Absolute quantification of CBF on rodent brain with D_2O as tracer of ^1H MRI

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Introduction. Deuterium oxide (D_2O) was utilized as an exogenous tracer of MRI for perfusion measurement in early study. [(1)] Due to the characteristic of free diffusion, the local volume of distribution of D_2O can be assumed as the whole voxel space, and hence make it as a suitable for measuring the cerebral blood flow (CBF). Recently, an alternative strategy of indirectly detecting of D_2O via ^1H perfusion MRI was reported, it was suggested that the image quality could be improved by combining RARE imaging and D_2O infusion. [(2)] In this study, we aimed to further perform absolute quantification of CBF with this method.

Materials and Methods. All experiments were conducted on a 4.7T Bruker MRI scanner (Biospec, 47/40). 4 Sprague Dawley (SD) rats weighting 250~350g were anesthetized by 1.5% Isoflurane with respiration rates in a range of 50~60 times/min. For each SD rat, 2ml /100g dose of isotonic D_2O saline was infused through tail vein by a syringe pump. The infusion duration lasted 2 minutes during the dynamic MRI. Dynamic RARE images was acquired with a surface coil with following parameters: centric ordering, TE/TR= 11.8/2000msec, RARE factor= 8, in-plane resolution= 0.273×0.273mm, slice thickness= 1.5mm, temporal resolution= 32sec. The raw image was first processed by sensitivity correction and then filtered by a spatial 3×3 averaging mask. The relative concentration-time curve of D_2O was estimated by subtracting the baseline level with intensity-time curve. The CBF of each pixel was measured by two method: 1) Calculate the time constant of exponential decay after the maximum concentration as *exp(-CBF/λ)* [(1)], where the λ was set as 0.9 as the partition ratio of water. The concentration-time curve was further applied with temporal filter before curve-fitting. 2) Use a singular value decomposition (SVD) method for arterial input function (AIF) deconvolution, and extract the height of residue function *r(t)* as CBF value by the equation: $c(t) = CBF \cdot AIF \otimes r(t)$. [(3)] Singular values were omitted if its value was lower than 20% of the first one. The measured CBF was normalized regarding to the presumed CBF at corpus callosum. The AIF herein was assumed to remain constant for steady D_2O infusion. All data were processed by MATLAB scripts.

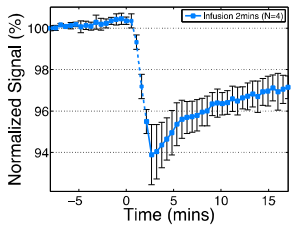

Fig 1. The dynamic D_2O intensity-time curve with 2mins infusion duration. Note the intensities decreased linearly during infution.

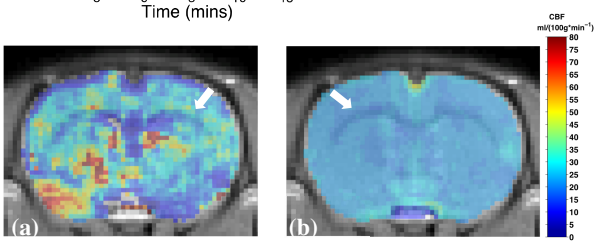

Fig 2. The CBF maps of the same rat evaluated from (a) single exponential fitting and (b) AIF deconvoltion by SVD methods, respectively. Both maps show clear contrast between the corpus callosum (white arrow) and other brain tissues.

Results. Fig 1. shows the averaged signal-time curve of dynamic RARE in the rat brain. During 2mins infusion, the ^1H signal intensity is linearly decreased. After stopped infusion, the intensities slowly recovered to a lower baseline than the intensities before infusion. By quantifying the CBF value pixel-by-pixel, Fig 2. (a) and (b) demonstrates the axial view of CBF maps, which were acquired from exponential fitting method and the SVD deconvolution method, respectively. It is noted the clear contrast of these CBF maps between the corpus callosum (white arrow) and other brain tissues.

Discussion and Conclusion. In this study, we demonstrated the feasibility of absolute quantification of CBF on rat brain. In comparison, the SVD method requires accurate AIF for deconvolution, while single exponential model simply fitting the D_2O washout curves. It could be difficult to extract correct AIF without partial volume effect on rat MRI. Therefore, we used a square wave as the AIF, and it might not be deviated from reality of slowly infused D_2O. Owing to the de-noising ability of the SVD method, the CBF map of SVD was smoother than the exponential fitting method. However, lesion model was needed in the future to test the ability of detection abnormal CBF. The measured CBF values were low, since anesthesia control, $PaCO_2$, and other physical situations have made the CBF value varied and hard to achieve consistent results. [(4)] Recently, clinical concern was raised on the cerebral perfusion in neurodegenerative disorders such as Alzheimer's disease. Due to the good quality of RARE imaging at the skull base region, the D_2O perfusion imaging method is promising for measuring the perfusion of lower brain regions.

References. 1. Detre JA et al. *Magn. Reson. Med.*, **19**:389-95, 1990. 2. Wang FN et. al., *NMR Biomed,* **26**: 692-8, 2013. 3. Ostergaard L et al. *Magn. Reson. Med.*, **36**:726-36, 1996. 4. Hendrich KS et al., *Magn. Reson. Med.*, **46**: 202-206, 2001.