Assessing the Evolution of Sodium MRI with Time After Onset in Human Stroke

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Introduction: One of the most critical determinants for treatment in stroke is the elapsed time since symptom onset (for example, the administration of tPA is only approved within 3 hours post onset). However, many people arrive at the hospital with an unknown time of onset. While diffusion weighted imaging (DWI) has become an important tool for the diagnosis of stroke, the apparent diffusion coefficient remains low from the onset of ischemia to several days post onset (1), and lacks significant temporal information during the acute period. Sodium MRI may be useful in this regard as linear increases with time past stroke onset have been observed in animals (2,3) and elevated tissue sodium has been observed in acute human stroke (4). The purpose of this study is to assess the potential of sodium MRI to differentiate time past symptom onset in human stroke by evaluating sodium signal intensity evolution over time.

Methods: Ischemic stroke patients (N=19, age 61 ± 15 years) were scanned 4 to 104 hours post known symptom onset. Several patients were scanned more than once yielding 29 total sodium scans. Standard proton images, including DWI, were first acquired from each patient on the 1.5T Siemens Sonata clinical scanner, after which patients were transferred immediately to the 4.7T Varian Inova scanner for sodium MRI. The sodium images generated for this study were acquired in 10 minutes using Na-PASS (projection acquisition in the steady-state) with a TR of 25 ms, and a nominal voxel size of 2.4 mm x 2.4 mm x 4.8 mm. Voxels were chosen to be anisotropic to somewhat match the slice thickness of DWI, to which the sodium images were coregistered and resliced (with SPM5) for analysis. Sodium images were acquired using 3D twisted projection acquisition and sampling density weighted apodization, yielding a TE of 0.6 ms. Four averages were acquired for each of the 5964 projections fully covering 3D k-space, sampled over a readout length of 18 ms. For each set of images a region of interest (ROI) was drawn to include all voxels with visibly increased intensity on DWI; another ROI was drawn to include corresponding tissue on the contralateral side. These ROIs were transferred to the registered sodium scan and an average intensity within each ROI measured to yield a percent sodium signal increase within the lesion relative to normal brain. Average signal intensity increases measured within each lesion were gathered into groups with statistically different ($p < 0.05$) mean values and plotted according to the mean time following symptom onset.

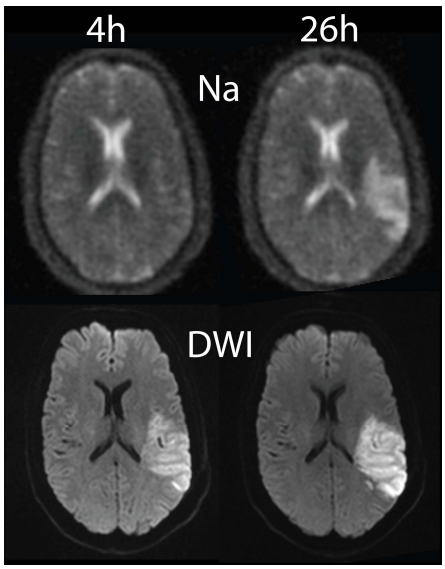

Figure 1: Representative sodium and proton diffusion weighted images from one stroke patient scanned at 4 hours and again at 26 hours post symptom onset.

Results and Discussion: Representative sodium and diffusion images from one patient are shown in **Figure 1**, highlighting sodium image quality and resolution. In **Figure 2** it can be seen that the average sodium MRI signal intensity within the lesion clearly increases with time following symptom onset, and appears to follow an exponential rise to maximum. Increasing variability of sodium signal intensity with time after onset may reflect not only the greater time span represented by each group but also differences in lesion size, location, and expansion during the disease time course, as well as treatments administered, other pathology, and relevant patient factors including age and other physiological variables. Despite this experimental heterogeneity, it is interesting to note the significant sodium MRI lesion intensity difference between the images in group **A** (mean time of onset 5.6 hours, and mean signal increase 5%) and images in group **B** (mean time of onset 13.3 hours and mean increase 26%). Given this preliminary substantial group difference it may be possible to estimate onset time with sodium MRI for stroke patients presenting with unknown time of onset.

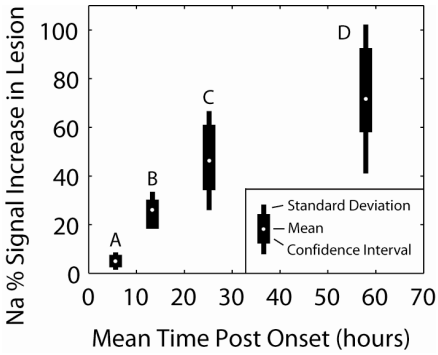

Figure 2: Average signal intensity increase in the lesion following known symptom onset in human stroke measured with sodium MRI. Scans are plotted in groups according to their mean time post onset. **A**) 5 scans, 4 – 6.75 hours. **B**) 4 scans, 9.25 – 17 hours. **C**) 8 scans, 18.5 – 29.5 hours. **D**) 12 scans, 36 – 104 hours.

References: **(1)** Schlaug, G., et. al., Neurology 49, 113 (1997) **(2)** Jones, S.C., et. al., Stroke 37, 883 (2006) **(3)** Bartha, R., et. al., MRI 22, 983 (2004) **(4)** Thulborn, K.R., et. al., Radiology 213, 156 (1999)