Hyperpolarized Water for Interventional Angiography

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Introduction

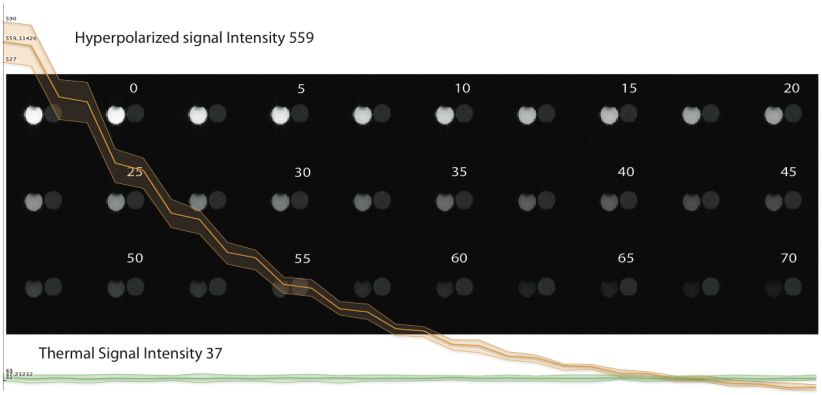
For more than a decade hyperpolarized water has been pursued for *in vitro* and *in vivo* applications (1-3). Here we demonstrate a novel method of hyperpolarizing water based on the dissolution-DNP method (4). The short T_1 and T_2 is a serious obstacle to the practical utility of the method, but this work suggests solutions to alleviate the problem. Protons have the highest gyromagnetic ratio of all nuclei providing high magnetization and high spatial resolution. Standard clinical MR equipment can be used as well as established pulse sequences. Hyperpolarized water would be ideally suited for interventional applications where the large magnetization of the bolus would allow fast imaging with high spatial resolution and SNR.

Methods

100 uL of water:glycerol 50:50 (w/w) with 30 mM TEMPOL was polarized for one hour in a Hypersense DNP polarizer. The sample was dissolved in degassed D_2O with 1 M ascorbate. The dissolved sample was manually transferred to a syringe and brought to the scanner for injection into either a phantom or rat. The transfer and injection took 8-10 s for phantoms and 10-15 s for rat experiments.
GRE with flip angle of 1º, 64x64, FOV 60x60x10 mm^3, TR/TE 5.6/1.9 ms were acquired on a 4.7 T Varian animal scanner. For phantom imaging two images were acquired back-back followed by a 5 s delay. A neat water sample was placed next to the hyperpolarized phantom as thermal signal reference. The hyperpolarized water (2.2 M) density is 2% of the thermal ionized water (110 M) density.

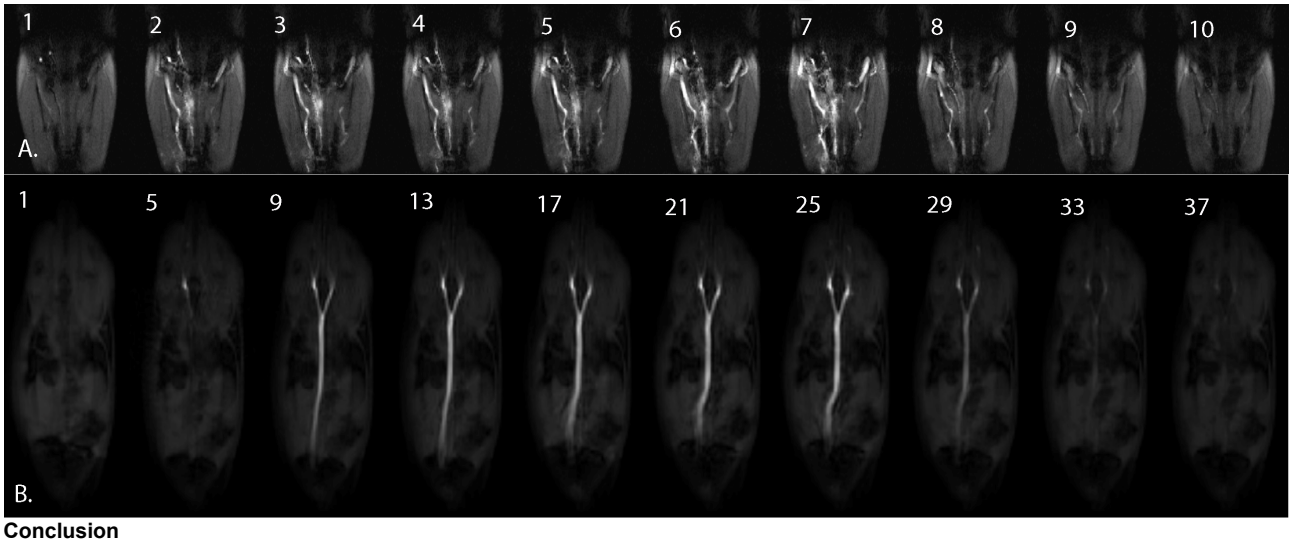
Results

T (°C)	H_2O	1:1 H_2O:D_2O	1:3 H_2O:D_2O	1:3 H_2O:D_2O *radical*	1:3 H_2O:D_2O *150 mM DMSO*	1:3 H_2O:D_2O *200 mM glycerol*
25	3.7 s	6.4 s	10.8 s	3.7 s	10.3 s	9.7 s
40	-	-	15.9 s	5.8 s	15.4 s	14.0 s
60	-	-	11.8 s	6.5 s	10.3 s	13.0 s



The relaxation time (T_1) of various relevant final product compositions were measured (all degassed). These results demonstrate that long relaxation times can be achieved by dilution into D_2O and that the radical is the main cause of relaxation. A series of images were obtained for a hyperpolarized water sample. The measured signal (magnetization) was 15 times thermal water at 4.7 T and room temperature. A decay (T_1) of ~20 s was measured showing the effective quenching of the radical. The effect of the 1º flip angle between pairs of images is small as seen from the ROI intensity plot overlaid on the phantom images. The total time for a pair of images is 0.7 s and the delay between pairs is 5 s.

In vivo angiographic images in the rat were acquired. The first row is after carotid artery injection. The scanner was setup for continous scanning and 10 frames are shown as the bolus is inejcted. The lower row shows a 5 mm coronal slice through the rat and 10 frames following tail vein injection. Every 5th image is shown. The vessel enhancement was ~5 times with high reproducibility. Other administration routes were tested with similar results.



Conclusion

The study demonstrates that water can be hyperpolarized by the dissolution-DNP method. The method has several advantages: a) very high polarization (tens of percent) and b) long relaxation times (by dilution in D_2O). The applicability of the method is demonstrated in the rat by several angiographic acquisitions. The method has potential for an order of magnitude further improvement in enhancement by optimizing the DNP, dissolution and transfer.

References: 1. US Patent 6,008,644 (1997), 2. McCarney et al, PNAS 2007, 3. Mishkovsky et al, JMR 2009, 4. Ardenkjaer-Larsen et al, PNAS 2003