3D MRI of the Hyperpolarized ^{129}Xe Distribution in the Rat Brain

J. Nouls[1,2], Z. I. Cleveland[1,2], M. S. Freeman[3], H. E. Moeller[4], L. W. Hedlund[1,2], and B. Driehuys[1,2]
[1]Department of Radiology, Duke University, Durham, NC, United States, [2]Center for in vivo Microscopy, Duke University, Durham, NC, United States, [3]Medical Physics, Duke University, [4]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Introduction: Hyperpolarized (HP) gas MR, in particular HP ^{3}He, is most typically associated with high resolution, functional imaging of the lungs. However, HP ^{129}Xe, unlike HP ^{3}He, is soluble in tissues and, after inhalation, can be observed in a variety of more distal organs including the heart **[1]**, kidneys **[2]** and the brain **[3, 4]** . HP ^{129}Xe studies of the brain may be particularly fruitful, because, unlike most conventional MR contrast agents, ^{129}Xe freely diffuses across the blood-brain barrier. Moreover, when dissolved in the brain ^{129}Xe, exhibits multiple resonance frequencies that have been attributed to ^{129}Xe dissolved in the blood, grey matter, and white matter **[4, 5]** . To make full use of these unique properties, it will be necessary to image the brain distribution of ^{129}Xe. While, ^{129}Xe brain MRI has been reported **[3, 6, 7]**, these earlier efforts typically required lengthy acquisitions, exhibited low resolution (16×16 matrix), and were limited to two dimensions. Here, we demonstrate the first fully isotropic 3D images of the ^{129}Xe distribution in the rat brain.

Methods: Rats (1, 300 g Sprague-Dawley CD; 1 180 g Fischer 344; Charles River, Wilmington, MA) were prepared according to a protocol approved by our IACUC. Animals were anesthetized with IP injections of pentobarbital/ butorphanol, intubated, and ventilated on a HP-gas compatible, constant-volume ventilator **[8]** at a rate of 1 breath/s with 20% O_2 and 80% N_2 or HP ^{129}Xe. Body temperature was maintained between 34 and 36 °C by warm air and heart rate was continuously monitored by ECG. Imaging was performed using a 2-T, 30-cm clear-bore magnet (Oxford Instruments, Oxford, UK) operated with a GE EXCITE console (GE Healthcare, Milwaukee, WI) and a 30-mm diameter, 40 mm long custom-made, dual-tuned ^{1}H-^{129}Xe birdcage coil. Isotopically enriched xenon (83% ^{129}Xe) was polarized to 6-10% in 500 ml batches using a prototype commercial polarizer (GE Healthcare, Durham, NC). Dissolved ^{129}Xe was selectively excited using a 1.2 ms 3-lobe since pulse centered 196 ppm from the gas-phase resonance. Spatial encoding of ^{129}Xe used a 3D radial acquisition [views =1201, FOV=128 mm isotropic, matrix=32^3, TR/TE=250/0.9 ms TE 0.9 ms, α=20°, BW 8 kHz, isotropic resolution = 4 mm]. 3D ^{1}H anatomical reference scans were acquired with the same sequence [views=400,001, FOV=10 cm isotropic, matrix=256^3, TR/TE=7/1.2m, α=15°, BW=31kHz, 0.4 mm isotropic resolution].

Results and Discussion: HP ^{129}Xe was readily observed from the brain tissue in both rats using an acquisition time of only 5 min. Comparison of the resulting 3D ^{129}Xe images with the corresponding anatomical ^{1}H MRI reveals, somewhat surprisingly, that the HP ^{129}Xe is heterogeneously distributed. For example, strong signal is observed from the olfactory bulb and mid-brain but is nearly absent in the cerebellum. These patterns as are not entirely consistent with known perfusion in the rat brain **[9]** and thus highlight the importance of 3D imaging in developing HP ^{129}Xe brain MRI. While the sources of the observed heterogeneity remain speculative, differences in transit times from the lung and washout rate from different regions of the brain likely play an important role. Additionally, differences in the ^{129}Xe partition coefficients and relaxation rates within different tissues types may also partially determine the observed signal distribution. Interestingly, dissolved ^{129}Xe signal is also is observed in the tissue of the nasal sinuses, which, to our knowledge has never been reported. Whether this signal originated from magnetization arriving via the vasculature or the dissolution of gaseous magnetization in the sinuses remains an open question.

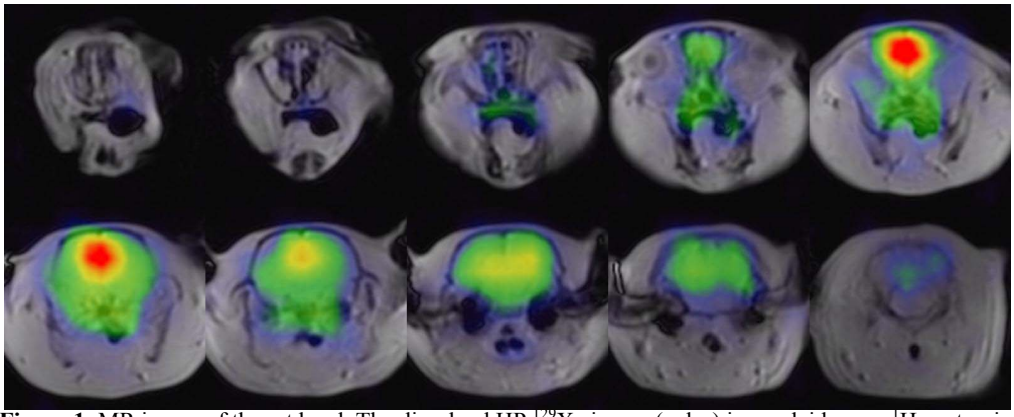

Figure 1: MR image of the rat head. The dissolved HP ^{129}Xe image (color) is overlaid on an ^{1}H anatomical image (grayscale). ^{129}Xe signal largely matches the brain tissue. ^{129}Xe signal is notably intense in the olfactory bulb and mid-brain regions. It is largely absent from the cerebellum.

References: 1. Z. I. Cleveland *et al.*, *PLoS ONE* 5, e12192 (08/16, 2010). **2.** S. D. Swanson *et al.*, *Magn. Reson. Med.* 42, 1137 (1999/12, 1999). **3.** S. D. Swanson *et al.*, *Magn. Reson. Med.* 38, 695 (1997). **4.** K. Nakamura *et al.*, *Magn. Reson. Med.* 53, 528 (2005). **5.** J. Kershaw *et al.*, *Magn. Reson. Med.* 57, 791 (Apr, 2007). **6.** G. Duhamel *et al.*, *Magn. Reson. Med.* 46, 208 (2001/08, 2001). **7.** X. Zhou *et al.*, *NMR Biomed.* 23, 1 (2010). **8.** J. Nouls *et al.*, *Concepts Magn. Reson. B* (submitted). **9.** H. Goldman, Sapirste.La, *Am. J. Physiol.* 224, 122 (1973).
Acknowledgements: Center for In Vivo Microscopy (NIH/NCRR P41 RR005959)