = .026255\); \(\text{logit}(p_x)\) correctly classified 76.3%, \(p = .000093\); \(\text{logit}(p_x)\) correctly classified 74.6%, \(p = .00169\). The summary data is presented in the following tables:

<table>
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<tr>
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<th>&lt;=5.7mm</th>
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<td>38</td>
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</table>

**Conclusions:** We used logistic regression models trained with specific patient data to predict needle deviation during transperineal prostate biopsies and implemented them in a 3D Slicer module, which returns the probability of the needle hitting the target and the horizontal and vertical deviation. It is expected that the output from this module can be used to find an optimal insertion position preoperatively and to make adjustments to the insertion intraoperatively.

**References**


12th Interventional MRI Symposium

October, 2018 Boston, MA
Using patient-specific data and machine learning techniques to predict targeting error in transperineal prostate biopsies

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Background: Prostate cancer (PCa) is the second most common cancer in men worldwide and the fifth cause of cancer death in men [1]. MRI-guided biopsy can be performed transrectally, transgluteally, or transperineally. The transperineal approach presents advantages such as better access to anterior and apical prostate regions and lower risk of sepsis over the transrectal approach. In the transperineal approach, the needle path is usually considered as a straight line from the insertion point to the target region. However, deviation from the intended path can occur due to the interaction between the needle and anatomical structures. This deviation usually leads to misplacement of the needle tip, which may result in missing the suspected cancerous tissue. Therefore, we hypothesize that a preoperative path planner that takes account of patient anatomy to select the best needle path can improve the overall accuracy of transperineal prostate biopsies. In this study, we demonstrate how machine learning techniques and patient-specific data can be used to identify the probability of success of a given insertion path and improve the planning phase.

Methods: We implemented a logistic regression and the k-nearest neighbors (KNN) techniques to classify the insertion paths according to the targeting error. We used the data from the MRI-guided transperineal prostate biopsy performed in 26 patients (50-80yo, average 64yo) using an MRI-compatible robot that aligned the needle guide with the target location [2]. A total of 188 insertions were performed, and after each needle insertion, a 3D validation MR image covering the entire pelvic region was obtained. Those images were used to reconstruct the needle path and segment anatomical structures such as the prostate, pelvic diaphragm, rectum and bulbospongiosus (Figure 1). The targeting error was defined as the Euclidian distance between the target coordinates and the final needle tip position. Each insertion was labeled according to the targeting error (below and above the average). The logistic regression model was defined as:

$$\text{logit}(p) = \alpha + \beta_1 L_1 + \beta_2 L_2 + \beta_3 L_3 + \beta_4 L_4 + \beta_5 L_5 + \beta_6 L_d,$$

where \(p\) is the probability of having a targeting error below the average, \(L_i (i = 1 \text{ to } 5)\) are the insertion length inside the prostate, pelvic diaphragm, bulbospongiosus, Ischiocavernosus and inside unsegmented tissue, respectively. \(L_d\) is the deviation of the needle path during the puncture of the perineum. The KNN algorithm uses the same data and \(k\) was set to 15. The insertions were randomly divided into one group with 100 (training dataset) and another group with 75 insertions (testing dataset).

Results: Both algorithms presented similar results, with the logistic regression model correctly classifying 75% of the paths and the KNN classifying 74% of the paths. Both the logistic regression and the KNN were able to accurately classify 82% of the needle paths with targeting error below the average. While the insertions above the average were correctly classified in 67% of the needle paths. The Chi-square test for both tables returned \(p < 0.001\). The summary data for both algorithms is presented in the following tables:

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<table>
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<td>Total</td>
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</table>

Conclusions: We presented a preliminary implementation of machine learning techniques to identify the probability of a given insertion path results in a targeting error below the average. Both algorithms were able to identify the paths resulting in targeting errors below the average in 82% of cases. The result presented in this abstract suggests that the patient-specific anatomical structures combined with machine learning techniques can be a powerful tool to reduce the incidence of targeting errors in transperineal prostate biopsies.

References
Magnetic Resonance Elastography to Image Prostate Anatomy in Patients with Known Prostate Cancer: Preliminary Findings

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Introduction and Objective: Measuring elasticity as a biomarker for prostate cancer has been a promising field of research. Magnetic resonance elastography (MRE) applies a modified phase-contrast imaging sequence to detect the propagation of shear waves in tissues of interest to measure elasticity differences. These waves are generated by a mechanical driver system. Mechanical drivers applied externally to the skin have shown limited success in prostate imaging due to attenuation of shear waves by soft tissues and intervening bones. Transurethral studies have been limited to ex vivo or non-human models. Our objective was to demonstrate the feasibility of prostate MRE using a transurethral actuator in human volunteers with a diagnosis of prostate cancer.

Methods: This was a HIPPA-compliant, IRB-approved prospective study. A total of 5 volunteers with a recent diagnosis of prostate cancer were recruited after obtaining an informed consent. After acquisition of standard clinical multiparametric (mp) MRI using a 3-Tesla magnet with endorectal coil, a transurethral catheter attached to an external pneumatic driver system translated longitudinal motion to the prostate at frequencies ranging from 150-233 Hz. Modified phase-contrast imaging sequences were utilized to detect the propagation of the resulting shear waves. Quantitative elastograms were then generated by post-acquisition processing and compared to standard multiparametric imaging. All proceeded with radical prostatectomy following the study.

Results: Gradient echo and echo-planar MRE images detected shear waves with peak motion amplitudes of up to +/- 5 um. Satisfactory MRE elastograms were generated from all 5 volunteers, and they appear to indicate regions of increased elasticity in areas of known prostate cancer (Figure 1). All patients reported little discomfort from catheter placement or vibration amplitudes. No patients experienced complications from transurethral catheter placement, and no prostatic injury was identified on the prostatectomy specimen.

Conclusions: Prostate MRE utilizing a transurethral actuator is a safe and feasible imaging modality in human patients. The MRE sequences demonstrated satisfactory propagation of shear waves and post-processing elastograms. MRE showed increased tissue stiffness associated with prostate carcinoma. Further analysis remains, including normal prostate MRE and gross correlation of histopathology with MRE in a larger number of patients undergoing radical prostatectomy.
**Pathological Outcomes of Complementary Biopsy of Negative Areas on Multiparametric Prostate MRI in the Setting of Targeted in-Bore MRI-Guided Biopsy**

Kareem K. Elfatairy, Christopher P. Filson, Adeboye O. Osunkoya, Sherif G. Nour

**Introduction and Purpose:** Although multiparametric MRI (mpMRI) shows a high negative predictive value for clinically significant cancers (CSC), areas deemed negative on multiparametric MRI (nvMRI) might still harbor CSCs. Thus, restricting biopsy to MRI-visible targets only may lead to inappropriately assigning patients to active surveillance or erroneously selecting them for focal therapy. The purpose of this study is to investigate the outcomes of complementary random biopsy for nvMRI areas in the setting of targeted in-bore MRI-guided biopsy (MRGB) in terms of 1) presence of cancer and its grade, 2) negative predictive value (NPV) for all prostate cancer as well as clinically significant cancers.

**Methods:** The study was approved by the institutional IRB and informed consents were obtained. We retrospectively analyzed our 244-case MRGB database for subjects who had mpMRI and subsequent MRGB at our institution from 2013 through 2017. We selected those who had biopsies for nvMRI areas (defined as those having PI-RADS v2 category 1 or 2 with no definite focal target), performed concurrently with targeted biopsies when visible targets are only present on one side and/or region to ensure obtaining a representative samples of the whole gland. The final population included in the analysis was 59 consecutive patients and 112 biopsied nvMRI areas. All cases had mpMRI in a separate session prior to the MRGB using 3T MRI scanner (Magnetom Trio, Siemens, Germany) with 32-channel surface phased-array pelvic coil. Scans were obtained in the supine position and consisted of high resolution axial, sagittal, and coronal TSE T2-WIs, Axial DWI (b-values 0-1000-1500 - 2000 s/mm2), DCE-MRI and pre- and delayed post-gadolinium VIBE scans. With the patients placed in the prone position, transrectal MRGBs were performed using the same MRI scanner and Dyna-TRIM (Invivo, Germany) guidance system. Each sampled area was reported to the pathology team as “having no image correlate.” Areas were selected on random basis from MRI negative areas. CSCs were defined as those with Gleason score ≥7 (≥Grade group 2). The pathology results were referenced to MRGB.

