Effects of Blood-Brain Permeability on CBF measured by arterial spin labeling and dynamic susceptibility contrast

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Introduction. Arterial spin labeling (ASL) and dynamic susceptibility contrast (DSC) techniques are widely used to image cerebral blood flow (CBF) in stroke. Stroke disrupts blood brain barrier (BBB), resulting in perturbed vascular permeability, and thus could affect CBF quantification (1,2). However, such effect is generally not taken into account in perfusion imaging of stroke. The aim of this study is to examine how changes in permeability affect ASL and DSC CBF measurements. We image CBF using the two CBF techniques on the same animals under three experimental conditions: 1) stroke animals where the CBF and BBB permeability are changed, 2) normal animals breathing 5% CO_2 where only CBF is changed, and 3) normal animals injected with mannitol to change BBB permeability with and without 5% CO_2 breathing. These experiments together allow us to investigate the effect of permeability change in perfusion images of ischemic stroke and how permeability affects the two commonly used CBF methods.

Methods. Rats (300-350 g) were anesthetized with isoflurane under controlled ventilation. CBF MRI was measured using continuous ASL and DSC technique on the same animals in three groups: 1) embolic stroke rats (n=5) (3) were imaged 2 days after stroke where hyperperfusion was observed, 2) animals (n=3) breathing air or 5% CO_2, and 3) animals (n=3) breathing air or 5% CO_2 with mannitol (1.1 mole/l) injected *via* a femoral vein. DSC measurements between air and CO2 in the same rats were separated by 1 hour.

MRI was performed on Bruker 7T using a 2.3-cm diameter surface coil. CBF was measured using ASL and DSC in the same rats. Both techniques used single-shot gradient-echo EPI, FOV = 25×25 mm, matrix = 64×64, slice thickness = 1.5 mm and TE = 13 ms. The ASL parameters were: separate neck labeling coil, labeling time = 2.3 ms, TR = 2.9 s. DSC parameters were: TR = 0.2 s and 3 corresponding slices. ASL (4) and DSC (5) CBF were calculated. Pixels of the CBF images were normalized to a single average value of the unaffected normal hemisphere. Pixel-by-pixel scatterplots of normalized ASL-CBF *vs* DSC-CBF were obtained for each experimental condition. Ratios of ASL/DSC CBF maps were also obtained to visualize the spatial differences between the two CBF methods. Note that absolute CBF comparisons between the two methods were not made.

Results. Figure 1 shows an ASL-CBF image, DSC-CBF image, and ASL/DSC ratio image. In group 1, the lesion hemisphere of the stroke rat showed hyperperfusion (left side of the image) and the ASL/DSC ratio was higher in the stroke hyperperfusion region (arrows) than in the contralateral normal hemisphere. In group 2, breathing CO_2 increased CBF globally but the ASL/DSC ratio was unchanged as expected. In group 3, breathing CO_2 with mannitol administration showed increased CBF globally detected by both methods. However, the increase detected by ASL was significantly higher than by DSC, resulting in a larger ASL/DSC ratio, similar to the stroke hemisphere. **Figure 2** shows the normalized ASL-CBF versus the DSC-CBF scatterplots. In the normal brain breathing air, all three groups showed a slope of close to unity. In the stroke hemisphere, the slope increased 25%. Breathing CO_2 *per se* did not change the slope. With mannitol under hypercapnic condition, the slope increased 60%.

Discussion and Conclusion. The major findings of this study are: 1) ASL and DSC are linearly correlated over the physiological ranges in normal brain. 2) High blood flow *per se* does not affect the CBF relation between the two methods. 3) Permeability change affects CBF values of both methods but affects ASL more significantly. And 4) in stroke animals, permeability changes affect CBF accuracy and quantitative CBF calculation should take permeability changes into account. The differential effects by permeability on the two methods can be explained as followed. Leakage of gadolinium shortens parenchymal T1 and thus underestimates DSC-CBF. In contrast, leakage of labeled water overestimates ASL-CBF. In conclusion, the two CBF methods are affected by permeability changes differently and thus caution must be exercise when comparing different CBF methods. Perfusion imaging of stroke should take into account permeability changes and is under investigation. These results have strong implications in perfusion imaging of stroke and other cerebrovascular diseases that involve BBB perturbation.

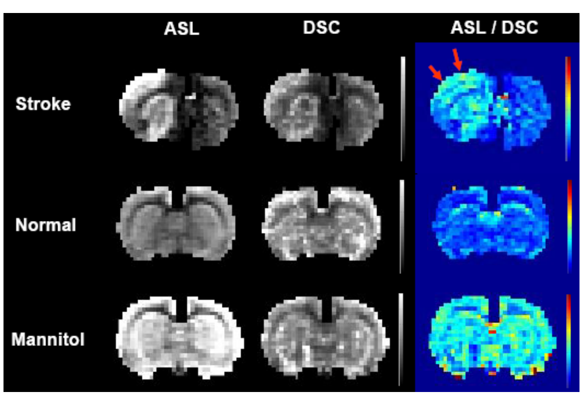

Figure 1. Blood-flow images obtained by ASL and DSC and their ratios from a stroke rat breathing air, a normal rat breathing 5% CO2, and normal rat breathing 5% CO2 injected with mannitol (iv).

References 1) Silva et al. MRM 35:58, 1997. 2) Parkes et al. MRM 48:27, 2002. 3) Tanaka et al. Brain Research 1165:135, 2007 4) Duong et al. MRM 43: 383, 2000. 5) Østergaard et al. MRM 36:715, 1996. 6) Thomas et al. JCBFM 26:274, 2006.

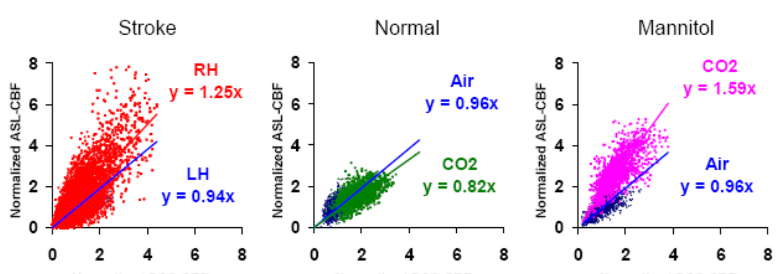

Figure 2. Pixel-by-pixel scatterplots of normalized ASL *vs* DSC CBF of stroke rats, normal rats, and normal rats injected with mannitol. ASL and DSC were measured on the same animals. In normal rats, air and 5% CO2 conditions were studied.