Physiological Noise in Acute Stroke MRI: A Measure of the Tissue Response to Ischemia?

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INTRODUCTION

Spontaneous low-frequency oscillations (<0.1 Hz, see Figure 1) in regional cerebral blood flow (CBF) and oxygenation have been observed using different detection techniques [1]. Studies have shown that, in humans, MRI time series data contain these low-frequency oscillations [2], often regarded as "noise". Although their biological basis is not completely understood, they are believed to indicate arteriolar vasomotion, an adaptive hemodynamic response that helps regulate blood flow. Vasomotion has been found to decrease in response to challenges to perfusion such as cerebral ischemia [3]. Thus, the ability to image vasomotion appears to be of high diagnostic and prognostic value in acute stroke in which the tissue response to ischemia is currently not well characterized. We have previously analyzed perfusion-weighted images (PWI) from stroke patients as time series data and quantified physiological noise by measuring the variance in signal intensity as a function of time [4]. Here, we extend these analyses to include a comprehensive comparison of variance with other PWI-based metrics.

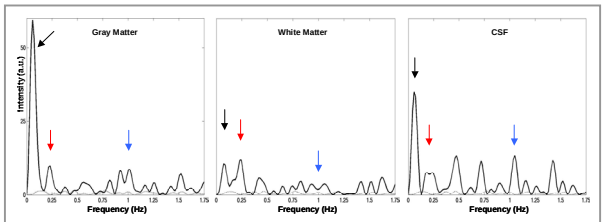

Figure 1: Spectra produced by performing time domain FFTs on time series data collected on a normal subject using a short TR (TR/TE=136/54 ms, single axial slice, 256 images). Note the different components of physiological noise (arrows) and their harmonics: vasomotion (0.1 Hz), respiration (0.2 Hz) and cardiac motion (1 Hz). Vasomotion is more prominent in gray matter and CSF than in white matter. The faint dotted line in each plot corresponds to a background voxel. Data such as this (i.e., long time series with a short TR) was not available in our stroke cohort.

METHODS

Patients were included in this study if they had undergone PWI within 12 hours of symptom onset of first-ever stroke and had follow-up T2 imaging performed a minimum of 5 days later. Patients who received thrombolytics or investigative therapeutics were excluded, as were those with visually apparent gross head motion. A total of 32 patients fulfilled these inclusion criteria. PWI was obtained at 1.5 T using an echo planar sequence with TR/TE=1500/65 ms. From these, maps of mean transit time (MTT), CBF and cerebral blood volume (CBV) were calculated. The variance in signal intensity as a function of time (Variance) was calculated from the pre-bolus PWI segment (approximately16 images) on a voxel-by-voxel basis to produce maps. A neuroradiologist outlined areas of abnormal MTT, CBF and CBV, representing the acute lesion, and the outlines were transferred to the Variance maps. Lesions were additionally subdivided into gray and white matter; voxels containing CSF or those from blood vessels were excluded. Normal gray and white matter regions were also outlined for each patient. The difference in Variance between ischemic and normal tissue for each tissue type was calculated for each patient. Areas of abnormal T2 representing the final infarct were also outlined for each patient and the outlines transferred to the Variance maps. We compared Variance values in regions that were "missed" on acute PWI to normal tissue. Only significant differences (determined via Student's t-test) are reported.

RESULTS

For 31 of 32 patients, normal white matter had significantly lower Variance than normal gray matter. This difference, as high as 20% in some cases, was 11.4 ± 4.3% (mean ± SD) on average. Shown in Figure 2 is an example of a brain slice with a lesion. There were typically no clear boundaries on the Variance maps between normal tissue and the lesion. We therefore used MTT, CBF and CBV maps to select regions of interest in order to assess whether SD reflects ischemia. When MTT was used to define the lesion, we found that for gray matter, Variance in the lesion was significantly lower than in normal tissue in most patients (20 of 32), by 6.4 ± 6.2%. When CBF was used to define the acute lesion, lesion Variance was again lower than normal for most patients (25 of 32), by 5.4 ± 5.0%. When CBV was used to define the acute lesion, lesion Variance was lower than normal for only half of the cases (15 of 32), by 5.1 ± 3.3%. For all three lesion outlines (i.e., MTT, CBF and CBV), for white matter, lesion Variance was generally indistinguishable from normal, presumably due to the fact that it had a lower baseline to begin with (i.e., white matter has lower Variance than gray in normal tissue). In addition, we examined Variance maps for their ability to detect ischemia in regions that appeared normal on acute PWI but went onto infarct on follow-up T2 (termed "missed" regions). Variance maps were able to detect ischemia in missed regions in approximately half of the cases for MTT, CBF and CBV, demonstrating that Variance maps contain information not seen on acute PWI.