**Results:** Fifty-nine patients met those inclusion criteria for this study with median age of 65 years (IQR 59-71), median PSA of 7 ng/mL (IQR 4.9-10.8). 16/59 (27.1%) patients were biopsy naïve, 24/59 (40.7%) had prior negative TRUS biopsy, and 19/59 (32.2%) had prior positive TRUS biopsy. Number of MRI-visible targets biopsied per patient ranged between 1-4 targets and number of nvMRI areas biopsied ranged between 1-11 areas per patient. 42 patients (71.2%) were diagnosed with prostate cancer. 8/42 (19%) were diagnosed with combined biopsy of MRI-visible targets and nvMRI areas. Only one case was diagnosed exclusively by MRGB of nvMRI areas. 20/112 (17.9%) nvMRI areas harbored prostate cancer (false-negative mpMRI) with 11/20 (55%) CSC (figure 1). NPV of mpMRI was ~78% for all cancers, and 88.1% for clinically significant cancers.

**Discussion and Conclusion:** nvMRI areas demonstrated a high NPV for CSC (88.1%). However, additional biopsy from those areas in the setting of targeted biopsy may be warranted especially in triaging patients for focal therapy or active surveillance.

**References:**

![Figure 1. Gleason grades for nvMRI areas.](image-url)
Transgluteal Free-Hand in-Bore 1.5T MRI-Guided Prostate Biopsy in Patients with no Transrectal Access - A Single Center Experience

Kareem K. Elfatairy, Christopher P. Filson, Adeboye O. Osunkoya, Sherif G. Nour

Purpose:

To describe the technique and report the feasibility and outcomes of transgluteal free-hand in-bore 1.5T MRI-guided prostate biopsy in patients with no transrectal access.

Materials and methods:

The study was approved by the institutional IRB and informed consents were obtained. We retrospectively searched our 255-patient in-bore MRI guided biopsy (MRGB) database for patients who had a transgluteal MRI-guided prostate biopsy between 2013-2018. All patients were referred for MRI-guided biopsy due to a rising PSA and suspicious lesion(s) on multiparametric MRI (mpMRI). Only one patient was on active surveillance for a Gleason 6 (Grade Group [GG] 1) disease. Patients had their diagnostic scans either at our institution or outside. The transgluteal biopsy procedures were performed on an open configuration cylindrical 1.5T MRI scanner (Siemens Espree, Erlangen, Germany) with an in-room monitor and control panel to facilitate real-time guidance. All patients had pre-procedure planning scans consisting of axial, coronal and sagittal TSE-T2WIs as well as axial DWIs. Fast tri-plane TrueFISP sequence was used for real-time guidance of a 16 G MR-compatible coaxial puncture needle. When needle position was deemed satisfactory, an 18 G automatic biopsy needle was introduced through the coaxial needle to obtain tissue cores, under near real-time image monitoring. Samples were labeled in reference to the initial diagnostic radiology report.

Results: Eight patients met our inclusion criteria. Median age was 70 years (range: 45-76), median PSA was 7.9 ng/ml (range: 3-35), median prostate volume was 28.8 gm (range: 14-65), and median number of targets per patient were 2 targets (range: 1-4). All patients had no transrectal access due to one of the following conditions: total colectomy for ulcerative colitis (n = 1); abdominoperineal resection for either rectal cancer (n = 2), ulcerative colitis (n = 3) or colorectal cancer (n = 1); or constructive surgery for a complicated decubitus ulcer eroding to the rectum (n = 1). Median interval between mpMRI and MRGB was 2 months (range: 1-7 months). 7/8 (87.5%) patients had prostate cancer with the following Gleason scores/Grade Groups (3+4=7/GG2-1/7 (14.3%), 4+3=7/GG2-2/7 (28.6%), 4+5=9/GG5-4/7(57.1%). Treatment options following MRGB were known in 6 patients; One patient had MRI-guided focal laser ablation, one patient had radical prostatectomy and 4 patients had external beam radiotherapy with androgen deprivation therapy. Median procedure time (calculated from the first acquired planning scan to the last core obtained) was 89 minutes (range: 55-97). Interactive free-hand needle guidance time under MRI fluoroscopy (calculated from the needle puncture time to the last core obtained) was 30.5 minutes (range: 13-46). No complications were observed except for one patient who had mild self-resolved difficulty in voiding. A total of 17 targets were biopsied; 5/17 were in the central gland (29.4%) and 12/17 were in the peripheral zone (12%). 6 targets were at apex (35.3%), 7 at mid gland level (41.2%) and 4 targets were at the gland base (23.5%). 8 targets were in the anterior gland (47.1%). Median largest transverse lesion diameter was 10 mm (range 5-34 mm). 11/17 (64.7%) lesions were prostate cancers with the following Gleason scores (3+4=7/GG2-4/11 (36.4%), 4+3=7/GG3-2/11 (18.2%), 4+5=9/GG5-5/11 (45.5%)). Median cancer core percent was 20% (range 5-90).

Conclusion: In patients with no suitable rectal access, freehand transgluteal in-bore MRI-guided prostate biopsy is a feasible and safe approach with a reasonable procedure duration and adequate tissue volume obtained.
Purpose: To evaluate the feasibility of MRI guided partial prostate gland cryoablation for localized prostate cancer.

Methods: A retrospective chart review was performed on all patients that underwent MRI guided partial prostate gland cryoablation for primary localized prostate cancer from January 2013 to August of 2017. Under general anesthesia and MRI guidance (wide-bore 1.5T MRI), 2-7 cryotherapy probes were placed in or around the prostate cancer lesion by transperineal approach and cryoablation was performed. Patients were included if they had at least 6 months of follow-up.

Results: Ten patients met inclusion criteria. All men had biopsy proven adenocarcinoma of the prostate and had either a single lesion visible on mpMRI or a mapping biopsy confirming the location and extent of disease. No patient had metastatic disease. Four patients underwent focal ablation, while 6 had hemigland ablations with median ages of 64 and 62 years respectively. Median pretreatment PSA was 7.6 ng/mL (IQR: 5.6-9.2). Median PSA follow-up was 15 months (IQR: 6.8-25.5). Nine patients (90%) have maintained a decrease in PSA with median decrease being 3.4 ng/mL (IQR: 1-8). No patients had recurrence within the treatment zone. Only one patient was referred for further treatment due to development of prostate cancer outside the treatment zone. No repeat cryoablation was necessary. There were no intraprocedural complications. Three patients developed urinary retention after Foley catheter removal on the day following treatment and required temporary replacement of the catheter. Following treatment, 3 patients (30%) reported initial worsening of erectile function with subsequent improvement at last follow-up. Two patients (20%) reported development of urinary incontinence immediately following treatment which had resolved to minimal or rare by last follow-up.

Conclusions: MRI guided partial prostate gland cryoablation is feasible and appears to be safe. Longer-term follow-up is needed to assess oncologic outcomes, but MRI-guided cryoablation appears to be a promising treatment option for patients.

