Bi-exponential 23Na T2* components analysis in the human brain

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Introduction

Total sodium measurements have been seen to provide an indirect indication of disease burden in MS [1] and relate to degrading cell metabolism, as demonstrated in stroke [2]. A better indicator of metabolism would be the intracellular 23Na-fraction, unfortunately not directly accessible by MRI without the use of toxic shift reagents or multiple-quantum filter techniques with very low SNR and resolution [3]. Here, we aim to measure the effective transverse relaxation time T_2^*, which is closely related to T_2, and may provide information on the underlying tissue environment. Previous attempts in characterising the bi-exponential sodium T_2^* in the brain used few echoes and insufficiently short echo times for accurate characterisation of the short component (T_{2S}^*~0.5-5ms) [4,5]. Lu et al. [6] improved this method in a short study and found the bi-exponential long T_2^* (T_{2L}^*=15-30ms) to vary significantly between white and grey matter (WM & GM) and to be much shorter than predicted. In this work, we scanned the brain of a healthy subject obtaining 18 echoes with echo times as short as 0.17 ms and fitted T_2^*s on a voxel-by-voxel basis. The sampling and fitting procedure was also tested using a simulated dataset matching the low SNR and Rice distributed noise of *in vivo* 23Na-images.

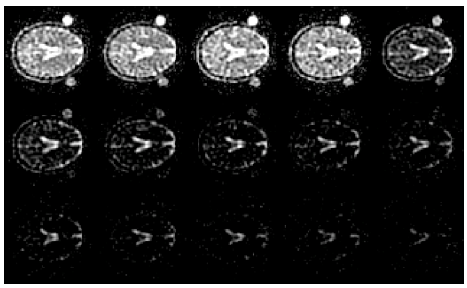

Figure 1: Exemplary slice showing the first 15 echoes, acquired from 0.17 (top left) to 52 ms (bottom right).

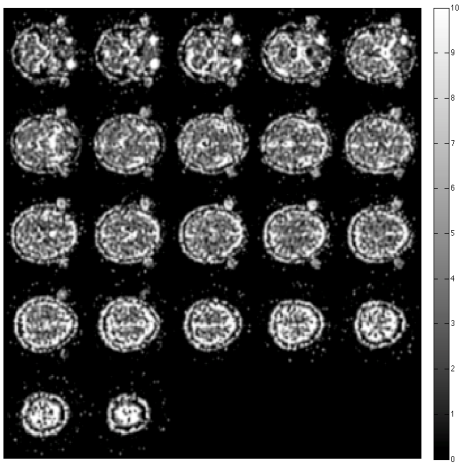

Figure 2: Short T_2^* map, scale bar 0 to 10 ms.

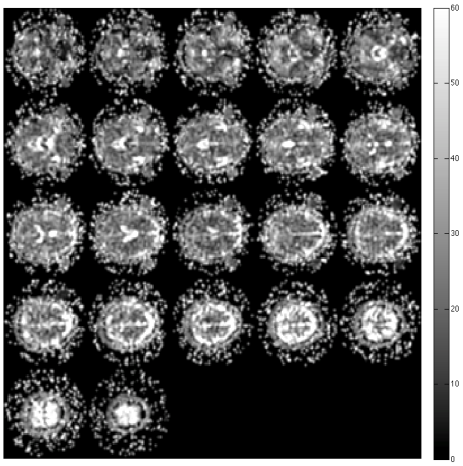

Figure 3: Long T_2^* map, scale bar 0 to 60 ms.

