Absolute T_1 and T_2 Relaxation Times; Proxies for Onset Time and Tissue Status Assessment in Acute Ischaemic Stroke

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Introduction: Quantitative MRI allows estimation of stroke onset time and assessing tissue status.[1,2,3] In preclinical models of stroke it has been shown that T_1, T_2 and $T_{1\rho}$ relaxation times respond to ischaemia almost instantaneously.[4,5] We have shown that $T_{1\rho}$ and T_2 increase in time-dependent manner thus, enabling estimates of stroke onset time with good accuracy.[2,6] SAR issues limit clinical use of $T_{1\rho}$ MRI, however, absolute T_2 and T_1 are routinely acquired by clinical MRI scanners. The exact nature of the time dependency of T_1 during ischaemia is unclear. Here, we have characterised the time courses of absolute T_1 and T_2 during the first four hours of ischaemia in rats with a view to improve stroke onset time estimation by MRI.

Methods: Male Wistar rats (n=5) underwent Middle Cerebral Artery Occlusion (MCAO) to induce focal ischaemia. Five hours after MCAO brains were extracted and stained with 1% triphenyletrazolium chloride (TTC). Animal procedures were conducted according to European Community Council Directives 86/609/EEC guidelines and approved by the Animal Care and Use Committee of the University of Eastern Finland. Using a horizontal 9.4T Varian MRI scanner, 12 slices (1mm, 0.5mm slice gap, FOV: 2.56 x 2.56cm, 128x128 matrix) of Diffusion (b-values = 0, 400, 1040; TE = 36ms, TR = 2000ms), multi-echo T_2 (12 echoes 10ms inter-echo spacing, TR = 2000ms) and FLASH T_1: TI_0 (from inversion to first FLASH sequence) 7.58ms,TI (time between FLASH sequences) 600ms, TR (time between each slice) 5.5ms, Trelax (time between inversion pulses) 10s, were acquired every hour up to 4 hours post MCAO. Total acquisition time was 20 minutes. Reciprocal Trace of Diffusion Tensor images (1/Dav = 3/Trace [D]), T_1 and T_2 maps were computed using in-house scripts written in Matlab.
Ischaemic tissue was identified as voxels with values 1 median absolute deviation outside the median value of the whole-brain 1/Dav distribution, and ischaemic volumes of interest (VOIs) were generated. Homologous regions in the non-ischaemic hemisphere were identified by reflecting ischaemic VOIs about the vertical axis. Ischaemic and non-ischaemic VOIs were loaded onto T_1 and T_2 maps, average relaxation times were extracted, and the percentage difference in T_1 and T_2 between hemispheres calculated. Regions of elevated T_1 and T_2 in the ischaemic hemisphere were identified as pixels in the ischaemic VOI with relaxation times exceeding the median value of the T_1 and T_2 distributions within the non-ischaemic VOI by more than one half-width at half-maximum. These thresholds were used to automatically generate elevated T_1 and T_2 VOIs. The volume of tissue displaying elevated T_1 and T_2 was calculated as a percentage of the ischaemic 1/Dav defined VOI for each rat and time-point. Pearson's correlations were carried out on relaxation time and volume data.

Results:
Both T_1 and T_2 relaxation times in 1/Dav defined ischaemic tissue increased linearly with time from ischaemia onset, T_1: $r = 0.83$, $p < .001$, and T_2: $r = 0.87$, $p < .001$ (Figure 1). As seen in Figure 2, T_1 and T_2 prolongation occurred in different regions of the 1/Dav defined ischaemic VOI during the first few hours of ischaemia. Over time these volumes began to overlap. Figure 3 shows the volume of tissue displaying both elevated T_1 and T_2 increased linearly with time post MCAO, $r = 0.84$, $p < .001$. TTC staining confirmed ischaemia in all rats.

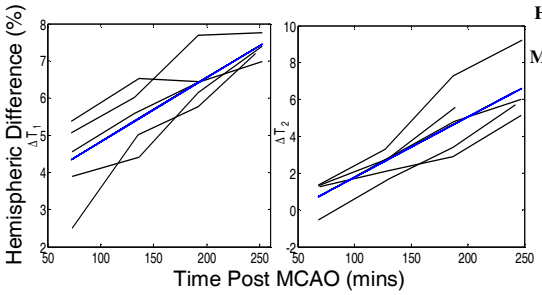

Figure 1. Percentage difference between hemispheres over time since MCAO for T_1 and T_2. For each rat (black) and linear trend line (blue).

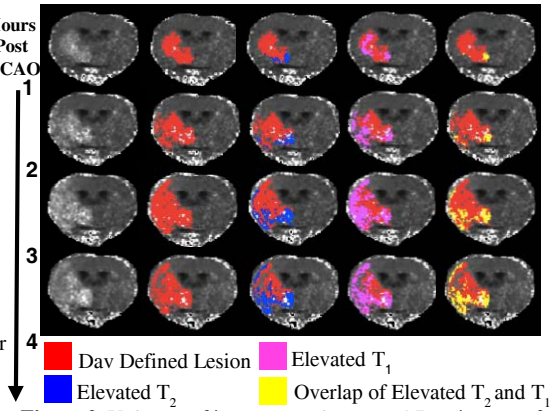

Figure 2. Volumes of interest are shown on 1/Dav images of a representative rat on a central slice over time since MCAO.

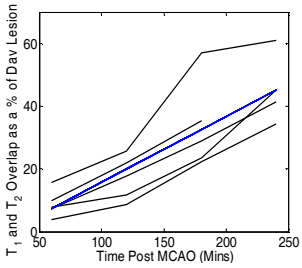

Figure 3. Volumes of the T_1 and T_2 overlap as a percentage of the 1/Dav defined lesion over time since MCAO for each rat (black) and linear trend line (blue).

Conclusions: The current data indicate that both T_1 and T_2 increase linearly with time in diffusion positive acute stroke. It is interesting that in the early hours of stroke, abnormal T_1 and T_2 volumes are distinct. This may reflect the fact that these two relaxations probe different factors of early stroke pathophysiology.[7] As the early changes in T_1 and T_2 are rather small combining these two could improve timing of stroke within the time window of thrombolysis. It should be also noted that especially in the first few hours, diffusion imaging over estimates the true extent of the infarct core, supporting conclusions of previous clinical and preclinical MRI studies.[6,8] Overall, quantification of absolute T_1 and T_2 could provide an estimation of stroke onset time and combined, provide information about tissue status. These techniques have the potential to be invaluable in stratification of acute stroke patients.

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