Figure 1. MRI Images from focal ablation. A Pre-Treatment Axial T2 imaging demonstrating a small area of marked focal low T2 signal (white arrow) in the left anterior mid prostate gland. B Pre-Treatment Axial DWI showing lesion (white arrow). C Axial imaging showing extent of iceball during treatment. D Sagittal imaging showing extent of iceball during treatment. E Immediate post-treatment Axial DCE Imaging. F Six months post-treatment Axial DCE Imaging.
Preliminary Evaluation of MRI-Guided In-Bore Transperineal Prostate Biopsy System with Disposable Needle Guide

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Background
In-bore transperineal biopsy of prostate cancer is useful particularly for patients undergoing repeat biopsy. The transperineal approach allows physicians to aim the anterior portion of the prostate gland which is difficult to reach for transrectal approaches. However, the key for successful, safe, and economical application of the in-bore transperineal biopsy of the prostate has not been achieved widely partly because there had been no FDA 510k-cleared software/hardware system specifically designed to support the clinical workflow of in-bore MR-guided transperineal biopsy. As a result, little effort has been made in organizing a multi-center study to evaluate the in-bore transperineal approach and compare its clinical outcome with other approaches. The objective of the study, therefore, is to investigate the feasibility of in-bore transperineal biopsy using an FDA 510K-cleared disposable needle-guide system (Fig.1) that was recently developed based on our prototype needle-guide system [1].

Methods
This study included 15 patients in BWH from Nov 2017 to May 2018 that underwent in-bore transperineal prostate biopsy. Both targeted biopsies (TB) and systematic biopsies (SB) were performed in all patients in a 3-tesla wide-bore MRI scanner (MAGNETOM Verio 3T, Siemens Heathineers, Erlangen, Germany). In each sample collection, a needle guidance template (Single-use ProBx Grid, Haromonus, Lowell, MA) was used to guide an 18-gauge core biopsy needle (Full-Auto Bx Gun, 175 mm, Invivo, Gainesville, Florida) into the prostate according to the plan. The software (Pro-Bx, Haromonus, Lowell, MA) was used to import pre-procedural and intra-procedural MR images to identify the targets. The software was also used to provide targeting plan including the identification of needle holes on the needle guidance template. The metrics collected from this preliminary study include average age, number of targets in the TB, number of needle placement attempts per target in the TB, accuracy of needle placement in the TB, and the total procedure time (time between the patient’s arrival and departure from the MRI room), and times required for patient setup, planning, and tissue sampling using the TB and SB approaches. For SB, tissues were sampled from six locations.

Results
All fifteen procedures using the system were completed safely. For TB, a total of 21 targets were sampled averaging 1.4 per patient; average 4.7 insertions were performed per target, and 2.9 cores were collected per target. The in-plane accuracy of needle placements was 4.6 ± 2.1 mm when biopsy samples were collected. The total procedure time was 109.6 ± 14.0 minutes including the times for patient setup (29.1 ± 10.3 min), planning (12.3 ± 4.4 min), tissue sampling for TB (28.1 ± 10.8 min) and tissue sampling for SB (15.7 ± 3.0 min).

Conclusions
Our preliminary evaluation showed that in-bore MRI-guided transperineal prostate biopsy using the FDA 510K-cleared disposable needle-guide system was feasible.

Acknowledgments
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References
In-bore transperineal MRI guided biopsy of prostate cancer: Exploratory data analysis in all 469 cases performed at Brigham and Women's Hospital

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Brigham and Women’s Hospital and Harvard Medical School

Introduction and Purpose:
Prostate cancer (PCa) is the most common non-cutaneous malignancy and is the second highest cause of cancer-related mortality among the male population in the United States. Although aggressive PCa can be serious, most men diagnosed with PCa have an indolent, low grade form, yielding a high survival rate of 100% in cases of localized disease. The main clinical issue in PCa diagnoses is the inaccuracy in the prediction of the cancer’s aggressiveness, leading to overdiagnosis and overtreatment of benign cases, and thus a waste of resources for both patients and hospitals and unnecessary complications during radical treatment. In addition, underdiagnoses of PCa often occurs when TRUS-biopsies are conducted. The purpose of this study was to use basic natural language processing (NLP) techniques to create semantically-rich machine-readable information from the pathology reports of a retrospective study of MR-guided biopsy patients and perform exploratory data analysis (EDA) to produce summary statistics of this cohort.

Methods:
The data used in this study consists of 469 patients who underwent transperineal MR-guided biopsy procedures between December 2009 to August 2017 at Brigham and Women Hospital. This retrospective study was HIPPA compliant and institutional review board approval (IRB) and informed consent was obtained from the patients. The patients from this cohort had a total of 1197 biopsy cores. Python data analysis and visualization libraries such as Seaborn, Matplotlib, Numpy, and Pyplot were used for NLP and data curation and production of summary statistics. NLP algorithms processed a spreadsheet containing procedure information such as enrollment number, target locations, prostate specific antigen (PSA) levels from lab reports, and pathology diagnosis reports. The Gleason score of each target was extracted and converted to Gleason Grading Groups (GGGs), the current system used in grading prostate cancer lesions. The number of patients and locations with prostatic intraepithelial neoplasia (PIN) was determined. The location of each prostate biopsy was parsed, separated using sector maps. Finally, the PSA levels were extracted, and summary statistics were calculated for each of the GGGs and biopsy locations.

Results:
469 patients yielded a total of 1197 biopsy locations. The average PSA level was 11.50 ng/mL. Patients with benign, GGG 1, GGG 2, GGG 3, GGG 4, and GGG 5 lesions averaged 8.00 ng/mL, 7.37 ng/mL, 9.95 ng/mL, 15.44 ng/mL, 15.68 ng/mL, and 12.57 ng/mL respectively. 25.15% of the targets tested positive for PCa. 83.29% are diagnostic, and 16.71% are nondiagnostic. 41.77% targets are located on the right side of the prostate, and 41.77% are located on the left side. 16.46% locations do not have a side assigned. 16.88% are in the posterior, and 16.71% of the targets are in the anterior. 66.42% were not assigned an area. 14.79% targets were located in the central zone, 37.60% were in the peripheral zone, and 7.85% were in the transition zone. 39.77% were not assigned a zone. 22.90% were in the apex, 44.53% were in the middle, and 23.06% were in the base. 9.77% were not assigned a level. 0.92% are positive for PIN. 57.22% are benign. 10.36% were not clinically significant. 8.19% were categorized as GGG 2. 4.18% were categorized as GGG 3. 1.75% were categorized as GGG 4. 0.67% were categorized as GGG 5.

Conclusion:
These techniques used resulted in machine readable data which were used to produce summary statistics of the population of Brigham and Women’s patients participating in this procedure. The next step is to improve the extraction by developing an NLP to incorporate more clinically relevant data points for each patient. In addition, we plan to further extend the method to other populations, including Prostatectomy patients and MR-ultrasound procedures.

References:
4. Gary J. Kelloff, Peter Choyke, and Donald S. Coffey, Challenges in Clinical Prostate Cancer: Role of Imaging. American Journal of Roentgenology; 2009 192:6, 1455-1470

Figure 1. Patient population breakdown. GGG 1 (GS ≤ 6) is not clinically significant cancer.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>469</td>
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<tr>
<td>Average PSA level at biopsy (ng/mL)</td>
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<tr>
<td>Patients nondiagnostic</td>
<td>43</td>
</tr>
<tr>
<td>Patients negative for PCa, positive for PIN</td>
<td>5</td>
</tr>
<tr>
<td>Patients positive for PCa, positive for PIN</td>
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<tr>
<td>Positive for PCa</td>
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<td>GGG 1</td>
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<td>GGG 4</td>
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Optimization of noninvasive absolute MR thermometry for knee joint cartilage using T1

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Background or Purpose
Thermal therapy for osteoarthritis is one of the options for pain-relief (1). Temperature monitoring of cartilage is indispensable for optimal treatment. We have demonstrated the possibility of temperature imaging of knee articular cartilage under hyperthermia therapy using phase mapping technique (2). However, when the joint moves, phase difference calculation becomes problematic. Since $T_1$ has an absolute dependence on limiting to cartilage, temperature distribution imaging independent of the position and shape of the joint can be expected. However, the influence of spatial inhomogeneity of $B_1$ in the multiple flip angle method has to be solved. Thus, in this study, we examined the $B_1$ correction technique suitable for the knee joint cartilage treatment.

