Combined Dynamic Susceptibilty Contrast (DSC) Imaging and Arterial Spin Labeling (ASL) for Quantitative Perfusion Measurements in Children with Diffuse Pontine Glioma

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Introduction: Accurate, absolute cerebral blood flow (CBF) quantification is desirable for many applications including longitudinal monitoring of tumor therapy. Dynamic susceptibility contrast (DSC) perfusion-weighted (PW) imaging and arterial spin labeling (ASL) are two established methods to measure CBF (1). Each method has its advantages and disadvantages: DSC can provide high resolution PW images of up to 1mm^2. Absolute quantification is, however, not yet established as there are many factors that influence the DSC-CBF accuracy such as arterial bolus dispersion, partial volume effects, and contrast differences between arteries and capillaries (2). ASL can provide quantitative CBF estimates without the use of exogenous contrast agents, but suffers from low intrinsic SNR, especially in areas of delayed transit times such as the white matter (3). This leads to the underestimation of CBF in these regions. Also, the overall resolution in ASL exams is poor at >3mm^2 when EPI-based sequences are used. For better CBF quantification, it has been recently proposed to calibrate the DSC to the ASL experiment by calculating a patient-specific correction factor, the ratio of ASL- and DSC-CBF, in areas where short transit times and short bolus arrival times are measured (4). In this work, we applied this algorithm to a large clinical trial in patients receiving both DSC and ASL perfusion exams during and after chemotherapy and radiation therapy. In an alternative method, the gray matter DSC perfusion values were calibrated to gray matter ASL values in a co-registered axial slice at the level of the basal ganglia. The goal was to determine if either approach would improve the quantification and precision of CBF in areas such as the white matter and in tumors particularly in the posterior fossa.

Methods: One-hundred and seventeen MR exams from 21 patients (mean age: 6.8 years; range: 3-13 years) in a Phase I clinical trial for treatment of diffuse pontine glioma were collected that contained both DSC and ASL perfusion data. All aspects of the exams were approved by the Institutional Research Board and were performed under general anesthesia on a 3T clinical MR system (Magnetom Trio, Siemens, Malvern, PA, USA). DSC data was obtained from dynamic acquisition of T_2*-weighted EPI images (TE/TR=28ms/1800ms, FOV=210x210mm^2, matrix=128x96, 1562 Hz/voxel, 15 slices, 1.6 x 1.6 x 5.0 mm^3) during injection of a paramagnetic contrast agent (Magnevist, Bayer, Montville, NJ, USA). DSC data was evaluated using software that utilizes a user-defined arterial input function (AIF) (PWI Task Card, MGH, Boston, MA, USA). ASL (Q2TIPS (5), TE/TR=23ms/2280ms, TI1/TI2=700ms/1400ms, FOV=210x210mm^2, matrix=64x64, 2004 Hz/voxel, 11 slices, 3.3 x 3.3 x 5.0 mm^3) was also used to calculate CBF. Gray matter and white matter was segmented automatically and all images in the exam were co-registered. As described in (4), DSC and ASL values were plotted at voxels with low time-to-peak (TTP) values (≤ 3 sec). In addition, DSC and ASL values were plotted at voxels that contain gray matter. The slope, intercept, and correlation coefficient were calculated for each plot using linear least-squares regression analysis. The slope of the line represented a correction factor with the ratio being the ASL measurement divided by the DSC measurement. This factor was multiplied by the DSC-CBF map to create a quantitative CBF map.

Results: Figure 1 displays the DSC and ASL maps from one patient in our study. Note that the ratio of the two maps is used for calibration for a quantitative perfusion map. There is high variability not only in areas of low TTP (≤3.0 sec) but also the gray matter. This leads to low correlation to be used for the ratio. Figure 2 shows the calibration plot for another patient using voxels with TTP≤3.0 sec. The slope of the regression line is 1.05, which means that ASL was 5% higher in value. However, the correlation was 0.34 which reduced the significance of the calibration with confidence intervals from 0.94-1.16 for the slope. High variations were also seen when gray matter was used for calibration. In six patients who had 5 or more exams (38 total), the coefficient of variation (CoV) of gray matter and white matter using the corrected CBF map was 16.8 ± 5.3% and 23.5 ± 7.9%, respectively. This was significantly lower than the DSC GM and WM CoV of 35.5 ± 7.2% (p=0.004) and 38.4 ± 10.4% (p=0.039). There were no statistical differences in CoV between the corrected CBF map and ASL.
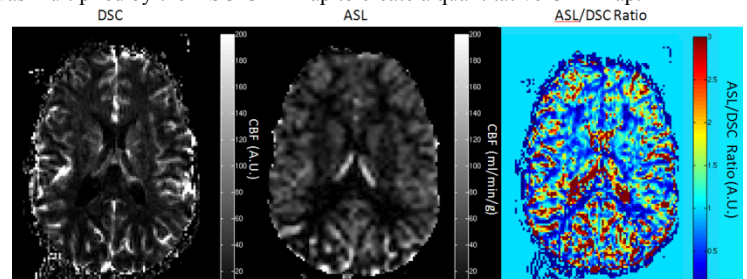

Figure 1: Example of a DSC (left) and an ASL (center) CBF map on one exam from our patient study. The image on the right is the ratio of the two maps. High variability was seen in the ratios.
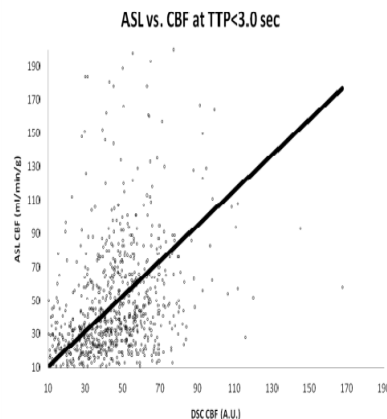
Discussion: For calibration purposes, areas in which there is a relatively constant ratio of ASL and DSC values are needed in order to quantify DSC maps using a correction factor. Although lower CoV values were measured in the combined ASL-DSC approach, the broad confidence intervals of the correction factor or ratio gave high uncertainty on the combined ASL-DSC maps for each patient exam. There are several factors that may account for this. Suboptimal performance in the ASL and/or DSC method may propagate the error in the combined map. It is also important to note that ASL and DSC measure perfusion through two different mechanisms: ASL relies on the tagging of blood whereas DSC relies on the susceptibility effect from a paramagnetic contrast agent that has different physical properties than blood. In conclusion, high uncertainties were observed when calculating the correction factor from ASL-DSC calibrations as reflected in plots relating ASL to DSC. At this point, based on our data and assessment of our acquisition and post-processing methods, we cannot conclude that calibration of DSC and ASL datasets in the same patient leads to reliable quantitative perfusion values in areas otherwise not obtainable.

Figure 2: Plot of ASL and CBF values in voxels with a TTP of ≤3.0 seconds as outlined in (4). The slope from the linear regression was calculated as 1.05 with a correlation of R=0.34 (CI: 0.94-1.16). Generally, it is difficult to obtain a reliable calibration with such a low correlation since the confidence interval is from approximately 6% underestimation to 16% overestimation.

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