9.4T

Sher I, Chandra RV, Daly C, Oehme D, Sher M, DSc PG, Smith J, Surg M, Goldschlager T. 9.4T MRI Assessment of Degenerative Disc Disease: Statistical Methodology. Spine (Phila Pa 1976). 2019 Mar 4. doi: 10.1097/BRS.0000000000003026. [Epub ahead of print] PubMed PMID: 30883452.

High field 9.4T MRI has been shown to provide superior resolution and anatomical detail. However, it has not been tested against current standard MRI techniques.

Disc degeneration was initiated in 36 skeletally mature ewes 6 months prior to necropsy via validated surgical IVD injury models using either scalpel injury or drill-bit injury techniques at lumbar spine levels L2/3 and L3/4 with L1/2, L4/5 and L5/6 serving as control discs. All ex vivo IVDs were examined with 9.4T MRI and 3T MRI. All scans were analysed using the Pfirrmann grading system by four independent observers. Intra- and interobserver reliability was assessed using kappa statistics and Spearman's correlation.

Inter- and intraobserver agreement for 9.4T MRI was excellent, both at κ 0.91 ($p < 0.001$). Comparatively, 3T interobserver reliability demonstrated substantial agreement at κ 0.61 ($p < 0.001$). Complete agreement was obtained in 92.7-100% of discs at 9.4T compared to 69.7-83.1% at 3T. A difference of one grade or more occurred in 6.7% at 9.4T and 39.3% at 3T. 9.4T MRI scored 97.3% of discs as grade 1-2 compared to 71.3% at 3T. 3T MRI tended to over-score the extent of disc degeneration with 28.6% of discs scored as grade 3 or higher compared with 2.7% at 9.4T MRI.

9.4T MRI study of IVD degeneration using the Pfirrmann grading system demonstrated excellent inter- and intraobserver reliability. Comparatively, 3T MRI demonstrated a tendency to over score the extent of disc degeneration. This improved reliability of 9.4T MRI holds great potential for its clinical applications [1)].

The high chemical shift separation at 9.4 T allows for selective saturation of proton pools in exchange with water protons. For the first time, highly selective and comprehensive chemical exchange saturation transfer (CEST) experiments were performed in the human brain at 9.4 T. This work provides insight into CEST signals in the human brain in comparison with existing animal studies, as well as with CEST effects in vivo at lower field strengths.

A novel snapshot-CEST method for human brain scans at 9.4 T was optimized and employed for highly-spectrally-resolved (95 offsets) CEST measurements in healthy subjects and one brain tumor patient. Reproducibility and stability between scans was verified in grey and white matter after B0, B1, and motion correction of the acquired 3D CEST volumes. Two-step Lorentzian fitting was used to further improve separation of spectrally discernible signals to create known and novel CEST contrast maps at 9.4 T.

At a saturation power of $B1 = 0.5\,\mu T$ most selective CEST effects could be obtained in the human brain with high inter-scan reproducibility. While contrast behavior of previously measured signals at lower field, namely amide-, guanidyl- and NOE-CEST effects, could be reproduced, novel signals at 2.7 ppm, and -1.6 ppm could be verified in healthy subjects and in a brain tumor patient for the first time.

High spectral resolution chemical exchange saturation transfer at 9.4 T allows deeper insights into the Z-spectrum structure of the human brain, and provides many different contrasts showing different correlations in healthy tissue and in tumor-affected areas of the brain, generating hypotheses for future investigations of in-vivo-CEST at UHF [2].

7T-MRI and 9.4T-MRI of human cerebral arterial plastic casts could proof feasible for acquiring detailed morphological data of the cerebral arterial tree in a time efficient method. One cast of the complete human cerebral arterial circulation embedded in gadolinium-containing gelatine gel was scanned at 7T-MRI (0.1 mm isotropic resolution). A small section of another cast was scanned at 9.4T-MRI (30 µm isotropic resolution). Subsequent 3D-reconstruction was performed using a semi-automatic approach. Validation of 7T-MRI was performed by comparing the radius calculated using MRI to manual measurements on the same cast. As manual measurement of the small section was not feasible, 9.4T-MRI was validated by scanning the small section both at 7T-MRI and 9.4T MRI and comparing the diameters of arterial segments. Linear regression slopes were 0.97 (R-squared 0.94) and 1.0 (R-squared 0.90) for 7T-MRI and 9.4T-MRI. This data shows that 7T-MRI and 9.4T-MRI and subsequent 3D reconstruction of plastic casts is feasible, and allows for characterization of human cerebral arterial tree morphology [3].