Methods
$T_1$ distribution in the cartilage tissues resected from swine knee joints were mapped in a 9.4T-MRI. In the multiple flip angle method, TR was set to 20, 50, 100, 150 and 200 [ms], and FA was changed from 10° to 90° with 10° steps to find the parameter combinations giving optimal $T_1$ accuracy versus imaging time performance. Heating experiment was conducted under the conditions of TR 100 [ms], FA 10° and 30°. Two holes of diameter 1mm were made in the swine cartilage sample to insert a laser fiber for heating and a probe fiber for temperature measurement. The sample was heated with a laser output power of 0.8w for time 99 seconds. During heating, $T_1$ and $B_1$ mapping was performed with TR of 100 [ms]; FA, 10°, 30°. Imaging was also continued for 350 sec during cooling.

Results
As a result of the $B_1$ mapping, the flip angle over the entire cartilage sample was in the range of 80 to 100% of the target value. In the scope of this study, if TR is 100 [ms] and FA is 10° and 30°, the $T_1$ value was closest to the value measured in advance with inversion recovery. A qualitative temperature change was observed in the heating experiment. However, the absolute temperature change of the objective could not be achieved.

Conclusions
The measurement accuracy of $T_1$ was improved with the $B_1$ inhomogeneity correction, suggesting the feasibility of temperature distribution imaging by $T_1$. In order to improve the accuracy of $T_1$, optimization of FA for TR and $T_1$ was necessary.

References (Begin text here)
Optimization of Strategy for Temperature Imaging of Water/Fat Mixed Tissue
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Background or Purpose
In HIFU treatment of breast, imaging of temperature distribution in both aqueous and fat tissues is necessary for maintaining safety and maximizing therapeutic effect. Proton Resonance Frequency (PRF) method is available for aqueous tissues including tumor. On the other hand, as fat tissue has no temperature dependence in proton resonance frequency, various techniques to use relaxation times have been investigated with and without considering variation of temperature coefficients of T1 and T2 among different chemical shift components of fat. The optimal method for simultaneous imaging fat and aqueous tissue temperature is not known yet. Thus, in this study, comparison of various strategies was performed.

Methods
Fat has nine chemical shift components according to the composition of the hydrogen sites. The primary components are stemmed from methylene chain (\(-\text{CH}_2\)) and terminal methyl (\(\text{CH}_3\)) included in all of fatty acids. If the fat chemical shift components are not separated, a synthesized temperature coefficient is observed as a mixture of each coefficient. Thus the accuracy of fat temperature estimation was compared between three strategies with numerical simulations of SPGR signals; (1) Multiple Dixon-type water/fat-components separation followed by the use of T1 or T2 of \((-\text{CH}_2\)) and \((\text{CH}_3)\) signals, and (3) Chemical shift selective water suppression followed by the use of T1 or T2 of the mixed \((-\text{CH}_2\)) and \((\text{CH}_3)\) signals.

Results
Multiple Dixon-type water/fat-components separation was sensitive to signal-to-noise ratio, and thus not suitable for separating chemical shift components including methylene chain and terminal methyl. On the other hand, chemical shift selective water suppression attained reasonable efficiency to extract the bulk fat signal including both \((-\text{CH}_2)\) and \((\text{CH}_3)\) signals. When spatial inhomogeneity of B0 field was compensated, T1 seemed to be advantageous compared with T2. The temperature estimation error induced by using T1 of bulk fat in comparison with using T1 of \((-\text{CH}_2)\) changed with the signal ratio between \((-\text{CH}_2)\) and \((\text{CH}_3)\). When the \((-\text{CH}_2)\) vs \((\text{CH}_3)\) ratio changed from 10:1 to 5:1, the temperature estimation error increased from 6 to 10 °C.

Conclusions
Comparison of MR temperature imaging strategies of water/fat mixed tissue was investigated. When bulk fat signal is observed, temperature estimation deviates largely unless appropriate calibration of T1 with temperature is performed.

References
A Temperature Controlled MR-Compatible Phantom for Validation of MR Thermometry Methods

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Background. In MR, different methods can be used to estimate temperatures. These methods vary in performance, also depending on the investigated sample material.1 In this study, a temperature-controlled MR-compatible phantom was developed for validation and comparison of different MR thermometry methods. To show its suitability, a method for fat-referenced thermometry proposed by Sprinkhuizen et al.2 was exemplarily evaluated in several fat-containing samples. For this technique, the temperature is modelled from multi-gradient-echo (mGRE)-sampled magnitude FID data.

Methods. The temperature-controlled phantom was built using an insulated container (Coleman Company, Wichita, KS, US) that provides space for up to seven sample tubes (see Fig. 1). Water with a specific temperature is piped through the lid of the container to the inside, where it is guided to the bottom of the cylindrical container with a plastic tube, ensuring high water circulation around the sample tubes and, therefore, enabling fast heat transfer. A fiber-optic thermometer (FOT) (LumaSense Technologies, Santa Clara, CA, USA) can be easily introduced into the container via an access catheter to monitor the temperature close to the test tubes. In our study, several emulsion and tissue samples were investigated (see caption of Fig. 2). A water circulator (Haake C25, ThermoFisher Scientific, Waltham, MA, USA) was used to raise the setpoint temperature inside the container from 5 °C to 65 °C in steps of 5 °C. At least 30 min were allowed for the samples to reach the new temperature. The setup was placed inside a 1.5 T whole-body MR scanner (MAGNETOM Aera, Siemens Healthcare GmbH, Erlangen, Germany) using a head coil. mGRE data were acquired for each temperature step and the fat/water PRF shift was estimated to model the temperature using Sprinkhuizen’s method.2

Results. The temperature in the investigated samples estimated from the fat/water PRF shift is plotted in Fig. 2 in comparison to the temperature recorded with the fiber-optic thermometer. The results show much higher deviations in estimated temperatures for the tissue samples than for the emulsion samples, probably due to increased fat/water inhomogeneity in the tissue samples.3

Conclusions. Accurate results for homogenous fat-containing samples were found for our exemplary implementation of Sprinkhuizen’s method. However, the more inhomogeneous tissue samples were more challenging and caused large temperature estimation errors. The proposed phantom setup allows for exact control of the phantom temperature. In conclusion, it provides a suitable and reproducible way to evaluate MR thermometry methods.

Figures.

Figure 1: The temperature-controlled phantom consists of an insulated cylindrical container (internal dimensions: diameter: 11.3 cm / height: 23.9 cm). The fibers of the FOT can be introduced to the inside of the container to measure the temperature close to the sample tubes (dimensions: diameter: 2.3 cm / height: 5.9 cm).

Figure 2: Temperatures acquired with the FOT and estimated with Sprinkhuizen’s method in comparison. Subfigures (1) to (7) show the results for all seven investigated samples: 1. water/canola oil (37% fat); 2. water/canola oil (26% fat); 3. water/canola oil (17% fat); 4. porcine abdominal wall; 5. egg yolk; 6. bovine bone marrow (defrosted after freezing); 7. porcine fatty tissue (defrosted after freezing).


