

First Results of Quantitative Cerebrovascular Reserve with MRI

Renee Qian¹, Parmede Vakil¹, Michael C Hurley², Sameer A Ansari², Christina Sammet², Jessy Mouannes-Sour², H. Hunt Batjer³, Bernard R Bendok³, and Timothy J Carroll^{1,2}

¹Biomedical Engineering, Northwestern University, Evanston, IL, United States, ²Neuroradiology, Northwestern University, Chicago, IL, United States, ³Neurosurgery, Northwestern University, Chicago, IL, United States

Purpose: Cerebrovascular reserve (CVR) measures the autoregulatory dilatation of intracranial vessels in the setting of ischemic pathologies. We developed an approach to quantify and score, for the first time, CVR (qCVR) based on acquisition of fully quantitative MRI cerebral perfusion images.

Materials and Methods: We performed a retrospective review of images acquired in patients with angiographically confirmed neurovascular disease (i.e. intracranial stenosis). All subjects were scanned on a 1.5T MRI scanner in this IRB approved study. Patients referred for acetazolamide (ACZ) challenge were scanned using a previously published quantitative perfusion pulse sequence [1]. Cerebral perfusion (Bookend Perfusion, TR/TE=1200 ms/54 ms, FOV/matrix=220 mm/128/ 13, 5.0 mm slices, 0.1 mmol/kg bw, scan time=3:00) was measure prior to and 10 minutes after administration of 1000 mg ACZ, a carbonic anhydrase inhibitor which serves as a clinical analog to CO2 reactivity. Healthy volunteers were scanned without ACZ as experimental controls.

Compartmentalization Effects: The intravascular compartmentalization of Gd-DTPA produces a predictable bias in quantification that depends on water exchange rate ($\tau_{ex} = 0.9 \text{ s}^{-1}$ [2]) and pre-contrast T1 value of blood. We derived a response curve relevant to the second contrast agent infusion and validated its accuracy in controls. QCVR ($(\text{qCBF}_{\text{baseline}} - \text{qCBF}_{\text{ACZ}}) / \text{qCBF}_{\text{baseline}} \times 100\%$) was calculated in normal and hemodynamically compromised vascular territories.

Statistical Analysis: The quality of the compartmentalization model was determined by a McNair F-test. We compared 1st and 2nd injection volunteer perfusion to verify the scan-to-scan variability of the techniques in the absence of ACZ challenge based on Wilcoxon signed rank test. In patients, we compared the degree of CVR in normal regions with expectations based on historical reference data. In all tests significance was defined at the 5% level.

Results: A series of N= 10 healthy controls were scanned to constrain the WCF response curve for the second injection. We found the second injection WCF modeling equation (Figure 1): $\text{WCF} = 0.003(\text{dR}_1)^2 + 0.8(\text{dR}_1) + 0.1$ at 1.5T ($F(3,14) = 14.0$, $P < 0.001$). Mean qCVR in controls was $3.9 \pm 8.1\%$, in agreement with the test-retest reliability of the technique ($0 \pm 14\%$). In patients normo-perfused territories exhibited the expected 30% flow augmentation for the dose of ACZ

applied (Figure 2). We derived a quantitative scale for the flow augmentation based on the severity of CVR reduction on a 4 point scale (Figure 2): I = Normal ($\text{qCVR} > 30\% / 1000 \text{ mg ACZ}$), II = mild impairment ($10\% < \text{qCVR} < 30\%$), III = moderate impairment ($-10\% < \text{qCVR} < 10\%$), IV = severe impairment (vascular steal) ($\text{qCVR} < -10\%$). In this small patient study we found that more pronounced steal was associated with more severe steal.

Conclusion: We found that quantification of CVR is possible with MRI with an ACZ challenge. Our proposed index correlates with the presence of hemodynamic compromise resulting from neurovascular disease. Assigning a quantitative CVR score has the potential to track longitudinal changes in hemodynamic status in response to therapy.

References: [1] Sakaie, K.E., et al, *JMRI* 21(5): 512-9 (2005). [2] Shin, W., et al. *MRM*, 56:138-145(2006), [3] Cashen, T.A., et al. *MRM*, 56(1): 138-45(2006).

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