Regional differences in cerebral perfusion parameters in non-human primates: comparison between DSC and ASL perfusion imaging

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Introduction Perfusion parameters can be measured by using dynamic susceptibility contrast (DSC) or by magnetically labeling the endogenous water in blood. While DSC MRI has been widely utilized in humans (1-3), perfusion imaging in non-human primates is sparse (4). With the increasing interests in MRI studies of more clinically relevant monkey models, perfusion imaging could critically impact monkey research. The goal of this study was to measure perfusion parameters using DSC MRI on anesthetized rhesus monkeys and to compare with those obtained using the continuous ASL MRI technique obtained in our lab (5).

Methods. Adult Rhesus monkeys (6.5-8.5 kg, N = 6) were anesthetized under 1% isoflurane during imaging. Gd-DTPA (0.1 mg/kg) was administered intravenously. MRI study was performed on a 3T Siemens Trio using a 5cm diameter surface coil. MRI parameters were: single shot gradient echo EPI, TR = 200 ms, TE = 20 ms, FOV = 96×96 mm, matrix = 64×64, slice thickness 2 mm, 3 slices, and total acquisition time was 50 seconds.

Image processing employed Matlab and Stimulate software to obtain maps of cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), time to peak (TTP), and tracer arrival time (Tstart). Singular value decomposition method was used to calculate CBF and CBV. MTT, TTP, and Tstart maps were calculated from time-ΔR_2^* curve. Tracer arrival time was defined as the ΔR2* value rose above 2 standard deviations of baseline value. Perfusion parameters were tabulated for different region-of-interest including the artery, caudate, putamen, white matter (WM), and cortical gray matter (GM). Quantitative CBV and CBF maps were calculated with an assumption of 45 mL/100g/min in WM (5).

Results. Perfusion parameter (CBF, CBV, MTT, TTP, Tstart) maps for a representative single slice are shown in **Figure 1**. CBF and CBV were heterogeneous with larger values in GM than WM as expected. Tstart map showed a larger dynamic range than MTT and TTP maps. The ΔR_2^* bolus traces for artery, caudate, cortical GM and WM are shown in **Figure 2**. MTT, TTP and Tstart were calculated and are summarized in **Table 1**. These time constants were shortest in the artery, followed by caudate and putamen and then cortical GM and WM as expected. Interestingly, putamen had no or small delay relative to artery. By comparison, Tstart showed the largest difference among different tissue types.

CBF in the caudate, caudate, cortical GM and WM were 95 ± 16, 104 ± 20, 82 ± 11, and 39 ± 2 ml/100g/min, respectively, consistently with those reported using the continuous ASL technique (5). The corresponding CBV values were 57 ± 22, 55 ± 23, 49 ± 15, and 26 ± 9 ml/100g, respectively. The cortical GM:WM CBF ratio was 2.1 ± 0.26, within the range of 1.7–2.7 reported in humans using MRI and PET.

Discussion and Conclusion. DSC MRI was applied to measure cerebral perfusion parameters in isoflurane-anesthetized monkeys. Tstart is less frequently used but it has a larger dynamic range compared to MTT and TTP. ASL technique to measure CBF generally does not take into account regional different in tracer arrival time. It has been suggested that tracer arrival time needs to be taken into account to obtain reliable perfusion image when SVD deconvolution is used (6).

CBF and CBV values reported herein were high compared to those in humans. This is likely because the anesthetic (isoflurane) used is a known vasodilator, as amply demonstrated in rats (7). While ASL MRI technique is completely non-invasive, MTT, TTP, Tstart and CBV could not be readily obtained using the ASL technique. DSC and ASL thus complement each other and provide cross validation of perfusion parameters. Future studies will include measurements of arterial input function to quantify CBF and CBV in awake and anesthetized monkeys.

References 1) Østergaard et al. MRM 36:715, 1996. 2) Wu et al. Magn Reson Med 50:856, 2003. 3) Calamante et al. MRM 44:466, 2000. 4) Pedersen et al., JMRI 20:930, 2004. 5) Zhang et al. NeuroImage (in press, 2006). 6) Ibaraki M et al. J Cereb Blood Flow Metab 25:378 2005. 7) Sicard & Duong, NeuroImage 25:850, 2005.

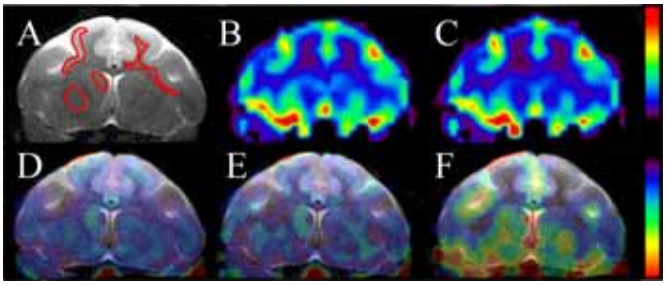

Figure 1. (A) T2W image, (B) CBF map, (C) CBV map, (D) MTT, (E) TTP and (F) Tstart color map. Typical ROIs were put on T2W image.

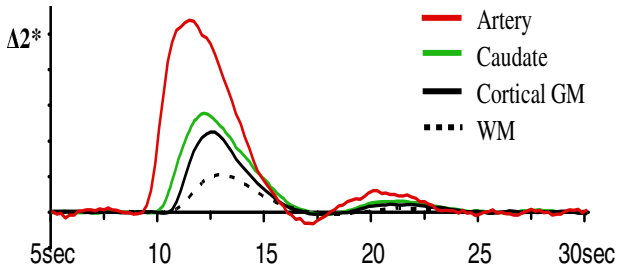

Figure 2. Gd-DTPA bolus traces for four different tissue types. The "artery" trace shows the highest peak, earliest start time, and steepest gradient.

Table 1. Perfusion parameters (in seconds, mean ± SD, N = 6). Delay values are relative to that of the artery.

	MTT	MTT delay	TTP	TTP delay	Tstart delay
Artery	2.53 ± 0.32	0	2.01 ± 0.11	0	0
Caudate	2.68 ± 0.30	0.15 ± 0.11	2.20 ± 0.22	0.13 ± 0.18	0.49 ± 0.22
Putamen	2.53 ± 0.34	0.00 ± 0.09	2.12 ± 0.31	0.06 ± 0.24	0.37 ± 0.13
Cortical GM	2.77 ± 0.33	0.24 ± 0.17	2.31 ± 0.27	0.25 ± 0.19	0.85 ± 0.43
WM	2.83 ± 0.39	0.30 ± 0.23	2.43 ± 0.32	0.37 ± 0.25	0.93 ± 0.31