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Novel technologies and applications of MR guided FUS and HiFU

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Focused ultrasound (FUS/HIFU) relies on ablation of pathological tissues, by delivering sufficiently high level of acoustic energy in situ of the human body. Magnetic Resonance guided FUS (MRgFUS/HIFU) and Ultrasound guided (USgFUS/HIFU) are image guided techniques combined with therapeutic FUS for monitoring purposes. Clinical applications FUS/HIFU gained CE and FDA approvals for the treatment of various benign and few malignant lesions in the last two decades. Current technical limitations of ultrasound guided and MRI guided Focused Ultrasound are related to challenges of ablating moving organs (Liver and Kidney). An outlook to possible new applications is provided. Among those are real-time MRI guided focused ultrasound of the liver through a novel controlling system (Fraunhofer MEVIS funded by the European grant TransFusimo) which allows combining for the MRI tracking of liver lesions with beamforming of a phased array TRANSDUCER. Ultrasound guided focused ultrasound supported by robotic positioning has been realized funded by the European grant FUTURA and new applications using to KUKA robot arms including wireless ultrasound devices will be presented. Support of radiation therapy through FUS and HiFU is currently being developed in Leipzig and Dresden (D) funded by a large grant from the German Ministry of science. Preliminary results of sonication of glioblastoma cells will be presented. The work includes the development of PET MRI compatible focused ultrasound (Fraunhofer IBMT) positioned by a PET MR compatible robot arm.
The Role of MR-guided Focused Ultrasound in Brain Disease: From Ablation to BBB Disruption

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Sunnybrook Health Sciences Centre

MR-guided Focused Ultrasound (MRgFUS) is an emerging ‘incisionless’ neurosurgical procedure allowing precise access to key nodes in aberrant circuits driving challenging brain conditions. Both ablative/lesional and non-ablative applications are in various stages of investigation. Ongoing clinical trials are in various stages of development covering a broad range of clinical indications. The advantages and challenges of MRgFUS as a potential treatment modality are now beginning to emerge.

This presentation will review our experience with current and emerging clinical applications of MRgFUS in human populations, in three major clinical domains: psychiatry, neuro-oncology and neurodegenerative disease. Ablative applications of MRgFUS obviate the need for open neurosurgical approaches, offering distinct advantages to some patients, and enhancing the safety of lesional surgery. The relative efficacy of MRgFUS vs. open lesional and other surgical approaches is under continued investigation, and will influence the more widespread adoption of these techniques. Non-ablative BBB applications, in early pilot trials, appear technically feasible and safe in human populations, including those with demonstrated oncologic and neurodegenerative pathology. Additional, larger trials are now needed to better characterize the brain's response to BBB opening and to determine what effects this has on brain pathology and clinical outcomes.

MRgFUS is a promising tool in the clinical neurosciences, permitting safe access to dysfunctional brain circuits across a broad range of conditions. Ablative applications have provided proof-of-concept evidence of discrete, anatomically precise targeting, with BBB applications now emerging as a potentially disruptive tool for the safe delivery of otherwise impassable therapeutic compounds.

References


Valéry Ozenne\textsuperscript{1,2,3}, Charlotte Constans\textsuperscript{4}, Pierre Bour\textsuperscript{1,2,3}, Mathieu Santin\textsuperscript{5,6}, Harry Ahnine\textsuperscript{5}, Romain Valabrègue\textsuperscript{5,6}, Stephane Lehéricy\textsuperscript{1,6}, Jean-François Aubry\textsuperscript{5,6} and Bruno Quesson\textsuperscript{1,2,3}

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**Purpose:** MR-guided High Intensity Focus Ultrasound (MRgHIFU) is an appealing technology in neurosurgery that has grown in popularity with the recent success of essential tremor therapy \cite{6} and for other emerging application such as the treatment Parkinson’s disease. More recently, neuromodulation by transcranial ultrasonic stimulation (TUS) came out and expanded the perspectives of transcranial stimulation by offering non-invasive deep targeting. For both HIFU and TUS applications, accurate targeting and monitoring are crucial. Acoustic Radiation Force Intensity (ARFI) is a promising sequence to identify the focal point location before starting the therapy \cite{5} and could also be combined with simultaneous temperature mapping \cite{3-5}. In this work, a recent sequence allowing simultaneous measurements of temperature and displacement measurements is used to identify in real-time both the focal point by ARFI and verify the absence of heating during ARFI sonications. The validation has been tested in vivo in a non-human primate under anesthesia with a single-element transducer.

**Methods:** Acquisition was performed at 3.0T on a clinical imaging system (MAGNETOM Prisma, Siemens Healthcare, Erlangen, Germany) using a modified single-shot gradient echo EPI with bipolar motion-sensitive encoding gradient \cite{3} (duration 4 ms, amplitude = 54 mT/m). Acquisition parameters were FA = 60°, GRAPPA acceleration of 2, 6/8 partial Fourier, 4 slices were acquired sequentially in transversal orientation at 1 Hz using two pad coils (8 channels). Other acquisition parameters were TE/TR=26 ms/124 ms. FOV=200x200 mm, leading to a spatial resolution of 1.8x1.8x2 mm\textsuperscript{3}, bandwidth = 1565 Hz/pixel. Image reconstruction and post-processing were performed in real-time in the Gadgetron framework \cite{4}. Magnitude and phase images were then transferred by TCP/IP to Thermoguide\textsuperscript{TM} (Image Guided Therapy SA, Pessac, France) for online computation and display of temperature images and displacement maps. HIFU ablation device: A single-element transducer \cite{7} (H115, Sonic Concepts, Bothel, USA) was operated at 850 kHz. For each slice, the displacement was generated by a 4 ms HIFU shot at 70Wac (200 V peak to peak applied to the transducer). Animal Preparation: The protocol was approved by the local Animal Research Ethics Committee “Darwin” according to the European rules for animal experimentation. In vivo validation was performed on primate near the caudate nucleus (Fig. 1). The animal was assisted for ventilation and maintained under general anesthesia with isoflurane (0.8%).

**Results:** Acquisition were done with pad a limited number of channels (8). Nevertheless, an accurate phase reconstruction with GRAPPA acceleration was obtained and resulted to a standard deviation (uncertainty) below 0.2 °C for temperature mapping and 0.4 µm for tissue displacement. HIFU sonications were emitted every second (4 ms shot per slice) during 40 s. Estimation of the focal point location was confirmed by the visualization (Fig. 2 & 3) of an ARFI spot (3*4 voxels) on two adjacent slices. Maximum displacement was 3 µm with average value around 2 µm (Fig. 2 top right). Acquisition was repeated three times after at least 2 min. In all cases, no temperature elevation were observed (Fig. 2).

**Conclusions:** The combination of thermal rise and displacement measurements allows to identify both the focal point location and the temperature changes and could improve safety during MRgHIFU therapies. The current real-time implementation is compatible with clinical practice. As proposed by Bour et al. \cite{2}, the sequence also allows to use the dead time in the window acquisition to emit HIFU energy for heating and to monitor simultaneously changes in temperature and elasticity.

Multichannel fast interleaved non selective free induction decay (FID) readouts for field drift correction of PRFS temperature mapping.

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Background/Purpose: Proton Resonance Frequency Shift (PRFS) MR Thermometry (MRT) is clinically used for guidance of multiple thermal therapeutic treatments. In the case of controlled mild hyperthermia it is essential to create long cycles of mild heating, for which highly accurate temperature feedback is needed. However, during long gradient-intensive dynamic scanning, B₀ drift is an issue. Recently, methods using multiple field probes have been proposed for spatial B₀ drift correction of PRFS Thermometry, but these require additional hardware. We propose a new method based on interleaving a PRFS MRT acquisition with non-selective FID readouts, using conventional receive coils and recombining information from single elements to allow spatio-temporal drift-corrected thermometry.