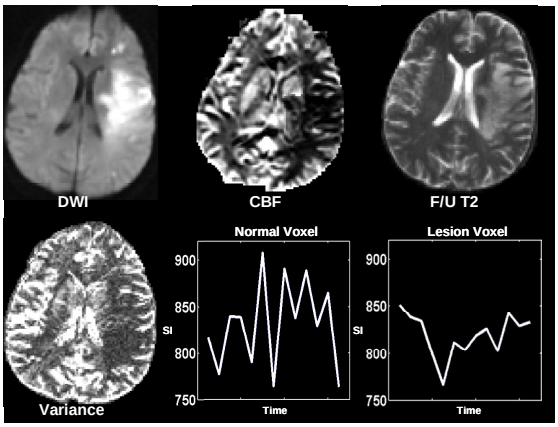

Figure 2: A typical patient who showed a decrease in Variance relative to normal in the acute CBF lesion. The Variance map is shown above along with acute DWI and CBF and follow-up T2 images. Also shown are signal vs. time curves for a normal gray matter voxel and an ischemic gray matter voxel. Note the decrease in fluctuations in the ischemic time series as well as the lower intensity in the ischemic region on the Variance map.

DISCUSSION

In summary, we report a different contrast mechanism to visualize ischemic tissue based on a post-processing method applied to pre-bolus PWI. We found that Variance maps of pre-bolus perfusion images show spatial variation both normally and in ischemia. Because thermal and scanner noise do not correspond to a spatial distribution, we assume that regional differences on the Variance maps are due to physiological noise. Furthermore, because we do not expect to find differences in cardiac and respiratory motion in ischemic regions relative to normal, we propose that the spatial differences we observed in Variance are due to the vasomotion component of physiological noise.

We found that white matter has a significantly lower Variance than gray matter in normal brain tissue, consistent with previous physiological noise studies [5]. This supports the notion that Variance reflects vasomotion, as both vessel density and autonomic modulation are lower in white matter, which would be expected to result in a lower measure of vasomotion. However, there are many biological differences between gray and white matter that could explain this difference. We expect that, while related, Variance should provide different information than CBF since the latter is sensitive to the macrovasculature (using the current acquisition methods) whereas we hypothesize that the former is sensitive to the microvasculature. We found that Variance indicated the same threatened tissue as CBF in most (25 of 32) but not all (7 of 32) patients. In addition, Variance was sensitive to tissue at risk "missed" on CBF, suggesting that Variance and CBF provide complementary rather than redundant information. This study strongly suggests that the use of long time series, short TR data (such as that used to image the normal subject in Figure 1) that enable the use of spectral filtering methods to more specifically examine the vasomotion component of physiological noise will improve upon the ability of acute stroke imaging to capture the tissue response to ischemia.

1. Hyde and Biswal, Functionally related correlation in the noise, Springer Verlag, 2000. 2. Biswal et al, Magn Reson Med 1995; 34:537. 3. Hudetz et al, Adv Exp Med Biol 1998; 454:551. 4. Wang et al, Proc 29th AHA Intl Stroke Conf 2004, #68. 5. Kruger and Glover, Magn Reson Med. 2001; 46:631. *This work was supported in part by Public Health Service grant NS38477, the National Center for Research Resources (P41RR14075) and the Mental Illness and Neuroscience Discovery Institute.*