D_2O Perfusion MRI: Investigation on the D_2O Infusion Method

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Introduction. In early days, pioneering studies demonstrated that the deuterium oxide (D_2O) could be utilized as an exogenous diffusible tracer for *in vivo* perfusion measurement by NMR and MRI. [1, 2] Recently, an indirect detection strategy for D_2O perfusion MRI was proposed by monitoring the ^1H signal attenuation, and opened a new way to re-investigate this technique. [3] Due to the characteristic of free diffusion across the BBB, the time course of D_2O perfusion is significantly longer than the conventional method using Gd-based contrast agent. In this study, we aimed to further utilize the long time course of D_2O by using a stable infusion instead of bolus injection and acquiring perfusion images with proton density weighted RARE sequence. Although the RARE sequence will cost longer time than EPI, the improved image quality and reduced artifacts were expected in the cerebral regions under severe susceptibility effect.

Materials and Methods. All experiments were conducted on a 4.7T Bruker MRI scanner (Biospec, 47/40). 9 Sprague Dawley rats weighting 250~350g were anesthetized by 1.5% Isoflurane with controlling respiration rates in a range of 50~60 times/min. During MR imaging, each rat was injected with a 2ml /100g dose of isotonic D_2O saline through tail vein by a syringe pump. For multi-slice EPI sequence, infusion time was set to 1 minute and the imaging parameters were as follows: spin-echo, TE/TR= 30/12000msec, Matrix size=128*128, FOV=3.5cm, inter-slice distance= 2mm; for multi-slice RARE images, 1, 4, and 6 minutes infusion time (N=3, 2,and 3, respectively) was set with following parameters: centric ordering, TE/TR= 11.8/2000msec, RARE factor =8, Matrix size=128x128, FOV=3.5cm, inter-slice distance= 2mm. A surface coil for rat brain was used for receiving signal, and the inhomogeneity of sensitivity was corrected for presented images. To observe the perfusion of infused D_2O, multi-slice signal drop maps were calculated by subtracting the average images during 3 minutes after the end of infusion from the baseline images. Finally, ROIs of rat brain were applied to depict the whole brain time-intensity curves. All data were processed via MATLAB scripts.

Results. Multi-slice EPI and RARE signal change maps with 1 minute for infusion are compared in Fig 1. The RARE images retained intact brain morphology and excellent perfusion contrast. Furthermore, Fig 2 shows brain coronal slices near skull base. The EPI images hardly outlined the brain tissues due to severe distortion, while RARE images could still specify detailed structures such as hypothalamus, amygdala, and substantia nigra. For various flow rates, Fig 3 displays similar maximum signal drop and slowly recovered time curves of 1min(●), 4(■), and 6mins(▲) infusion. These results suggest that reproducible signal drops by infusion method are feasible for perfusion analysis.

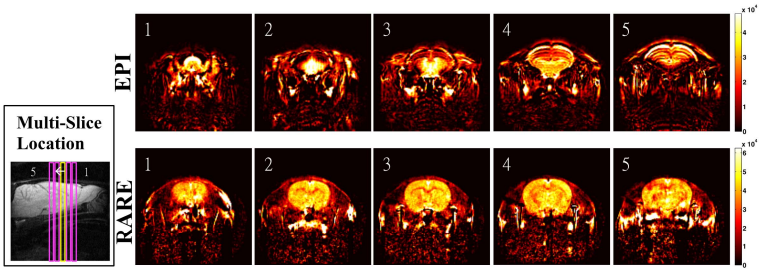

Fig 1. EPI (upper row) and RARE (lower row) axial multi-slice signal drop maps, where Anterior Commissure (AC) is on the 3rd slice. RARE images retained intact brain morphometry and excellent perfusion contrast.

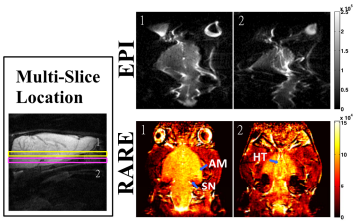

Fig 2. In contrast with the distorted EPI images (upper row), RARE coronal signal drop maps (lower row) showed perfusion contrast for detailed structures such as hypothalamus (HT), amygdala (AM), and substantia nigra (SN).

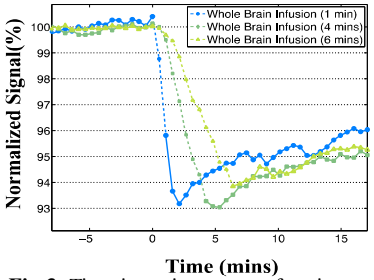

Fig 3. Time intensity curves of various infusion times: 1, 4, and 6 minutes. Dashed lines (--) depict the duration of D_2O infusion.

Discussion and Conclusion.

The proton-density weighted RARE images were used to show perfusion contrast on important brain structures near skull base. Therefore, the D_2O perfusion MRI by indirect detection of ^1H signal attenuation has potential for applications of observing blood supply in these critical regions. The 2ml/100g dose of D_2O is relative high, but far under the level of possible harm. Care should be taken for further applying D_2O administration on human subjects, due to possible of vertigo in some people. [4] The infusion method can provide consistent signal drop after D_2O administration, and a longer infusion time may alleviate the physiological stress. However, the wash-out of D_2O may not be ignored during longer infusion time, which may complicate the quantification of perfusion. Further studies are needed for dose optimization and absolute perfusion quantification.

References. 1. Ackerman JJ et. al. PNAS 84:4099-102, 1987. 2. Detre JA et. al. Magn Reson Med 14:389-953, 1990. 3. Wang FN et al, Proc. of ISMRM, 2012. 4. Price JC et. al. Analy Biochem 420:73-83, 2012.