Methods: Experiments were performed on a clinical 1.5-T scanner (Achieva, Philips Healthcare, The Netherlands). PRFS MRT was performed with a dynamic spoiled gradient echo pulse sequence: TR = 100 ms, TE = 19 ms, FA = 20°, voxel size = 2.5x2.5x8 mm³. Before every phase map, an FID was acquired per channel, using automated dynamic alternation (Fig 1). To maintain a steady-state, TR, FA and gradient spoiling parameters of the FID’s were as those in the PRFS acquisition. The readout window was [1.4-9.4ms], and FID’s were acquired after a full volume excitation. Phantom experiment: Spatio-temporal drift correction was assessed in an agar/silica gel phantom, with HIFU heating. HIFU power was applied with a 70-watts, 16-mm sonication cell. HIFU power was applied for one minute followed by 4 minutes of cool-down, this protocol was repeated 6 times. Two optical temperature probes, one at the center of the sonication and one in an unheated area, were used for independent temperature measurements. Phase images were used to compute non-drift corrected PRFS temperature maps: \[ ΔT = Δ\phi / (αTE2πγ B₀) \], with α the temperature coefficient of the shielding constant (-0.01-10⁻⁵/°C), B₀ the main field in T, Δ\phi the phase difference between incoming phase and reference phase image in rad and γ the \[^1\text{H}\] gyromagnetic ratio 42.58MHz/T. Drift correction: The phase of the FID was used to estimate the ΔT drift due to B₀ spatio-temporal drift. Two correction methods were investigated: 1) using the average ΔT drift, over all available coil elements, and 2) accounting for spatial differences using sensitivity map, as illustrated in Fig 1. These are respectively referred to as 0th and 1st order correction.

Results: In the phantom experiment, uncorrected B₀ drift led to corruption of the temperature map. Within the 25cm black ROI, after 2500s, the error ranged from -9 to -11°C, and showed a smooth spatial pattern (Fig 2a). While the 0th order already reduced the error substantially, only the 1st order correction could correct for the spatial variations of the B₀ drift. The measured PRFS temperature in the center of the HIFU cell with both 0th and 1st order correction were in accordance with the optical probe readings, while in the control area only the 1st order correction was in accordance with the optical probe.

Conclusions: Using independent information from individual receive coil elements combined with fast interleaved FID acquisitions allows to spatially compensate B₀ drift in PRFS-based MRT.

Achieving acoustic coupling with adjustable blades in high intensity focused ultrasound
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Background or Purpose Treating musculoskeletal tumors with high intensity focused ultrasound requires an optimal acoustic windowing and contact between the transducer and the target in order to achieve efficient conduction of energy into the target and to avoid adverse off-target effects such skin burns. Usually degassed water or gel is used between the transducer unit and skin when the surface is flat. This is an issue in curved areas, such as limbs.

Methods To solve the coupling issue we applied agarose gel pads (4cm x 27.5cm and 1.5cm x 27.5cm, Aquaflex, Parker Laboratories Inc., Germany) shaped using curved blades manufactured by our technical division. Two adjustable blades were produced, smaller (25.5cm x 1.5cm) for thinner body parts and bigger (43cm x 3cm) for thighs and trunk. Adjustability was gained by 7mm diameter threaded rod through the blades sides, that can be adjusted by butterfly nuts at both ends. All parts were MRI compatible aluminium. The blade adjustments were approximated according to the shape of the treatment area in the pretreatment MRI.

Results Three patients with osteoid osteoma of tibial bone were treated. Two of the lesions were on the anterolateral aspect of mid tibial and of the lesions on the side of medial condyle. The treatment was performed either on prone position or the side towards the HIFU -treatment table. First a pretreatment MRI was obtained for planning. On the treatment day the patient would arrive on the preparation room where gel pad was carved into suitable form according to pretreatment imaging and applied on top of the HIFU transducer. General anesthesia was introduced and the planned treatment position on the HIFU-table was obtained. Degassed water and sentrifuged gel were poured on the groove carved on the gel pad to have faultless acoustic contact. In order to drive all possible air bubbles out from ultrasounds path the leg was mildly pressed against the pad to in order to have a firm contact. Before the initiation of the treatment a routine air bubble detection scan was made with minimal amount of residual air observed. With slight manipulation residual bubbles were also driven out and the treatments were carried out without adverse effects and the patients remain symptomless at the present.

Conclusions Careful planning and custom tailored gel pads ensure a sound acoustic contact between HIFU-transducer and treatment focus in body parts with challenging geometry thus allowing optimal heating of target area and avoiding adverse effects. Described techniques can be applied in treatment of both benign and malignant lesions of the bone and soft tissue.

References

Figure 1. Post treatment T1 axial enhanced with gadolinium showing gel pad architecture. Nonperfusing area along the bone surface (arrow) in sonicated area.
Combining MR-Acoustic radiation force and temperature imaging with simultaneous multislice imaging during MR guided HIFU procedures

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Purpose: Magnetic resonance-guided High intensity focused ultrasound (HIFU) offers an unrivaled combination of therapeutic and monitoring systems providing the information of temperature (MR-THERMOMETRY) and displacement (MR-ARFI), during the treatment [1]. Despite a great variety of sequences (2D and 3D), their implementations lack to combine spatial coverage and temporal resolution. These characteristics are of particular interest during treatment monitoring. In this work, we have investigated the benefits of simultaneous multislice (SMS) acquisitions to address this limitation. Validation was performed on fresh ex vivo pig samples.

Methods: A prototype single shot gradient-echo-planar imaging (EPI) sequence was combined with simultaneous multislice and GRAPPA accelerations using the Blipped-Controlled Aliasing in Parallel Imaging (blipped-CAIPI) technique. A coil combination based on Souheil et al. [3] work was implemented and added in the reconstruction pipeline. In the sequence a bipolar Motion Encoding Gradient (MEG) was integrated before the EPI readout to encode micrometric tissue displacement induced by HIFU (see Figure 1a). Magnitude and phase images were reconstructed and data were transferred online to a separate workstation (Thermoguide™, Image Guided Therapy SA, Pessac-France) for computation and visualization of temperature and displacement images. Sequence parameters were: FOV = 260x260 mm², spatial resolution = 2.3x2.3x3 mm³, TE/TR = 36 ms/101 ms, GRAPPA acceleration factor of 2, 50 % phase oversampling, 6/8 partial Fourier and pixel bandwidth = 1955 Hz/pixel. Flip angles were set to the Ernst angle. The protocols were divided in 2 steps: 40 s of sonication (S_{ARFI} = 330 W, S_{THERMO} = 190 W) and a post sonication step during the rest of the acquisition time (S_{ARFI} = 330 W, S_{THERMO} = 0 W).

Results: The temporal resolution for acquiring the 12 slices were 1130 ms, 608 ms for MB = 1 and 2, respectively. The spatial averaged standard deviation (ROI of 21x21 pixels centred at the focus in slice #6) of temperature and displacement were [0.3 0.3] °C and [1.1, 1.3] μm, for MB = [1, 2], respectively. In Figure 2a displacement and temperature spatial profiles for MB = 2, taken at the end of the sonication, were similar to those found for MB = 1. In Figure 2b the displacement and temperature estimates for the same pixel of interest were close (Note that with MB = 2, the temporal resolution was doubled).

Conclusions: The study demonstrates the feasibility of sub-second volumetric sonication monitoring of the tissue displacement and temperature evolution, by combining slice-acceleration and GRAPPA-acceleration. Results have shown good agreement in displacement and temperature estimations between MB = 1 and MB = 2. Results in temperature and displacement estimates for MB = 3 were more degraded due to shorter repetition times (loss in SNR) and need further investigations. In addition a more in-depth noise enhancement study will be conducted to assess more precisely the spatial noise variations inherent to SMS reconstruction algorithms (Slice-GRAPPA).

References:
Multispecialty treatment center for uterine fibroids with MR-HIFU option: Clinical setup and initial experience

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Purpose To describe our clinical setup of a multispecialty treatment center for uterine fibroids with MR-HIFU option and to report on our initial procedural and clinical experience with our first applications.

