Sodium 'Invisibility' in Single Quantum Sodium Imaging of the Human Brain

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Introduction: To accurately measure tissue sodium concentration (TSC) in the human brain with sodium MRI, the acquired signal must be free from NMR contrast unrelated to sodium concentration. Minimization of relaxation weighting has been of primary concern for the past ~20 years as the sodium nuclei in brain tissue exhibit rapid biexponential T_2 relaxation with a fast component (60%) as short as 1-2 ms, as well as rapid T_1 relaxation (~37 ms at 4.7 Tesla). Various projection imaging variants have been implemented to minimize relaxation weighting, each having ultra-short echo times (TE) <0.6 ms, and full T_1 relaxation (i.e. 'standard TSC imaging'). However, spin 3/2 sodium NMR is complicated by more than rapid relaxation as the sodium spectrum may be split in environments with long range order. It has been demonstrated before with double quantum imaging that some sodium nuclei within the human brain exist in environments with long range order (**1**). When a spectrum splitting residual quadrupole interaction (ω_Q) exists, the transverse magnetization generated by an excitation pulse does not necessarily follow an $M_o\sin(\alpha)$ dependence (where α is the prescribed flip angle) (**2**). If $\omega_Q >> \omega_{RF}$ the transverse magnetization following an RF pulse is $0.2M_o\sin(2\alpha)$. A 1987 paper on excised cat brain testing this effect did not show an altered signal intensity dependence on flip angle (**3**); however, that is not the case for our study. We show that 'standard TSC imaging', particularly in ordered white matter, has additional contrast (i.e. regional signal intensity loss) that is independent of relaxation.

Methods: To determine whether a spectral splitting effect exists for 'standard TSC imaging' of the human brain, two images were acquired on a Varian 4.7T from two healthy volunteers with $\alpha = 90^o$, and 53^o respectively. An RF pulse length of 0.5 ms was implemented for each yielding identical TE values of 0.31 ms; TR was 150 ms for each case. With these parameters, relaxation weighting should be small and constant for each implementation in all brain tissues. 1500 twisted projections with a twist parameter of 0.14 and a readout length of 16.15 ms produced a nominal resolution, defined as $1/(2k_{max})$, of 3.2 mm x 3.2 mm x 6.4 mm. Two averages gave a scan time of 7.5 minutes per image. The images were aligned using SPM5 to compensate for any volunteer movement during the imaging session. Signal intensities, relative to cerebral spinal fluid (CSF) in the ventricles, were measured using the same regions of interest on each image, which included: cortical gray matter (GM), corpus callosum (CC), thalamus, and posterior limb of the internal capsule (PLIC).

Results: In the absence of spectral splitting and relaxation weighting effects, the relative signal intensities between all brain tissue and CSF should remain constant for both flip-angle implementations. However, a regional signal decrease on the $\alpha = 90^o$ images when compared to the $\alpha = 53^o$ images can be seen in **Figure 1**. This relative decrease is 4% and 2% for GM (for each volunteer respectively), 1% and 4% for the Thalamus, 8% and 5% for the CC, and 12% and 12% for the PLIC. The altered signal intensity dependence on flip angle is greatest in white matter regions, especially those with tracts running superior-inferior (i.e. parallel to the B_0 field), like the PLIC.

Discussion: An altered signal intensity dependence on the prescribed flip angle is demonstrated for 'standard TSC imaging' in the highly ordered white matter regions of the human brain. This effect points to residual quadruple spectral splitting on the order of, or greater than, the RF bandwidth used in this experiment (500 Hz); splitting on this order has been demonstrated in bovine nasal cartilage (**4**). It is not surprising that the greatest effect is observed in fibres running parallel to the B_o field, given the orientational dependence ($3\cos^2\theta - 1$) of the static quadrupole interaction. A similar 1987 study (**2**) did not demonstrate a `flip angle effect` in excised cat brain; however, this regional effect may have been obscured by the prevalence of unordered gray matter in a 1 dimensional experiment. In our study, the existence of a spectral splitting effect for `standard TSC imaging` is demonstrated as reduced relative white matter signal intensity on the $\alpha = 90^o$ image when compared to the $\alpha = 53^o$ image, however, signal loss likely exists on the $\alpha = 53^o$ image as well (and may exist for only a portion of the sodium nuclei within the tissue). Spectral splitting is not a new proposal for sodium NMR 'invisibility' in biological tissue (**5**). To minimize this loss for TSC imaging of the human brain much narrower RF bandwidths may be required, a potential difficulty at high field.

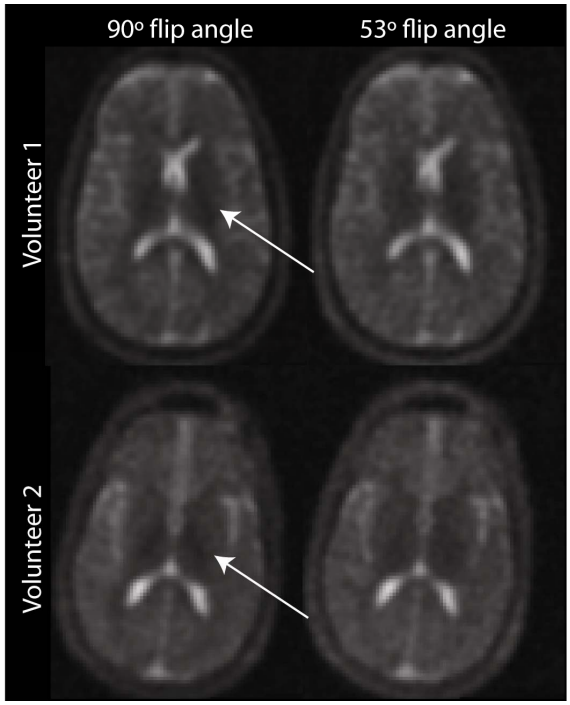

Figure 1: Brain images from 2 volunteers demonstrating regional relative signal decrease proposed to be the result of quadrupole spectral splitting. Notice the darker signal intensity in the posterior limb of the internal capsule (white arrows) relative to CSF on the 90^o flip angle images as compared to the 53^o flip angle images. This signal intensity decrease on the 90^o flip angle images cannot be explained by relaxation weighting.

References: **(1)** Reddy, et. al., MRM 33,134 (1995) (**2**) Pandey, et. al., J Chem Phys, 85, 6923 (1986) (**3**) Joseph, Summers, MRM 4, 67 (1987) (**4**) Hancu, et. al., JMR 147, 179 (2000) (**5**) Shporer, Civan, 12, 114 (1972)