

# Arterial Transit Time Effects in Pulsed Arterial Spin Labeling CBF Mapping: Insight from a PET and MR Study of Normal Human Subjects

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**Introduction** Arterial transit time (ATT) in ASL is one of the major factors that affect the mapping from the image intensity difference to the absolute CBF value. The previously proposed methods for ATT measurements using the PALS sequence suffer from low signal-to-noise ratio and contamination from intravascular signals [1, 2] and protocols to measure the relevant parameters are too lengthy to fit in a reasonable scan session. In practice, empirical ATT values on a per-slice basis were either borrowed from the previous ATT studies or assumed to be linearly related to TI as in QUIPSS II [3]. Since arterial transit time in ASL is dependent on the geometric setup, such as the slice thickness, imaging location and orientation, and the gap between labeling and imaging slabs, several issues still remain to be further elucidated. By fusing both PET and MRI data from the same subjects we were able to investigate the extent to which the per-slice ATT values depend upon the location of the imaging slab and the gap between the imaging and labeling volumes. Secondly, this analysis allows estimation of the errors that arise in CBF due to errors in the ATT. Thirdly, the significance of within-slice variations in ATT, are investigated as are the errors in task-induced changes in CBF measured by ASL when activation induced changes in ATT are ignored. Clarification of these issues will provide researchers with the necessary information to set up optimum ASL imaging parameters and minimize errors in absolute CBF quantification.

**Materials and Methods** Pulsed ASL and PET imaging were performed on the same group of 14 healthy normal subjects. ASL data including perfusion weighted images, proton-density weighted images, and  $T_1$  maps were acquired using QUIPSS II on a 3T whole-body scanner Trio (Siemens Medical Systems, Erlangen, Germany) with a circularly polarized head coil. ASL imaging was performed separately for the upper and lower parts of the brain, and each part had 10 AC-PC aligned slices (thickness 6 mm; gap 3 mm). In the ascending order, the 1<sup>st</sup> slice passed through AC-PC for the upper part and the 7<sup>th</sup> slice passed through AC-PC for the lower part, with 4 slice overlap, which allowed us to address the ATT dependence on GAP. The thickness of labeling/control slab was 100 mm; the gap between the imaging and labeling slabs was 20 mm. Other parameters: TR=2s; TE=20ms; TI=1.4s;  $T_1$ =700ms; FOV=240x256mm<sup>2</sup>; matrix=60x64; EPI acquisition duration for each slice  $t_{\text{acq}}=55$ ms; crusher=5cm/s;  $\lambda=0.9$ ml/g;  $\alpha_\pi=0.95$ . PET imaging was performed using High Resolution Research Tomograph (HRRT) which acquires 207 slices (1.2 mm slice separation) with reconstructed image resolution of ~3 mm. A 6-min transmission scan was acquired for attenuation correction. List mode data were acquired on the HRRT for each scan. The arterial input function was measured with an automated blood counting system (PBS-101, Veenstra Instruments) using continuous withdrawal system with a peristaltic pump (4 ml/min). The same sensorimotor and visual stimuli were used for both ASL and PET. All ASL and PET images were coregistered and regridded to a common brain space (MNI-3mm) using BioimageSuite.org. ATT mapping was done using an iterative algorithm based on the ASL CBF quantification equation [e.g., 4] but here we solved it for ATT assuming that CBF was known from PET.