Methods A total of 47 patients with symptomatic uterine fibroids have been screened in our multispecialty fibroid center since October 2017. After proper consultation and consensus for a therapy option, seven of them underwent MR-HIFU [1,2] (Sonalleve, Profound Medical, Mississauga, ON) in an otherwise diagnostic 3-T MRI (Ingenia 3.0T, Philips Healthcare, Best, Netherlands). Patients received analgesic and sedative medication and their vital parameters were monitored continuously. T2-weighted and special bowel sequences were used for planning. Therapeutic and adverse tissue heating during sonication was controlled by multiplanar MR temperature mapping (6 slices in 3.5 s) in the treatment cell as well as the so-called near (skin) and far field (sacrum). Patients will be followed up by ultrasound (3 months) and MR imaging (6 months) with regard to fibroid volumes and remaining vascularization (some exams still pending).

Results Mean age (range) was 36 (28–52) years. Patients typically suffered from dysmenorrhoea, hypermenorrhoea, pollakisuria or conception difficulties; four of them had large solitary and three multiple smaller fibroids. Bowels frequently happened to lie in the beam pathway on the day of treatment only. Filling of the bladder, rectum or both was then required to properly manipulate bowel and uterus positions. Five patients were treated successfully, taking 3–6 h, with non-perfused volumes ranging from 71 to 100%. One treatment was discontinued after various MRI system errors had substantially delayed the procedure—that patient was later treated with uterine artery embolization. Another patient (discontinued) developed an abdominal wall edema after cumulative near-field heating in a weakly thermosensitive fibroid; pain symptoms resolved completely after 2 months. All patients were discharged on the next day.

Conclusions We have successfully established a treatment center for symptomatic uterine fibroids and already performed the first MR-HIFU ablations. Patient comfort and compliance have so far been good enough but are still compromised by long procedure times. Adequate supervision of the first clinical cases is considered mandatory. One future goal is to extend our service to other clinical entities as well, in particular to bone metastases.

Transcranial MR-guided Ultrasound Neuromodulation

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Ultrasound is well known as a diagnostic imaging modality, but it offers much more than that. It has recently emerged as a powerful and flexible tool for completely non-invasive deep neuro ablations, for targeted drug delivery, and for localized neuromodulation. For each of these, an ultrasound beam can be transmitted through the intact skull and focused to a point deep in the brain. The equipment to do this is an array of ultrasound transducer elements fixed on a hemisphere, and coupled to the head via degassed water. The effect on the brain is different depending on the ultrasound intensity level and the presence of microbubbles.

Low intensity modulation is presumably due to the ultrasound acting via radiation force on stretch-sensitive ion channels. Studies have shown the ability of ultrasound to modulate behavior in non-human primates, to modulate evoked potentials in sheep and pigs, to affect behavior in rodents and the C-elegans nematode, and to activate ex vivo retina. In this presentation, these results will be described, as well as the ongoing need to develop accurate methods to calibrate the beam after traversing the skull.
Magnetic Resonance-guided Focused Ultrasound (MRgFUS) combines focused ultrasound, a minimally invasive technique that can be used to ablate tissue focally within the body, with MR imaging, which is used for targeting, thermometry for intra-operative verification, and post-operative confirmation of treatment effect. We routinely use MRgFUS as an option for patients with uterine fibroids, bone tumors, soft tissue tumors, prostate cancer and essential tremor. For each of these pathologies, we have introduced a Center of Excellence model, whereby multidisciplinary teams of physicians evaluate patients’ suitability for MRgFUS among other options. As an example, this talk will discuss the impact of MRgFUS in the setting of our Fibroid Center. In addition, treatment results will be presented for patients with bone tumors, including metastases and osteoid osteomas, and soft tissue tumors, including desmoid tumors and vascular malformations.

References (Begin text here)


Magnetic resonance imaging–guided high-intensity focused ultrasound (MRI-HIFU) is a novel technology that integrates magnetic resonance imaging with therapeutic ultrasound. This unique approach provides a completely noninvasive method for precise thermal ablation of targeted tissues with real-time imaging feedback. Over the past 2 decades, MRI-HIFU has shown clinical success in several adult applications ranging from treatment of painful bone metastases to uterine fibroids to prostate cancer and essential tremor. Although clinical experience in pediatrics is relatively small, the advantages of a completely noninvasive and radiation-free therapy are especially attractive to growing children. Unlike elderly patients, young children must deal with an entire lifetime of negative effects related to collateral tissue damage associated with invasive surgery, side effects of chemotherapy, and risk of secondary malignancy due to radiation exposure. These reasons provide a clear rationale and strong motivation to further advance clinical utility of MRI-HIFU in pediatrics. An introduction to MRI-HIFU technology and clinical experience in adults will be provided. Next, we will describe our early institutional experience in using MRI-HIFU ablation to treat benign, locally aggressive, and metastatic tumors in children and young adults. Specifically, results of osteoid osteoma, desmoid tumor, and relapsed sarcoma ablation will be reviewed. We also review some limitations and challenges encountered in treating pediatric patients and highlight additional applications such as hyperthermia-enhanced local drug deliver and mechanical tissue destruction (histotripsy), which may be also be feasible in the near future using clinical systems.

References:


MRI guided Trans-rectal Focused Ultrasound as Focal Therapy for Intermediate Grade Prostate Cancer: Single Center Preliminary Biopsy Results

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Background: Prostate cancer focal therapy is being employed by multiple academic and private practices to minimize the side effect profile for treatment of localized intermediate grade prostate cancer. MRI guided ablation therapies provide a unique approach to this quest with multi-planar real time imaging during the therapy. As a contributor to the first USA, prospective, multicenter (12 site) focal therapy trial for intermediate grade prostate cancer using MRI guided trans-rectal focused ultrasound (Insightec, Ltd, Tirat Carmel, Israel) we present our preliminary treatment zone biopsy data for 9 patients.

Methods: Between 2016 and 2018 a total of 10 patients were treated for localized, small volume Gleason 3+4 or 4+3 disease. Per protocol, all patients are to have image guided mapping biopsy at 6 and 24 months following treatment. Multi-parametric MRI was obtained and at least 2 cores were taken from the treatment zone at both biopsy sessions.

Results: Nine of the ten patients have undergone biopsy at 6 months post treatment. Two of ten have completed 24 month follow up including mapping biopsy. All treatment target biopsies have returned with no visible carcinoma on histopathology. At 6 months, 19 of 19 cores in the treatment zone were consistent with treatment effect with no viable carcinoma. At 24 months, 6 of 6 cores in the treatment zone showed no viable carcinoma. The remaining systematic mapping biopsies showed no new clinically significant prostate cancer.

Conclusions: This preliminary, single site, post-treatment biopsy data following MRI guided trans-rectal focused ultrasound supports complete, effective targeting and destruction of low volume intermediate grade prostate cancer through 24 months of follow-up.
A Combined PRF/T<sub>1</sub> Golden-Angle-Ordered Stack-of-Radial Sequence to Monitor HIFU Ablation

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**Background** High-intensity focused ultrasound (HIFU) is currently the only entirely non-invasive therapeutic modality used for the treatment of tumors including prostatic and breast cancers<sup>1,2</sup>. To monitor and calculate thermal dose, proton resonance frequency shift (PRF) is widely used for MR temperature mapping. However, PRF fails in adipose tissue due to the lack of hydrogen bonds. Alternatively, T<sub>1</sub> measurement by the variable flip angle (VFA) scheme has been used in combination with PRF for Cartesian MRI techniques<sup>3,4</sup>, but it is still prone to motion corruption. Non-Cartesian sampling such as golden-angle-ordered (GA) 3D stack-of-radial can potentially improve motion robustness and accelerate acquisition speed<sup>5</sup>. Here we propose a new GA radial technique for PRF-T<sub>1</sub> temperature mapping and describe initial results from pilot studies.