Diffusion-weighted imaging and arterial spin labeling perfusion MR imaging were performed on rats with middle cerebral artery occlusion (MCAO) by using a 9.4T MR imaging scanner to measure the volume of infarction and relative cerebral blood flow (rCBF) after infarction. Twenty-five rats were assigned to either a dehydration group or normal hydration group, and dehydration status was achieved by water deprivation for 48 h prior to MCAO. Results: The volume of the infarction was significantly larger for the dehydration group at the 4th h after MCAO ($p = 0.040$). The progression in the infarct volume between the 1st and 4th h was also larger in the dehydration group ($p = 0.021$). The average rCBF values of the contralateral normal hemispheres at the 1st and the 4th h were significantly lower in the dehydration group ($p = 0.027$ and 0.040, respectively). Conclusions: Our findings suggested that dehydration status is associated with the progression of infarct volume and decreases in cerebral blood flow during the acute stage of ischemic stroke. This preliminary study provided an imaging clue that more intensive hydration therapies and reperfusion strategies are necessary for the management of acute ischemic stroke patients with dehydration status [4].

Using a 9.4T magnetic resonance imaging (MRI) system, a whole-cord FP-DDE spectroscopic voxel was acquired in 3 minutes at the lesion site and compared to DWI at 48 hours postinjury. Relationships with chronic (30-day) locomotor and histological outcomes were evaluated with linear regression.

The FP-DDE measure of parallel diffusivity (ADC||) was significantly related to chronic hind limb locomotor functional outcome ($R2 = 0.63$, $p < 0.0001$), and combining this measurement with acute functional scores demonstrated prognostic benefit versus functional testing alone ($p = 0.0007$). Acute ADC|| measurements were also more closely related to the number of injured axons measured 30 days after the injury than standard DWI. Furthermore, acute FP-DDE images showed a clear and easily interpretable pattern of injury that closely corresponded with chronic MRI and histology observations.

Collectively, these results demonstrate FP-DDE benefits from greater specificity for acute axonal

damage in predicting functional and histological outcomes with rapid acquisition and fully automated analysis, improving over standard DWI. FP-DDE is a promising technique compatible with clinical settings, with potential research and clinical applications for evaluation of spinal cord pathology. Ann Neurol 2018;83:37-50 [5)].

An ex vivo monkey brain was scanned in a 9.4T MRI scanner at 0.3mm resolution with b values of 3000, 6000, 9000 and 12000 s/mm2. K-means clustering on each thalamus was implemented using maps of dMRI models fitted to the same data. Meanwhile, histological nuclei were identified by AChE and Nissl stains of the same brain. Overall agreement rate and agreement rate for each nucleus were calculated between clustering and histology. Sixteen thalamic nuclei on each hemisphere were included.

Clustering with the DKI model has slightly higher overall agreement rate but clustering with other dMRI models result in higher agreement rate in some nuclei.

dMRl models should be carefully selected to better parcellate the thalamus, depending on the specific purpose of the parcellation [6)]

---

23 brains were selected from the Queen Square Brain Bank (10 controls, 8 progressive supranuclear palsy, 5 Parkinson's disease) and imaged using high field 9.4Tesla spin-echo MRI. Subsequently brains were cut and stained with Luxol fast blue, Perls stain, and immunohistochemistry for substance P and calbindin. Once the anatomy was defined on histology the dimensions and volume of the substantia nigra were determined on high field magnetic resonance images.

The anterior border of the substantia nigra was defined by the crus cerebri. In the medial half it was less distinct due to the deposition of iron and the interdigitation of white matter and the substantia nigra. The posterior border was flanked by white matter bridging the red nucleus and substantia nigra and seen as hypointense on spin-echo magnetic resonance images. Within the substantia nigra high signal structures corresponded to confirmed nigrosomes. These were still evident in Parkinson's disease but not in progressive supranuclear palsy. The volume and dimensions of the substantia nigra were similar in Parkinson's disease and controls, but reduced in progressive supranuclear palsy.

Massey et al., presented a histologically validated anatomical description of the substantia nigra on high field spin-echo high resolution magnetic resonance images and were able to delineate all five nigrosomes. In accordance with the pathological literature we did not observe changes in the nigrosome structure as manifest by volume or signal characteristics within the substantia nigra in Parkinson's disease whereas in progressive supranuclear palsy there was microarchitectural destruction [7)].

DSC and arterial spin-labeling perfusion MR imaging were performed by using a 9.4T MR imaging scanner in nude rats with glioblastoma. Rats were randomly assigned to the following 3 groups: control, 3-day treatment, and 10-day treatment after bevacizumab injection. One-way analysis of variance with a post hoc test was used to compare perfusion parameters (eg, normalized CBV and normalized CBF from DSC MR imaging and normalized CBF based on arterial spin-labeling) with microvessel area on histology. The Pearson correlations between perfusion parameters and microvessel area were also determined.

