Identification of Diaschisis Post Stroke with Rest-Stress Quantitative CASL MRI

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Introduction: Stroke typically results in neurometabolic activity defects in regions distal but functionally connected to the infarct, usually representing deafferentation effects of the lesion, a physiological phenomenon known as diaschisis. The regions of reduced metabolic activity show more substantial increases in rCBF compared to healthy tissue during CO2 or Diamox stress on SPECT [1]. Cerebrovascular stress thus provides a way to distinguish between reduced rCBF due to vascular constraints versus that due to parenchymal dysfunction. In this paper we present the clinical feasibility of using a continuous arterial spin-labeled (CASL) perfusion MRI, during resting baseline and cerebrovascular stress induced by 5% CO2 inhalation to non-invasively identify and quantify regional activity reductions outside the lesion in post acute stroke as a measure of recovery potential.

Materials and Methods: We studied 6 patients (mean age 57, range 19-72 years) within 2-4 weeks post unilateral stroke involving the middle cerebral artery (MCA), with some variation in the extent of cortical and deeper white and gray matter involvement.

MR Sequences: All subjects were imaged on a 3T, Philips Intera clinical scanner, using a transmit/receive head coil. Supratentorial slices covering from cerebrum to cerebellum (single shot spin echo planar imaging; acquisition matrix 64x64, TR/TE: 5 sec/42 msec; acquired spatial resolution: 3.59 x 3.65 x 8 mm^3; interslice gap 1.5 mm; adiabatic-through-fast-passage labeling pulse; labeling offset 80 mm; labeling delay 1400 msec; labeling duration 2400msec; 10 sec per dynamic; 30 dynamics)[2] were acquired continuously in ascending order during resting baseline and inhalation of 5% CO2, 21% O2, 74% N2. Glucose PET was performed on a GE 8-slice discovery LS PET-CT using intravenous injection of 10 mCi F-18 FDG. After a 40 min wait, emission scans were performed for 10 minutes in a 3-D acquisition mode.

Data Analysis: CASL data was stored as raw echo amplitudes and transferred to a separate workstation for rCBF computations [3] using custom software written in MATLAB™. The 30 pairs of labeled and control images were first corrected for motion and then averaged to produce a single set of perfusion sensitive images. Changes in rCBF were analyzed using a local ROI method, a method for estimating relative functional versus anatomical defect size [4], and compared to 10 controls with Statistical Parametric Mapping (SPM) analysis.

Results: Figure 1 depicts an angulated transverse section from a patient for T1 weighted MRI, CASL at rest and during CO2 stress, and F-18 PET. Figure 2 plots rCBF values in ROI segments formed by a cortical circumferential profile analysis (mean rCBF control rest L: 80.3, R: 81.5; patient rest L: 45.8, R: 63.5; patient stress L: 64.5, R: 72.7). All patients showed a significant increase in rCBF ($p < 0.01$) between rest and stress. Table 1 shows lesion sizes and rCBF "defect" volume sizes using MRI, rest-stress CASL and F-18 FDG PET scans. All CASL studies showed significant reduction in rCBF defect volume (37.1 ± 8.1 %) by CO_2 stress. The reduced defect volume quantifies an extended penumbra in the affected hemisphere. On F-18 FDG PET studies the areas with reduction in activity distal to the infarct coincided with the resting state rCBF reductions. Figure 3 shows an SPM analysis of the case shown in Fig. 1 compared to 10 normal controls. Some significant ($p < 0.001$) contralesional as well as ipsilesional hemispheric reductions are seen. Similar analysis of the CO_2 scan showed differences only within the lesion perimeter.

Discussion: The dramatic improvement in rCBF seen during CO2 stress outside the perimeter of the infarcted region strongly suggests primary neurometabolic reduction at rest and represents diaschisis or deafferentation effects. These regions also represent viable brain with recovery potential and probably account for some portion of the patients' current cognitive and motor deficits. These results, obtained in only 15 minutes in non-invasive fashion, have important clinical relevance: not only are they potentially predictive of recovery, but they could help optimize rehabilitation strategy – for example, facilitatory techniques, applied either to affected limbs or cognitive operations, may be of greater benefit to patients with a significant diaschisis component.

Conclusion: The present study provides substantial evidence that quantitative rest-stress rCBF measurement using the CASL-MRI technique is an excellent clinical tool in evaluating the extent of permanent versus temporary cerebral damage post stroke and thus help guide rehabilitation techniques.

References: 1. J. Mountz et al: Sem Nucl Med 2003; 33(1):56-76. 2. X. Golay et al: S. Topics in Magnetic Resonance Imaging 2004; 15(1) : 10-27. 3. Alsop & Detre: J. Cereb. Blood Flow Metab. 1996; 16: 1236-49. 4. J. Mountz: Clin Nucl Med 1989; 14:192-196.

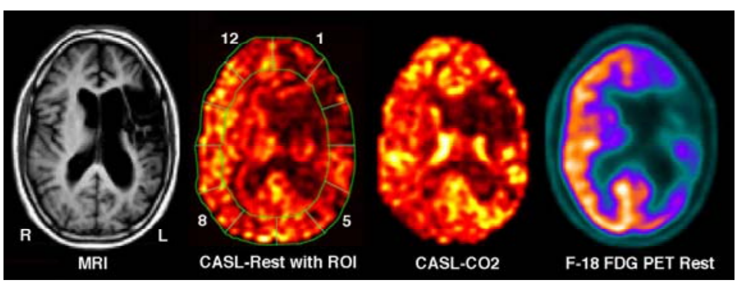

Figure 1: Representative slice from patient with cortical circumferential ROI drawn on rest CASL.

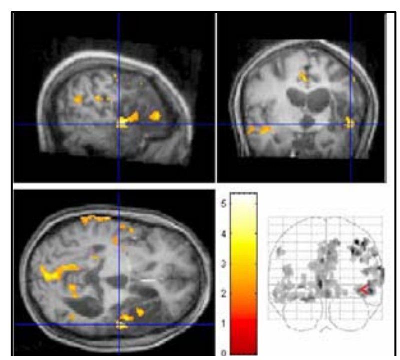

Figure 3: Patient CASL rCBF pattern compared with 10 normal controls using SPM.

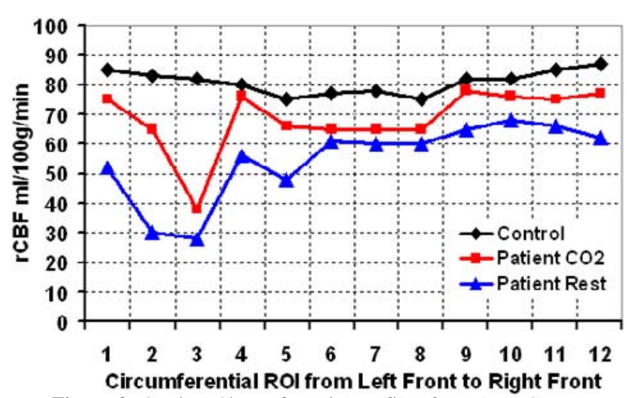

Figure 2: Cortical Circumferential Profile of absolute rCBF

Case	MRI lesion	rCBF Defect		PET
		Rest	CO_2	
1	15	31	20	-
2	5	18	9	16.3
3	19	45	26	39.8
4	18	41	30	68.0
5	18	38	26	60.8
6	27	49	31	69.5

Table 1: Lesion volumes (cc) from MR and total defect (cc) calculated for rCBF at rest and during CO2 stress using CASL and for FDG PET at rest for 6 patients.