Methods

A radial 3D UTE sequence with 5mm nominal isotropic voxel size, TR of 120ms, BW/pixel=250Hz, FOV=240mm^2 was performed in 14 minutes with a TE=0.17ms and 14 echoes spaced at ΔTE 4.7ms on a 3T Philips Achieva Tx. Three individual 14 mins scans with 0.3, 0.5 and 1ms echo times were performed and added to the first scan after realignment (SPM8, WTCN, UCL, London, UK). Phantoms containing 33 and 66 mM NaCl in 4% agar were positioned within the field of view for literature value comparison. A non-linear least squares fit was implemented in Matlab (the MathWorks, Natick, US) on a voxel by voxel basis using positive constraints and correcting for low SNR quadrature noise [7]. ROIs were carefully selected to avoid partial volume contamination [5]. In total, 5 ROIs in each phantom, 35 ROIs in the WM and 6 ROIs in the GM were analysed. An 8x8 voxel simulated dataset with 3 tissue types (single exponential T_2^*=60ms, representing cerebrospinal fluid (CSF); bi-exponential T_{2S}^*=5ms, T_{2L}^*=18ms with 60 and 40% amplitudes respectively, representing brain tissue; bi-exponential T_{2S}^*=0.5ms, T_{2L}^*=20ms with 60 and 40% amplitudes, representing a different brain tissue) as well as a no signal air region was created to assess if our sampling and fitting could recover short as well as long echo times accurately. Artificial Rice-distributed noise [8] was used in the simulation to match SNR with that of experiments (SNR-range 15-1, arb. units).

Table 1: Mean results for the individual ROIs.

REGION OF INTEREST	SHORT T_2^* (±SD)	LONG T_2^* (±SD)
Frontal WM (n=12)	3.19 ± 1.06	22.3 ± 2.62
Periven. WM (n=6)	1.98 ± 0.61	19.43 ± 1.67
WM splenium CC (n=3)	3.26 ± 1.22	21.99 ± 2.91
Parietal WM (n=12)	3.21 ± 0.75	22.41 ± 2.29
Occ. WM (n=2)	3.22 ± 0.31	22.76 ± 0.02
GM putamen (n=4)	2.96 ± 0.6	22.81 ± 2.6
GM cerebellum (n=2)	2.68 ± 0.02	19.53 ± 2.31

Results and Discussion

In the simulation, T_2^*s were recovered voxel-wise with small standard deviations for the two tissue types with a difference of ±10% for T_{2L} and max. ±20% for T_{2S}, the CSF region could only be described by a single exponential or free fraction fit. On the volunteer a bi-exponential fit with fixed 60 and 40 % amplitudes, for the short and long components respectively, minimized the χ^2-statistics as opposed to single exponential or bi-exponential free fraction fitting. Fitting results worsened for CSF rich regions and the vitreous humour, were possibly motional averaging make the signal more appropriately described by a single exponential [5]. The mean T_2^*s for the 33mM NaCl in 4% agar phantom (n=5) were found to be T_{2S}^*=4.83±1.03ms, T_{2L}^*=24.52±1.16ms; and to be T_{2S}^*=6.48±0.49ms, T_{2L}^*=23.21±1.99ms, for the 66mM phantom. Mean WM (n=35 ROIs) values were T_{2S}^*=3.05±0.98ms, T_{2L}^*=21.85±2.45ms, and mean GM (n=6 ROIs) values were T_{2S}^*=2.87±0.49ms, T_{2L}^*=21.71±2.82ms. The results for the individual regions are summarised in table 1. The signal decayed rapidly after a TE of 5ms (see figure 1), and at this bandwidth and SNR, the resulting T_2^*-map for the short decay component (0.1 to 10ms, see figure 2) is characterised by less noise and higher SNR compared to the long component (15 to 60ms, figure 3). Little variation was found throughout WM and GM regions and they appear homogenous with 3 and 22ms decay times for the long and short component respectively; apart from ROIs in the periventricular WM and cerebellar GM, where values are slightly lower. Previously observed significant differences of long T_2^*s between WM and GM regions were not observed, possibly due to lower SNR in the long T_2^*-map or the previously postulated independence of structure and concentration on sodium T_2^* [5]. Independence of concentration for the long component was observed in the phantoms.

Conclusions

We have measured the short and long components of the bi-exponential transverse decay for sodium in the human brain and present the first high SNR T_2^*-map of the short component. Assuming that in the limit of fast relaxation, $T_2^* \approx T_2$ [9], we estimate the short T_2 component in the brain to be of the order of 3ms. Further work needs to be performed to assess the intra- and inter-subject reproducibility of these measures.

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