

## Impact of equilibrium magnetization of blood on ASL quantification

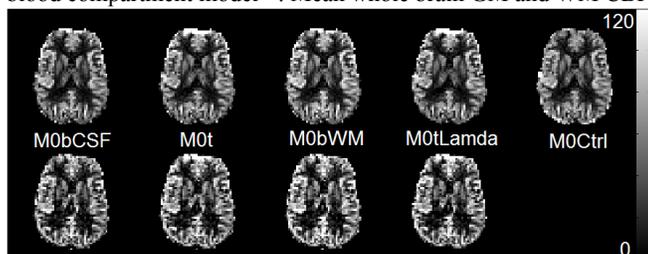
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**Introduction** Arterial spin labeling (ASL) is a noninvasive technique capable of measuring cerebral blood flow (CBF) in absolute physiological units. In the single blood compartment ASL model<sup>1</sup>, the term  $M_{0b}$  represents the equilibrium magnetization of blood, which is difficult to measure given the low resolution of ASL images. Most ASL studies are divided into two groups regarding  $M_{0b}$ : one group calculates  $M_{0b}$  based on either cerebrospinal fluid (CSF) or white matter (WM) signal on a separately acquired  $M_0$  image, the other uses the entire  $M_0$  image to generate a  $M_{0b}$  map based on  $\lambda$ , the partition coefficient of tissue-to-blood. Continuous ASL (CASL) studies have the additional choice of using the control images as an estimate of  $M_0$ , thus eliminating the need for a separate acquisition. To date, no systematic comparison between the methods has been presented. In this study, we compare the quantitative CBF values generated using these different  $M_{0b}$  estimates.

**Methods** Ten healthy subjects (age  $25 \pm 6$ , 3F, 7M) were scanned on a whole-body 3.0T MR scanner (Siemens TIM Trio, Erlangen Germany) equipped with a 32-channel receive-only head coil. All subjects were scanned with both FAIR<sup>2</sup> (T1/T2=600ms/1600ms) and pseudo-continuous ASL<sup>3</sup> (pCASL, labeling duration 1.5s, postlabeling delay 1s) using gradient-echo EPI (TR/TE/FA=4s/18ms/90°, 18 axial slices of 6mm thickness and 1.2mm gap), 60 pairs of control/tag. An additional  $M_0$  image was acquired using the same EPI parameters without any ASL preparation. A minimum contrast image was also acquired for coil sensitivity correction. Finally, high resolution MPRAGE images were collected for co-registration purposes.

The mean difference images and  $M_0$  images were corrected for inhomogeneities in coil sensitivity by division with the minimum contrast image. To assess the effect of different  $M_{0b}$  calculations on CBF estimates, the following  $M_{0b}$  values were used: 1)  $M_{0b\_CSF}$ :  $M_{0b}$  estimated using the equation  $M_{0b} = R * M_{0CSF} * \exp(TE/T_{2CSF} - TE/T_{2b}^*)$ , where R was set to 0.87<sup>4</sup>,  $M_{0CSF}$  was signal of CSF voxels (designated as those with top 20% of signal in the center of the image),  $T_{2CSF}^*$  and  $T_{2b}^*$  were set to 74.9 and 43.6<sup>4</sup>. 2)  $M_{0t}$ : The  $M_0$  image was divided by 0.9, designated as mean  $\lambda$  between gray (GM) and white matter (WM). 3)  $M_{0b\_WM}$ :  $M_{0b}$  estimated using the same equation as  $M_{0b\_CSF}$  with  $R=1.19$  and  $T_{2WM}^*=44.7^4$ . 4)  $M_{0tLamda}$ : The  $M_0$  image was segmented into gray and white matter, gray matter voxels were divided by  $\lambda_g=0.98$ , white matter voxels divided by  $\lambda_w=0.84^5$ . 5)  $M_{0ctrl}$ : Mean of the control images divided by 0.9. This was only available for pCASL. CBF maps were generated using the single blood compartment model<sup>1,6</sup>. Mean whole brain GM and WM CBF were generated using the segmented tissue masks thresholded at 0.75.



**Results** Sample CBF maps calculated using the different  $M_{0b}$  values are shown to the left (top: pCASL, bottom: FAIR). No apparent difference was observed between the various CBF maps. Barplots of mean ( $\pm$ standard error) values of  $M_{0b}$ , GM CBF and pCASL GM:WM CBF ratio are shown below. Map-based  $M_{0b}$  values were extracted from whole-brain GM masks. Although mean  $M_{0b\_CSF}$  was the highest of all  $M_{0b}$  estimates, resulting in the lowest CBF value, the effect size was small. However, the use of different  $M_{0b}$  estimates altered the GM:WM contrast of the qCBF maps, as is evident in the 3<sup>rd</sup> barplot. While both  $M_{0bCSF}$  and  $M_{0bWM}$  preserved the intrinsic contrast of the difference images, both  $M_{0t}$  and  $M_{0tCtrl}$  resulted in lower contrast as a result

of using a single  $\lambda$  for the entire brain. The contrast was restored when tissue-specific  $\lambda$  was used in  $M_{0tLamda}$ .

**Discussion** Our results demonstrate minor differences between the various  $M_{0b}$  estimates. The largest discrepancy was observed between  $M_{0bCSF}$  and  $M_{0bWM}$ , likely due to the assumed values of  $T_2^*$  which is known to be highly variable. Interestingly,  $M_{0tCtrl}$  was very similar to  $M_{0t}$ , suggesting that the concern about magnetization transfer effects of the long labeling pulse train is minimal, possibly due to the long labeling duration + post labeling delay used in the current study.

Although the GM CBF values appear similar, visible differences were observed in the GM:WM ratio between the various  $M_{0b}$  methods. Notably, the map-based methods:  $M_{0t}$  and  $M_{0tCtrl}$  which use a single  $\lambda$  for the entire brain reduce the GM:WM contrast. Although the correct contrast can be restored by using tissue-specific  $\lambda$ s, this approach requires additional tissue segmentation step, which is subject to partial volume effects at the image resolution of typical ASL studies. In conclusion, the  $M_{0bCSF}$  and  $M_{0bWM}$  approaches may be more accurate, though care must be taken to eliminate coil inhomogeneity and accurately measure  $T_2^*$ . Though the two methods are interchangeable in healthy subjects, patient populations with WM pathology may be limited to the  $M_{0bCSF}$  method.

**References** (1)Buxton, R. B. *J Magn Reson Imaging* **2005**, *22*, 723-6. (2)Kim, S. G. *Magn Reson Med* **1995**, *34*, 293-301. (3)Dai, W. et al., *Magn Reson Med* **2008**, *60*, 1488-97. (4)Cavusoglu, M. et al., *Magn Reson Imaging* **2009**, *27*, 1039-45. (5)Herscovitch, P.; Raichle, M. E. *J Cereb Blood Flow Metab* **1985**, *5*, 65-9. (6)Alsop, D. C.; Detre, J. A. *J Cereb Blood Flow Metab* **1996**, *16*, 1236-49.