**Methods** The proposed sequence is illustrated in Fig. 1A. Groups of 64 GA radial spokes (i.e., a segment) were acquired with alternating flip angles. Multiple segments were obtained where spokes in adjacent 4 segments were grouped together in a sliding window fashion during image reconstruction (Fig. 1C). 6 volunteers were scanned on a 3T scanner (Prisma, Siemens) to study the brain, prostate, and chest (including breast) where motion and/or fatty tissues pose challenges to traditional PRF methods. For chest scans, water and fat images were separated using multiple echoes (Fig. 1B)<sup>6</sup>. B<sub>+1</sub> maps were acquired before scanning sessions during breath hold to calibrate flip angles. Thermal ablation was conducted for 5 minutes on a chicken breast phantom on a HIFU system (Image Guided Therapy, Bordeaux, France) interfaced with the MRI scanner with an acoustic power of 80W.

**Results** Fig. 2 shows the temporal coefficient of variation (CoV) of T<sub>1</sub> and PRF temperature errors caused by fluctuations in phase in human subjects. Figs. 3A and 3B show changes in T<sub>1</sub> and PRF between baseline and peak temperatures during HIFU, while Fig. 3C compares the relative temperature and T<sub>1</sub> changes measured by the sequence to the absolute temperature measured by a temperature probe.

**Discussion and Conclusions** In non-heating subject scans, the sequence demonstrated good stability in T<sub>1</sub> and PRF measurement with 3- to 4-fold undersampling, especially in the brain and prostate where motion was on a minimal scale. Chest proved challenging due to breathing motion that also led to mismatch between dynamic images acquired at different times and the B<sub>+1</sub> map. Motion correction algorithms can be incorporated to address this issue as the center of each spoke can be used as a navigator. HIFU ablation results showed PRF closely tracking thermal probe readings. T<sub>1</sub> was noisier due to the low loading of the coil leading to low SNR. The T<sub>1</sub> temperature coefficient of chicken breast was ~8.5ms<sup>{°C}</sup>, similar to findings in previous studies<sup>5</sup>. In conclusion, preliminary data of our proposed GA radial PRF-T<sub>1</sub> technique demonstrated promising temperature accuracy with dynamic 3D coverage.

Intraoperative, diffusion-weighted, magnetic resonance imaging for transcranial focused ultrasound thalamotomy

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Abstract: We present a novel, intraoperative, diffusion-weighted MRI sequence and its application to FUS thalamotomy. During surgery, it produces high contrast, diffusion-weighted and T2-weighted images of thermal FUS lesions in the thalamus-despite technical challenges introduced by the FUS device.

Background or Purpose: Essential tremor (ET) is a debilitating movement disorder affecting up to 10% of the population. Transcranial focused ultrasound (FUS) thalamotomy can reduce ET symptoms in many patient populations. This procedure uses clinical and magnetic resonance imaging (MRI) feedback to guide the lesioning process. However, feedback is limited by both technical difficulties that suppress image quality and delayed lesion maturation. For example, T2-contrast-generating edema takes tens of minutes to develop and cannot differentiate between coagulation and vasogenic edema.¹,² We hypothesize that diffusion-weighted MRI (dw) contrast forms minutes after sonication and differentiates between coagulation and edema. Previous studies indicate dw contrast formation—³ but are limited by the use of a dedicated head coil—which requires removing the transducer and, consequently, delaying image acquisition to at least 30 minutes after treatment³,³.

Here, we introduce a novel T2-w and dw-MRI sequence designed for immediate image acquisition with the transducer remaining in place. We report its use during clinical FUS thalamotomy procedures.

Methods: Magnetic and transmit field in homogeneities remain primary impediments to quality intraoperative dw-MRI during FUS thalamotomy. Eddy current fields and an artificially large field-of-view induced by the coupling water bath remain secondary impediments. To mitigate these difficulties, we have developed a multi-shot, twice-refocused, adiabatic, dw-MRI pulse sequence that employs a retraced, spiral acquisition scheme. The adiabatic RF pulses partially mitigate the transmit field inhomogeneity effects; the multi-shot, retraced spiral acquisition mitigates the effects of patient motion, magnetic field inhomogeneities, and the large field of view; and the twice-refocused design mitigates eddy current field artifacts. T2-w images can be acquired by deactivating the diffusion-encoding gradients. This pulse sequence is shown in Figure 1.

ET patients underwent a standard FUS thalamotomy procedure³. After sonication, the water bath was drained but the transducer remained installed on the patient. The proposed sequence acquired dw and T2-w MR images using the scanner’s body coil. Data were acquired for 2 minutes for the dw and T2-w versions of the sequence, respectively. After acquisition, magnetic field inhomogeneities were corrected using a semi-automatic method.⁵

Results: Example T2-w and dw images are shown in Figure 2 with the thalamotomy lesion demarcated by an arrow. Contrast-to-noise ratios of the lesion are also provided. The lesion is hyper-intense in both the T2-w and dw images, consistent with previous observations using a head coil².

Conclusions: We found intraoperative dw-MRI to be feasible for FUS thalamotomy procedures using the proposed sequence. The resulting images are both sensitive to thalamic lesioning and robust against technical challenges such as field inhomogeneity, patient motion, and eddy current fields. Future work includes imaging with the water bath in place.

References

Figure 1: A multi-shot, twice-refocused, adiabatic, dw-MRI pulse sequence that employs a retraced, spiral acquisition scheme. This sequence produces intraoperative dw and T2-w MR images during FUS thalamotomy.

Figure 2: T2-w and dw images acquired in an ET patient using the proposed sequence. The arrows indicate the thermal lesion. Contrast-to-noise ratios are also provided. The lesion is hyper-intense in both the T2-w and dw images.
Magnetic Resonance-Guided Focused Ultrasound (MRgFUS) focal treatment of localized prostate cancer: Initial experience and follow up from a multi-center trial.


PURPOSE
To evaluate the initial experience, safety and feasibility of MR targeted focused ultrasound treatment of localized prostate cancer

METHOD AND MATERIALS
Patients with biopsy proven prostate cancer enrolled in a prospective multi-center pivotal trial of the ExAblate 2100 prostate system. Eligibility criteria include men of 50 years or older, PSA < 20 ng/mL with either low or intermediate risk prostate cancer (Gleason Score 3+3, 3+4 or 4+3). A multi-parametric MR must confirm localized prostate cancer (Stage T1-T2) and tumor distance < 4cm from rectal wall. All men were treated in 3T GEHC MR device with ExAblate system under general anesthesia. Pre-treatment MR defined the target volume and multiple focal sonications were delivered followed by post contrast imaging after IV gadolinium after the procedure.

RESULTS
38 eligible men have been enrolled and treated from 7 sites. Mean age 62.8 years, mean PSA 6.0 ng/mL. Prostate MR demonstrated dominant lesions in 32 men, no lesion in 4 men and MR data was not available in 2 cases. Pre-treatment prostate biopsy results showed Gleason 3+3 in 14, 3+4 in 19 and 4+3 in 9. All men successfully underwent MR-guided FUS ablation of their focal lesion. All men were dismissed home within 24 hours of treatment. Currently 6 men have completed 2 year follow up, 34 men are at 9 months, 27 at 12 and 12 at 18 months. There were 131 protocol related adverse events, which were Grade 1 (mild) in 117, Grade 2 (moderate) in 13 and Grade 3 (severe) in 1 (severe suprapubic pain 1 week post treatment, resolved the following day without permanent injury). Overall 77 events were procedure related, 48 were transient, 5 biopsy related and 1 device related.

CONCLUSION
Initial experience indicates that Prostate MRgFUS appears to be both feasible and safe. Enrolling men in a trial using image-guided focal therapy in prostate cancer is feasible. Accrual is ongoing in this pivotal trial.