**Results and Discussion** During arterial spin labeling imaging, a 54 mm upstream shift of the imaging and labeling slabs resulted in an increase of  $255.1 \pm 22.9$  ms in ATT. When the gap between the imaging and labeling slabs increased from 20 mm to 74 mm for upper part of the brain, the arterial transit time value increased  $630.7 \pm 28.7$  ms from to  $1224.8 \pm 27.3$  ms for the 1<sup>st</sup> slice, with a slab-average difference of  $613.0 \pm 17.8$  ms. For the upper part of the brain, over 37% of the voxels were underestimated by at least 20% or overestimated by at least 34% of its resting CBF value if spatial variations in ATT were ignored. The reduction in the ATT due to focal activation was of similar magnitude for both visual and motor tasks (~80 ms), and when the change in ATT is ignored, in the visual ROI, the task-induced increase in CBF is ~44% but when the changes in ATT were considered, the increase was reduced to 23% of the baseline CBF value. In the sensorimotor ROI, these two numbers were 40% and 25% respectively. The results of this study can be used to obtain a set of ATTs on a per-slice basis to avoid slice dependent errors. The assumption is that the linear interpolation/extrapolation holds true in Figure 2, such that a line of the ATT values could be derived when a set of imaging parameters are given.

**Conclusion** There is a marked dependence of arterial transit times upon the location of the imaging and labeling slabs and the gap in-between. Spatial variability in ATT causes errors in the quantification of CBF. The results of this study should aid in the interpretation of ASL-based CBF studies, while also providing spatially specific data on ATT values that may aid in optimizing the imaging parameters in ASL acquisitions.

**References** [1] Gonzalez-At JB, et al., MRM 2000;43(5):739-746. [2] Wang J et al., MRM 2003;50(3):599-607. [3] Wong EC et al., MRM 1998;39(5):702-708. [4] Yang Y et al., MRM 2000;44(5):680-685.

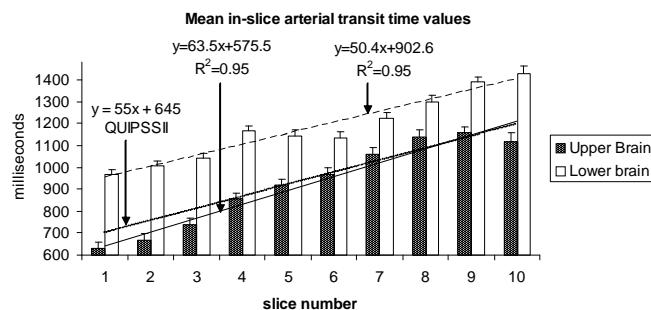


Figure 2 Linear regression of the per-slice ATT values for both parts, with comparison with those assumed in QUIPSS II.

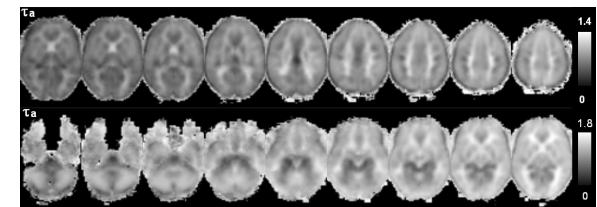


Figure 1 ATT values on a per-voxel basis.

| Motor ROI  | ASL $\Delta M$  | PET CBF           | ATT              |
|------------|-----------------|-------------------|------------------|
| rest state | $2.06 \pm 0.13$ | $41.3 \pm 1.7$    | 904.0            |
| finger tap | $2.88 \pm 0.17$ | $51.8 \pm 1.6$    | 821.2            |
| difference |                 | $0.82 \pm 0.06^*$ | $10.5 \pm 1.1^*$ |
|            |                 |                   | -82.8            |

| Visual ROI | ASL $\Delta M$  | PET CBF         | ATT             |
|------------|-----------------|-----------------|-----------------|
| rest state | $1.35 \pm 0.12$ | $48.2 \pm 1.9$  | 1251.5          |
| CB         |                 | $1.94 \pm 0.17$ | $56.9 \pm 1.9$  |
| difference |                 | $0.59 \pm 0.09$ | $8.6 \pm 1.1^*$ |
|            |                 |                 | -81.5           |

PET CBF is in ml/100grams/minute, ASL  $\Delta M$  in a.u., and ATT in milliseconds; CB: checkers board; \*  $p < 0.05$ .

Table 1 Task-induced changes in  $\Delta M$ , CBF, and ATT with both the sensorimotor (a) and visual (b) ROIs.