

Hyperpolarized water as an MRI contrast agent: Feasibility of *in vivo* imaging in a rat model

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Purpose

The ability to monitor flow and perfusion is important for a wide range of biomedical problems. While there are several flow and perfusion MRI methods in clinical practice, there is still a need for higher sensitivity and contrast. In addition, many of these methods rely on gadolinium-based contrast agents, which may not be safe for certain classes of patients.

To overcome these challenges we have developed a new MRI technique that utilizes Overhauser dynamic nuclear polarization (DNP) to continuously deliver contrast agent-free hyperpolarized water to a subject inside a standard 1.5 T clinical MRI. While there are multiple ways to hyperpolarize substances (e.g., dissolution DNP and parahydrogen), Overhauser DNP is the only method capable of operating in a continuous-flow system, making it well suited for the imaging of flow and perfusion. This method is also inherently safe, as the only substance injected is pure water, and the hyperpolarization process does not change the physical properties of the water. We have previously demonstrated this technique with phantoms [1], and here we present the first *in vivo* demonstration of our method.

Materials and Methods

According to protocols approved by the local institutional animal care and use committees, male Wistar rats were anesthetized and prepared by placing injection tubing in the subcutaneous layer ($n = 3$), the peritoneum ($n = 3$), the aorta ($n = 3$) or the right carotid artery ($n = 3$). The water was hyperpolarized via Overhauser DNP at room temperature in the 0.35 T fringe field of a 1.5 T MRI magnet, using a custom-built system to continuously deliver radical-free hyperpolarized water to the subject at flow rates of 1.5 mL/min [1]. The hyperpolarization process creates water with enhanced and inverted signal, and image contrast comes from differences in the intensity and phase of signal. Images were acquired with standard gradient echo sequences.

Results

Images of all injection locations showed clearly enhanced flow contrast. For subcutaneous and intraperitoneal injections, the water perfusion trajectory was observed within ~5 s of injection (images not shown). When injecting into the aorta, the hyperpolarized water could be visualized traveling through a 4.2 cm length of the aorta and femoral arteries (Fig 1). The carotid injections showed the modification of signal intensity in the right hemisphere of the brain and lateral ventricles (Fig 2).

Conclusion

This exploratory study shows that perfusion contrast for MR imaging can be enhanced by continuously infusing hyperpolarized water, providing localized angiography or brain perfusion information for *in vivo* rat models. This technique has potential to enhance human perfusion MRI, especially for patients with contraindications for Gd-based contrast agents, as the contrast is provided solely by pure water. However, before clinical application further improvements are necessary, such as higher quantities of hyperpolarized water and greater enhancement levels.

Reference

1. M.D. Lingwood, et al., *J. Mag. Reson.* 205 (2010) 247–254.

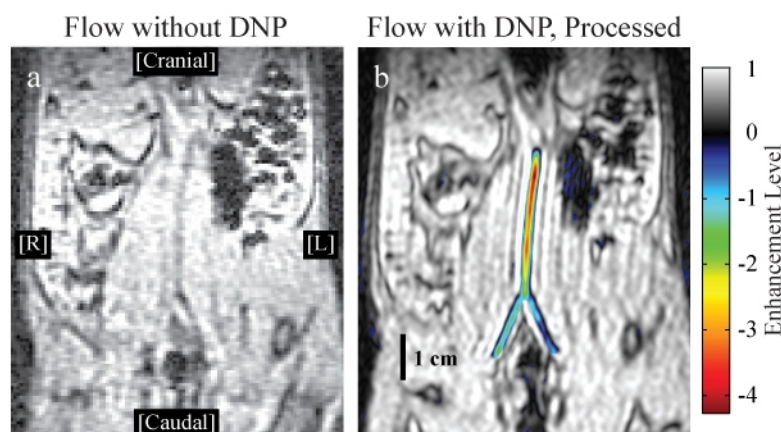


Figure 1: Image acquired while injecting (a) non-hyperpolarized and (b) hyperpolarized water into the aorta of a live rat. The water is injected at the top of the image, and after the hyperpolarized water leaves the small catheter it can be seen in the aorta and femoral arteries. Image (b) is specially processed to show the inverted, enhanced signal in color. Coronal SPGR images, 300 ms TR, 3.1 ms TE, 50 s acquisition.

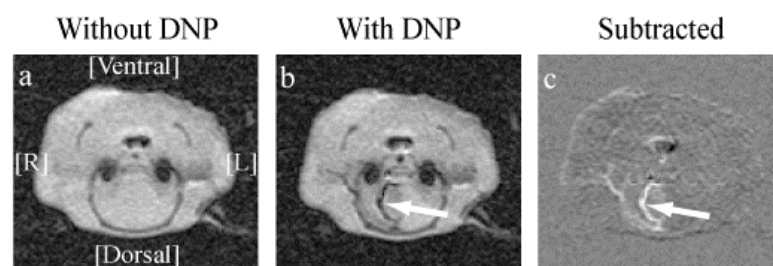


Figure 2: Images acquired while injecting (a) non-hyperpolarized and (b) hyperpolarized water into the right carotid artery of a live rat. Panel (c) is the subtraction image of (a) – (b). After injection, hyperpolarized water enters the right hemisphere of the brain, causing a decrease in signal due to the negative phase of the enhanced water, which when diluted across a large volume of bulk water (positive phase) results in a net reduction of the observed signal. Water then passes from the right hemisphere into the lateral ventricles, noted with the arrow in (b) and (c). Axial SPGR images, 300 ms TR, 3.1 ms TE, 1.6 min acquisition.