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CEREBRAL ANGIOGRAPHY IN RATS: COMPARISON OF ^{1}H TOF-MRA, SPIO ENHANCEMENT AND HYPERPOLARIZED ^{13}C BSSFP

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Introduction Magnetic resonance angiography (MRA) is an important tool in the diagnostics of abnormal vasculature, and proton imaging can provide excellent sub-millimeter resolution of blood vessels in small animals[1]. MRA can be further optimized with Gd-based or blood pool agents[2]. However the acquisition time is several minutes at best, and thus the technique fails in cases that require subsecond temporal resolution, e.g. imaging within a single heartbeat or breath hold to avoid movement artifacts. Several attempts to shorten the acquisition time have applied hyperpolarized ^{13}C-substances[3,4]. As the signal is increased by orders of magnitude and the background signal is negligible due to the low natural abundance of ^{13}C, the repetition time can be lowered significantly. We demonstrate that subsecond, submillimeter resolution can be achieved with hyperpolarized ^{13}C-enriched agents and provide important information about the cerebral vasculature in the rat.

Methods *Pulse sequence design:* Data were acquired on a 4.7 T imaging system (Agilent, Direct Drive, VnmrJ 3.2) using a ^{13}C/^{1}H RF volume coil combined with a ^{13}C four channel array coil (receive-only) (RAPID Biomedical GmbH, Germany). The receive coil was placed dorsal with the animal supine. The hyperpolarized signals were acquired using a bSSFP sequence with an $\alpha/2$ preparation pulse and a flip back pulse in a 30 mm slab with field of view of 60×60 mm^2, matrix 128×128 and 60° flip angle. The dependence on acquisition bandwidth was investigated by performing series of experiments with bandwidths of 20, 50 and 100 kHz, respectively. Higher SNR can be obtained by lowering the bandwidth, however the echo time is increased correspondingly resulting in artifacts in the image. A bandwidth of 50 kHz has proven to give a large SNR and minimal artifacts. The repetition time and the echo time were the shortest possible on the system, corresponding to TR/TE = 6.65 ms / 3.32 ms for 50 kHz bandwidth, yielding a total image acquisition time of 851 ms. The flip angle dependence was also investigated and the 60° was found to provide optimal image quality. The proton angiographic time-of-flight (TOF) images were acquired with a 3D gradient echo sequence with TR/TE = 90 ms / 1.09 ms, α = 40° and magnetization transfer of 1200°, duration of 6 ms and 3 kHz offset. The FOV and resolution were similar to the hyperpolarized measurements, with a resolution RO×PE×PE2 = 64×128×128 and FOV = 30×60×60 mm^3. The total scan time for the ^{1}H image is 24 minutes. 50 µL Clariscan™ was injected before scanning in the contrast enhanced images. *Hyperpolarization:* 50 µL of HP001 (bis-1,1-[hydroxymethyl]-[1-^{13}C]cyclopropane-d$_8$) was polarized using a Hypersense 3.35 T, 1.4 K, for more than 1 hr, (polarization time constant ~1800 s) at a microwave frequency of 94.112 GHz. The final polarization was measured to be 24 %. The hyperpolarized substance was injected within 30 seconds after dissolution, and the acquisition was initiated immediately after injection. *Animal preparation:* Male Spraque Dawley rats (200 - 500 g, n = 10) were anesthetized with isoflurane and a catheter was inserted in a tail vein for injection of the hyperpolarized substance.

Results and Discussion The image in Fig. 1 was acquired in less than a second. The signal is highest in the superior sagittal sinus (sss) and the transverse sinuses (trs), the anchor-like shape, which are the large vessels closest to the surface coil. An SNR of 15 is observed in the coronal orientation, whereas SNR above 30 are obtained in axial orientation of the slab. Due to the coil sensitivity, only the vessels within ~10mm from the surface coil appear on the ^{13}C-MRA. The MIP of a ^{1}H-TOF-MRA in the slab is shown in Fig. 2. The arteries dominate due to larger blood flow velocities and hence larger TOF effect, especially the carotids arteries are apparent, and none of the large veins appear. The large veins are shown in Fig. 3, where the vessels are enhanced with SPIO. Only the top 12 mm have been used in the MIP in Fig. 3 in order to avoid the carotids arteries etc. and only show the anchor-like sinuses. Fig. 4 shows an anatomical spin-echo image for navigation, the rat brain is centered in the FOV.

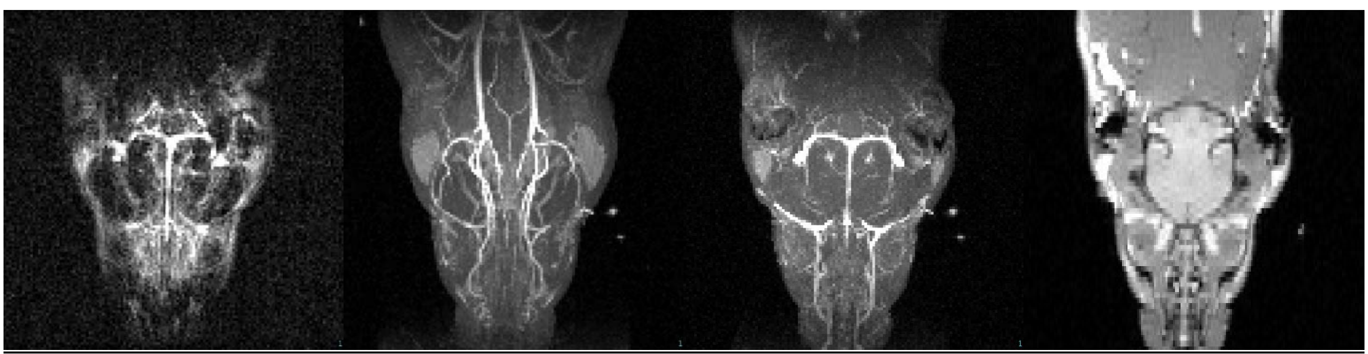

Fig. 1: Hyperpolarized ^{13}C MRA 0.85 s | *Fig. 2: Proton TOF-MRA 1475 s* | *Fig. 3: TOF-MRA with Clariscan™ 1475 s* | *Fig. 4: Anatomical spin echo image*

Conclusion: The signal from the large veins above the brain dominate the ^{13}C images due to the surface coil geometry. These veins are not visible in the TOF-MRA and high quality MRA images is only possible with extensive averaging. The study demonstrates that hyperpolarized ^{13}C angiography is able to provide high quality MRA images on the second time scale. Higher sensitivity (e.g. polarization and coil) and better coil coverage is needed to capture the smaller arteries and improve SNR and coverage further.

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