All of the normalized CBV from DSC, normalized CBF from DSC, normalized CBF from arterial spin-labeling, and microvessel area values showed significant decrease after treatment ($P < .001$, $P < .001$, $P = .005$, and $P < .001$, respectively). In addition, normalized CBV and normalized CBF from DSC and normalized CBF from arterial spin-labeling strongly correlated with microvessel area (correlation coefficient, $r = 0.911$, 0.869, and 0.860, respectively; $P < .001$ for all).

Normalized CBF based on arterial spin-labeling and normalized CBV and normalized CBF based on DSC have the potential for evaluating the effect of antiangiogenic therapy on glioblastomas treated with bevacizumab, with a strong correlation with microvessel area [8)].

Bisdas et al., examined in vivo metabolic alterations in the isocitrate dehydrogenase (IDH) mutated gliomas using magnetic resonance spectroscopy (MRS) at magnetic field 9.4T.

Spectra were acquired with a 9.4T whole-body scanner with the use of a custom-built head coil (16 channel transmit and 31 channel receive). A modified stimulated echo acquisition mode (STEAM) sequence was used for localization. Eighteen patients with brain tumors of probable glial origin participated in this study. The study was performed in accordance with the guidelines of the local Ethics Committee.

The increased spectral resolution allowed us to directly address metabolic alterations caused by the specific pathophysiology of IDH mutations including the presence of the oncometabolite 2-hydroxglutarate (2HG) and a significant decrease of the pooled glutamate and glutamine (20%, $P = 0.024$), which probably reflects an attempt to replenish α-ketoglutarate lost by conversion to 2HG. We also observed significantly reduced glutathione (GSH) levels (39%, $P = 0.019$), which could be similarly caused by depletion of dihydronicotinamide-adenine dinucleotide phosphate (NADPH) during this conversion in IDH mutant gliomas.

Bisdas et al., demonstrated that MRS at 9.4T provides a noninvasive measure of 2HG in vivo, which may be used for therapy planning and prognostication, and may provide insights into related pathophysiologic metabolic alterations associated with IDH mutations. J. MAGN. RESON. IMAGING 2016;44:823-833 [9)].

Unclassified

11: Heo H, Kim S, Lee HH, Cho HR, Xu WJ, Lee SH, Park CK, Park S, Choi SH, Kim H. On the Utility of Short Echo Time (TE) Single Voxel Proton magnetic resonance spectroscopic imaging in Non-Invasive Detection of 2-Hydroxyglutarate (2HG); Challenges and Potential Improvement Illustrated with Animal Models Using MRUI and LCModel. PLoS One. 2016 Jan 28;11(1):e0147794. doi: 10.1371/journal.pone.0147794. eCollection 2016. PubMed PMID: 26820720; PubMed Central PMCID: PMC4731570.

12: Reeves C, Tachrount M, Thomas D, Michalak Z, Liu J, Ellis M, Diehl B, Miserocchi A, McEvoy AW, Eriksson S, Yousry T, Thom M. Combined Ex Vivo 9.4T MRI and Quantitative Histopathological Study in Normal and Pathological Neocortical Resections in Focal Epilepsy. Brain Pathol. 2016 May;26(3):319-33. doi: 10.1111/bpa.12298. Epub 2015 Sep 6. PubMed PMID: 26268959; PubMed Central PMCID: PMC4950048.

13: Jirjis MB, Vedantam A, Budde MD, Kalinosky B, Kurpad SN, Schmit BD. Severity of spinal cord injury influences diffusion tensor imaging of the brain. J Magn Reson Imaging. 2016 Jan;43(1):63-74. doi: 10.1002/jmri.24964. Epub 2015 Jun 10. PubMed PMID: 26094789.

14: Mishra AM, Bai X, Sanganahalli BG, Waxman SG, Shatillo O, Grohn O, Hyder F, Pitkänen A, Blumenfeld H. Decreased resting functional connectivity after traumatic brain injury in the rat. PLoS One. 2014 Apr 18;9(4):e95280. doi: 10.1371/journal.pone.0095280. eCollection 2014. Erratum in: PLoS One. 2014;9(8):e105899. PubMed PMID: 24748279; PubMed Central PMCID: PMC3991600.

15: Nikas JB, Low WC. Application of clustering analyses to the diagnosis of Huntington disease in mice and other diseases with well-defined group boundaries. Comput Methods Programs Biomed. 2011 Dec;104(3):e133-47. doi: 10.1016/j.cmpb.2011.03.004. Epub 2011 May 6. PubMed PMID: 21529982; PubMed Central PMCID: PMC3166551.

