^{1}H Perfusion MRI with the Replacement Effect of D_2O

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Introduction

Deuterium oxide has been used as an exogenous tracer in early perfusion MRS/MRI studies, by using a coil for receiving signal at the resonant frequency of deuterium [1,2]. The nonradiative D_2O molecule, with a similar size and chemical characteristics as H_2O, has the advantage of low toxicity and high permeability, and it could represent the realistic behavior of small molecules perfusion in tissue. However, the sensitivity of deuterium is only about 1% of ^{1}H, and thus the image resolution and quality were not comparable to ^{1}H images [2,3]. RF labeled H_2O has also been utilized as a freely diffusible tracer by the arterial spin labeling technique, which is also suffered from the low SNR. The most popular perfusion method in clinical use is the dynamic imaging of Gd chelates, which has a limited permeability due to its size. In this study, we proposed a new method to use D_2O as a contrast agent for ^{1}H MRI.

Materials and Methods

All experiments were conducted on a 4.7T Bruker MRI scanner (Biospec, 47/40). 99.9% D_2O (Cambridge Isotopes, MA, USA) was mixed with deionized H_2O to five concentrations: 10%, 30%, 50%, 70%, and 90%. 1-ml syringes were filled with these five concentrations of D_2O, and then inserted into a 50-ml centrifuge tube. The empty space inside the centrifuge tube was then filled with pure deionized H_2O. The T1 and T2 of the phantom were measured by an IR-EPI and a MSME sequence, respectively. Furthermore, spontaneously breathing male Sprague-Dawley rats (n=5) weighting 250~370 g were anesthetized with 1.5% Isoflurane. One tail vein was catheterized with a 30 cm long PE-50 polyethylene tube for D_2O injection inside the MRI scanner. Axial brain slice at the anterior commissure point was scanned with dynamic gradient echo EPI with parameters: TR=1000 ms, TE=17.5 ms, echo position 30%, Flip angle=90°, FOV=35mm, slice thickness=2mm, acquisition matrix=96x96, bandwidth = 200kHz, NA=1, and number of repetition = 540. 1 ml of isotonic saline D2O was injected as acquiring the 120~125th image.

Results

A ^{1}H MRI image of the multi-concentration phantom was showed in Fig 1a. The SNRs within ROIs of 5 syringes and the surrounding water was measured and plot as a function of D_2O ratio in the Fig 1b. The SNRs were decreased as the water molecules replaced by D_2O and the exchanged HDO. Also note that the SNRs were further suppressed than the water ratio (dashed line). The relaxation rate R1 and R2 of ^{1}H were plotted regarding to the D_2O ratio in Fig 2a and 2b, respectively. Negative relaxivities were observed for using D_2O as ^{1}H contrast agent. For in vivo rat experiments, an intensity time course of one rat's brain was showed in Fig 3a to demonstrate the wash-in and wash-out of the injected D_2O. Due to its high permeability, the time course was prolonged than conventional dynamic susceptibility contrast MRI using Gd chelates. The averaged intensities of 50 points at the baseline and minimum peak were subtracted pixel by pixel to generate a map of maximum water replacement in Fig 3b, which was a representative map of cerebral blood perfusion. The averaged maximum signal drop of 5 rats was 5.3±1.6%. Due to the high SNR of ^{1}H image and efficient contrast provided by D_2O, the map showed high quality and good resolution for providing perfusion information.

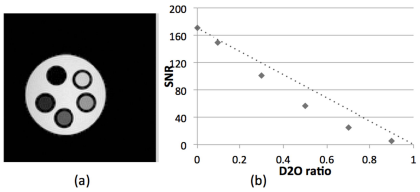

Fig 1 (a) An ^{1}H MRI image of the multi-concentration phantom. (b) The SNR decreased as a function of D2O ratio. The dashed line indicated the theoretical effect of ^{1}H replacement.

Discussion and conclusion

To the best of our knowledge, it is the first study to use D_2O as a contrast agent for ^{1}H perfusion MRI. The replacement effect was the dominant factor of contrast. The T1 and T2 were also slightly lengthened when the D_2O ratio increased. Due to the sensitivity difference between ^{1}H and deuterium, the negative contrast by replacing ^{1}H signals is theoretically 100 times larger than directly measuring the deuterium signal. The toxicity of D_2O has been discussed in early literature, and the dose of D_2O used in this study was far beyond the limit of possible harm [4]. On the other hand, the conventional Gd chelates could lead to nephrogenic systemic fibrosis for patients with kidney disorder. D_2O could be a potential substitution without the cost of hardware upgrade. Furthermore, the high permeability of D2O could provide different information than Gd chelates [3]. With the improved contrast by the proposed method, it is worthy to re-investigate the D_2O contrast perfusion MRI on tumor, stroke, and other applications.

References

1. Ackerman JJH et al., Proc Natl Acad Sci U S A 84:4099-102, 1987.
2. Muller S and Seelig J, J Magn Reson 72:456-66, 1987.
3. Bogin L et al., J Magn Reson Imaging 16:289:99, 2002.
4. Barbour HG, Yale J Biol Med 9:551-65, 1937.

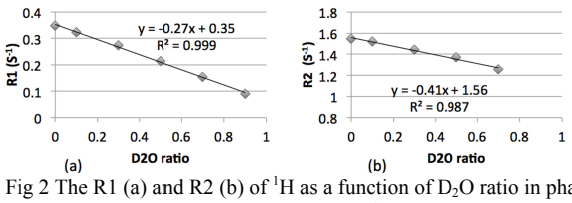

Fig 2 The R1 (a) and R2 (b) of ^{1}H as a function of D_2O ratio in phantoms were showed. Note that the D2O was an ^{1}H contrast agent with negative relaxivities.

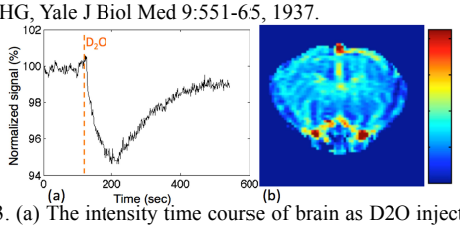

Fig 3. (a) The intensity time course of brain as D2O injected at 120~125 s. (b) A color map of maximum signal drop was showed.