Introduction: The arterial spin labeling (ASL) signal reflects a mixture of perfusion and arterial transit delay (ATD) effects. Techniques to reduce or eliminate ATD contribution have been proposed and validated with young healthy volunteers. Preliminary studies have reported lengthened global ATD in elderly populations, indicating that perfusion measurement without taking into account the longer ATD will suffer from systematic errors. Here we systematically study the regional variation of ATD, the effect of vessel suppression and its effect on perfusion measurement in an elderly, presurgical cohort.

Methods: Pulsed-continuous arterial spin labeling (PCASL) was used with 3.5 s labeling and 1.5 s post-labeling delay. An additional reference image was appended after the ASL sequence to provide necessary M_0 values for quantification. A low-resolution transit time acquisition (labeling duration of 2 s and five post-labeling delays of 0.7 s, 1.3 s, 1.9 s, 2.5 s, 3.0 s) was performed both with vessel suppression and without vessel suppression.

The perfusion images were acquired as a part of the Successful Aging after elective surgery (SAGES) study to investigate the potential cerebral damage associated with post-surgical delirium. Fifty-nine elderly patients over 70 years old scheduled for elective surgical procedures were scanned at baseline. Nine young healthy subjects (27.9±6.3 years old), scanned for ATD maps with vessel suppression from another study, were used to compare the regional ATD values with the elderly subjects.

ATD maps were calculated voxel-by-voxel from the ASL data with five post-labeling delays. Perfusion maps were calculated both with standard quantification methods (assuming the applied post-labeling delay of 1.5 s is equal to the ATD everywhere in the entire brain) and the method with ATD correction. All ATD and perfusion maps were normalized to a standard space using SPM. Voxel-based statistical analyses were performed to compare the ATD maps with a fixed delay of 1.5 s, and the perfusion maps with and without ATD map correction. Standard deviation and mean maps were calculated across subjects for the perfusion maps with and without ATD correction. Maps of coefficient of variation (CV = standard deviation/mean) were created to evaluate the voxel-wise perfusion variability for both perfusion quantification methods.

Results & Discussions: ATD varied across brain regions in the elderly population (Fig. 1). Posterior regions had longer ATD than anterior regions. Basal ganglia regions had shorter ATD value than other cortical gray matter regions. ATD values are longer with vessel suppression than without vessel suppression. Elderly subjects showed significantly longer ATD values for all the regions except the parietal and occipital regions (Table 1). Histograms of ATD values showed that ATDs distributions are relatively narrow in young subjects but broader in the elderly with a tendency towards a skewed distribution with a fraction having much longer values (not shown).

For the elderly subjects, perfusion increased after ATD correction in frontal regions, and especially in parietal an occipital regions, consistent with the regions where ATD was longer than the applied post-labeling delay of 1.5 s (Fig. 2a and 2b). This confirms that without ATD maps perfusion was systematically underestimated in the regions with significantly longer ATD values. The ATD was significantly shorter in only the basal ganglia on the ATD maps with vessel suppression, Fig 2d. Without vessel suppression, ATD was underestimated around the Circle of Willis, where large vessels contaminated the ATD estimate, Fig 2c. With ATD correction, perfusion variability across subjects was reduced in frontal regions and even more in parietal and occipital regions, but was increased in the cerebellum and pons regions (Fig 2a). The regions with increased perfusion variability are close to the labeling region and therefore may suffer from decreased accuracy of ATD. Overall, these results indicate that ATD measurement can improve the reliability and accuracy of perfusion measurement in elderly populations.

Conclusions: ATD can be measured in elderly populations using the transit time mapping method. ATD is heterogeneous across different brain regions and significantly longer than the young in all regions except posterior regions. ATD measurement with vessel suppression can reduce the systematic error of perfusion measurement in large vessel regions. Correction of ATD can improve the reliability and accuracy of perfusion measurement and thus should improve the sensitivity of clinical research studies involving elderly subjects.

Table 1. Regional ATD values of the young and elderly subjects

<table>
<thead>
<tr>
<th>ATD (s)</th>
<th>Inf Frontal*</th>
<th>Mid Temporal*</th>
<th>Inf Parietal</th>
<th>Occipital</th>
<th>Basal Ganglia*</th>
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<tbody>
<tr>
<td>Young</td>
<td>1.35±0.20</td>
<td>1.60±0.17</td>
<td>1.92±0.18</td>
<td>1.91±0.19</td>
<td>0.91±0.20</td>
</tr>
<tr>
<td>Elderly</td>
<td>1.63±0.23</td>
<td>1.76±0.26</td>
<td>1.96±0.27</td>
<td>1.94±0.21</td>
<td>1.26±0.29</td>
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</tbody>
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* Regions with statistically different ATD values with p < 0.02.

Fig. 1. (Left) The perfusion signal from five different post-labeling delays: (a) 0.7 s, (b) 1.3 s, (c) 1.9 s, (d) 2.5 s, (e) 3.0 s and (f) calculated ATD map based on the delays.

Fig. 2. (Right) (a) Perfusion difference map between with ATD correction and without ATD correction, and regions where (b) ATD is significantly longer than 1.5 s, (c) ATD is shorter than 1.5 s without vessel suppression, and (d) coefficient of variation (CV) of perfusion across subjects is reduced (red-yellow color) and increased (green color) with ATD correction compared to without ATD correction.