16: Doan BT, Autret G, Mispelter J, Méric P, Même W, Montécot-Dubourg C, Corrèze JL, Szeremeta F, Gillet B, Beloeil JC. Simultaneous two-voxel localized (1)H-observed (13)C-edited spectroscopy for in vivo MRS on rat brain at 9.4T: Application to the investigation of excitotoxic lesions. J Magn Reson. 2009 May;198(1):94-104. doi: 10.1016/j.jmr.2009.01.023. Epub 2009 Jan 25. PubMed PMID: 19289293.

1)
Sher I, Daly C, Oehme D, Chandra RV, Sher M, Ghosh P, Smith J, Goldschlager T. Novel Application of the Pfirrmann Disc Degeneration Grading System to 9.4T MRI: Higher Reliability Compared to 3T MRI. Spine (Phila Pa 1976). 2018 Dec 11. doi: 10.1097/BRS.0000000000002967. [Epub ahead of print] PubMed PMID: 30540717.

2)
Zaiss M, Schuppert M, Deshmane A, Herz K, Ehses P, Füllbier L, Lindig T, Bender B, Ernemann U, Scheffler K. Chemical exchange saturation transfer MRI contrast in the human brain at 9.4 T. Neuroimage. 2018 Oct 1;179:144-155. doi: 10.1016/j.neuroimage.2018.06.026. Epub 2018 Jun 15. PubMed PMID: 29894826.

3)
Helthuis JHG, van der Zwan A, van Doormaal TPC, Bleys RLAW, Harteveld AA, van der Toorn A, Brozici M, Hendrikse J, Zwanenburg JJM. High resolution 7T and 9.4T-MRI of human cerebral arterial casts enables accurate estimations of the cerebrovascular morphometry. Sci Rep. 2018 Sep 24;8(1):14235. doi: 10.1038/s41598-018-32427-w. PubMed PMID: 30250281; PubMed Central PMCID: PMC6155186.

4)
Tsai YH, Yang JL, Lee IN, Yang JT, Lin LC, Huang YC, Yeh MY, Weng HH, Su CH. Effects of Dehydration on Brain Perfusion and Infarct Core After Acute Middle Cerebral Artery Occlusion in Rats: Evidence From High-Field Magnetic Resonance Imaging. Front Neurol. 2018 Sep 20;9:786. doi: 10.3389/fneur.2018.00786. eCollection 2018. PubMed PMID: 30294297; PubMed Central PMCID: PMC6158308.

5)
Skinner NP, Lee SY, Kurpad SN, Schmit BD, Muftuler LT, Budde MD. Filter-probe diffusion imaging improves spinal cord injury outcome prediction. Ann Neurol. 2018 Jul;84(1):37-50. doi: 10.1002/ana.25260. Epub 2018 Jul 3. PubMed PMID: 29752739; PubMed Central PMCID: PMC6119508.

6)
Gao Y, Schilling KG, Stepniewska I, Xu J, Landman BA, Dawant BM, Anderson AW. Tests of clustering thalamic nuclei based on various dMRI models in the squirrel monkey brain. Proc SPIE Int Soc Opt Eng. 2018 Mar;10578. pii: 1057805. doi: 10.1117/12.2293879. PubMed PMID: 30467451; PubMed Central PMCID: PMC6241534.

7)
Massey LA, Miranda MA, Al-Helli O, Parkes HG, Thornton JS, So PW, White MJ, Mancini L, Strand C, Holton J, Lees AJ, Revesz T, Yousry TA. 9.4T MR microscopy of the substantia nigra with pathological

validation in controls and disease. Neuroimage Clin. 2017;13:154-163. doi: 10.1016/j.nicl.2016.11.015. Epub 2016 Nov 17. PubMed PMID: 30240348.

8) Yun TJ, Cho HR, Choi SH, Kim H, Won JK, Park SW, Kim JH, Sohn CH, Han MH. Antiangiogenic Effect of Bevacizumab: Application of Arterial Spin-Labeling Perfusion MR Imaging in a Rat Glioblastoma Model. AJNR Am J Neuroradiol. 2016 Sep;37(9):1650-6. doi: 10.3174/ajnr.A4800. Epub 2016 May 12. PubMed PMID: 27173366.

9) Bisdas S, Chadzynski GL, Braun C, Schittenhelm J, Skardelly M, Hagberg GE, Ethofer T, Pohmann R, Shajan G, Engelmann J, Tabatabai G, Ziemann U, Ernemann U, Scheffler K. MR spectroscopy for in vivo assessment of the oncometabolite 2-hydroxyglutarate and its effects on cellular metabolism in human brain gliomas at 9.4T. J Magn Reson Imaging. 2016 Oct;44(4):823-33. doi: 10.1002/jmri.25221. Epub 2016 Mar 11. PubMed PMID: 26970248.