# IDENTIFYING CEREBROVASCULAR VERSUS PARENCHYMAL DISEASE COMPONENTS IN DEMENTIA WITH REST-STRESS CASL MRI

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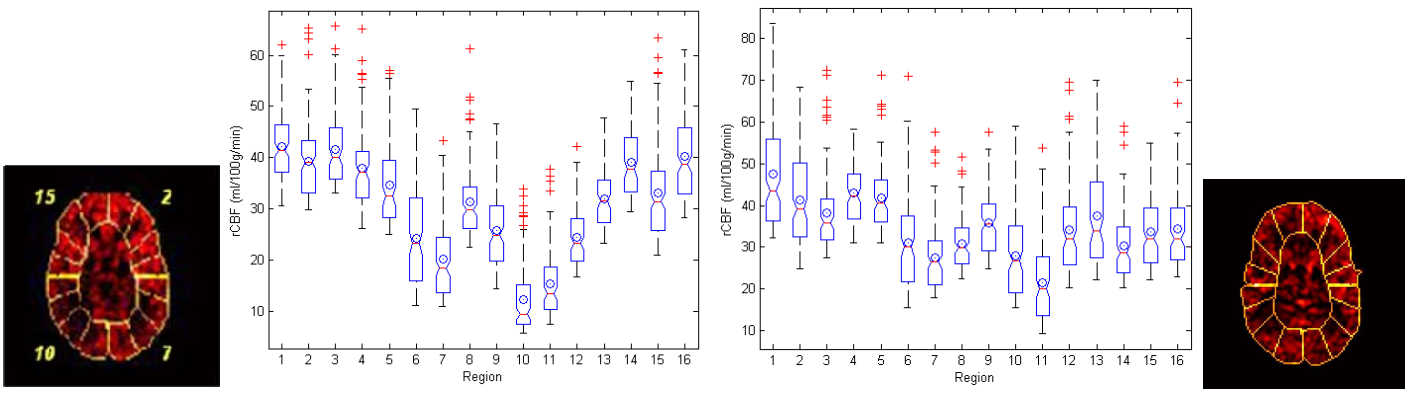
**Introduction:** The role of vascular disease in dementia, including in patients diagnosed with Alzheimer's disease (AD), has become more controversial lately, with growing evidence that vascular disease is present among many subjects with pathologically proved AD. Some new models propose that subclinical vascular disease may provide an environment conducive to AD or that there may even be a more causal relationship [1]. We have shown that regions of reduced metabolic activity show more substantial increases in rCBF during CO2 or Diamox stress compared to healthy tissue [2]. We now provide preliminary data using CASL MRI based measurement of quantitative rCBF, that cerebrovascular stress procedures can help confirm the diagnosis of a primary degenerative dementia and help discriminate between vascular disease and primary degenerative processes (such as pure AD) through an almost paradoxical effect on cerebrovascular reactivity in cases of primary neurometabolic reduction.

**Materials and Methods:** 7 patients initially diagnosed as either early Alzheimer's disease (AD) or a variant typically called fronto-temporal dementia (FTD) were recruited from an Alzheimer's screening service at the University of Alabama at Birmingham Medical Center. Informed consent was obtained from all subjects, including 20 healthy controls. *MR Sequences:* All subjects were imaged on a 3T, Philips Achieva 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)[3] were acquired continuously in ascending order during resting baseline and inhalation of 5% CO2, 21% O2, 74% N2. *Data Analysis:* CASL data was stored as raw echo amplitudes and transferred to a separate workstation for rCBF computations [4] 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 and compared to 20 controls with Statistical Parametric Mapping (SPM5) analysis.

**Results:** All patients showed some regional reductions at rest-baseline measures compared to the 20 controls consistent with a dementing etiology involving either temporal-parietal or frontal-temporal degenerative disease. Of these, five patients also had excellent rCBF reactivity during CO2 stress, showing in fact an overall "improvement" in overall activity pattern. Fig 1 shows a case example along with a box-plot analysis of the changes in absolute rCBF in each of 16 ROIs at the transverse level showing the most affected regions. Additional SPM analysis of each of these patients versus the control group confirmed the significance of the rest-baseline reductions and a lack of significant *pattern* differences (normalized mean rCBF) compared to controls in the C02 stress condition. Two patients, one involving a rest-baseline reduction in activity in parietal-occipital cortex and one with a frontal pattern of impairment at rest, did not show improvement in rCBF during CO2 stress.

**Discussion:** In 5 of the patients**,** the dramatic improvement in rCBF seen during CO2 stress in the most affected areas suggests a primary neurometabolic reduction at rest without vascular constraint and helps confirm the diagnosis of a primary degenerative dementia in these patients (either AD or FTD or PCA.) In the two cases where there was questionable or absent rCBF reactivity, there is good reason to suspect a more complex scenario, involving at least a mixture of cerebrovascular disease and primary degenerative disease, if not a dominant cerebrovascular disease etiology that was not properly diagnosed. Further analysis of such patients involving more detailed morphometric analysis and other measures of vascular disease, such as TCD, should reveal reasons for the lack of vascular reserve and how that may interact with parenchymal degenerative processes.

**References 1.** DeCarli C. Vascular factors in dementia. J Neurol Sci. 2004;226:19-23 **2**. J. Mountz et al: Sem Nucl Med 2003; 33(1):56-76**. 3.** X. Golay et al: S. Topics in Magnetic Resonance Imaging 2004; 15(1) : 10-27. **4.** Alsop & Detre: J CBF Metab. 1996; 16: 1236-49.




**REST Scan** **Absolute rCBF (ml/100g/min) for sectors 1-16 during rest and during CO2** **CO2 Stress Scan**

**Figure 1. AD case example.** Regions 1-16 on each boxplot start at the right frontal sector of transverse slice and run clockwise around the brain to the left frontal sector 16. Parietal sectors 7, 10 and 11 are most affected. CO2 increases rCBF in a manner that makes overall pattern look normal. SPM5 comparison vs controls showed significant rCBF pattern abnormalities at rest but none during stress.