Full 3D mapping of T2* relaxation times from mid to late gestation of the normal fetal brain

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Target audience Clinical and Basic Neuroscience researchers interested in developmental changes in the relaxation properties of fetal brain tissues.

Purpose Quantitative T2* measurements in early brain development after premature birth (1,2) have been shown to be elevated in relation to adult values. A better understanding of normative values in-utero will help to understand the nature of these measurements and also may provide useful markers for clinical evaluation of brain abnormalities in-utero. In addition, the recent interest in the possibility of functional MRI of the fetal brain highlights the need to know T2* values of different tissue zones at different stages of development, in order to optimize fMRI protocols for BOLD contrast. To date only one T2* study has been performed on the human fetal in-utero, showing the feasibility of slice-based multi-echo T2* measurements using a mixture of clinical and healthy fetal subjects (3). The technique employed in this early study acquired multiple echoes at each slice location before proceeding to imaging the next slice location. Such an approach minimizes motion between the subsequent echoes, but makes it less feasible to recover between-slice motion in order to reconstruct a 3D volume, because of the time between spatially neighbouring slices. Here, we examine an approach using one or more dual echo multi-slice acquisitions that are themselves then repeated. Between-slice motion is estimated and the repeated dual echoes combined to increase signal, allowing 3D mapping of T2* values in the presence of fetal head motion. We applied the methods to a cohort of healthy fetuses from mid-gestation onwards. This importantly provides a full 3D image and extends previously published measurements below 26W into the 20-26W period where many clinical MRI's are acquired after an earlier ultra-sound evaluation of pregnancy.

Methods Thirteen fetal scans (20-36GW), including three re-scan sessions with 5-9 weeks delay, were imaged on a 1.5T Philips Achieva using a torso coil. The protocol consisted of T2*w EPI double gradient echo acquisitions with TE1=15ms, TE2=~43ms TR=3000ms, spatial resolution 3.0x3.0x3.0mm, 90-150 time frames, acquisition time ~6m. To compare T2* maps estimated from 2 and 5 echoes, in a subset of six subjects and one re-scan (20-35GW) we acquired four additional 30 frames scans with TE1=19ms and varying TE2=51, 60, 70 and 80ms, acquisition time ~1.5min. Additionally, each session included three 3-4 stacks T2w HASTE scans acquired in 3 orthogonal planes each with spatial resolution 1.0x1.0x3.0mm, TE/TR=150-250/1000-3000, acquisition time ~5min. Phase of the EPI images was unwrapped and correction of the susceptibility distortions that can arise from air spaces in the maternal digestive system was performed using both echoes (4). The images of different acquisitions were collectively aligned and volume registered, and cascaded slice to volume registration was applied to each acquisition (5). T2* maps were calculated using voxel wise least square regression for each double echo acquisition (2E) and separately for combined four short acquisitions (5 echoes, 5E) with applied normalisation of the intensity to the first sequence based on the image acquired in TE1. Values of the signal averaged across first 30 frames were used in calculations in order to correct for the possible presence of BOLD effect. Brain masks were initially manually segmented on the T2*w images with the longest TE available within the acquisition, as having the highest tissue contrast. Further correction of the masks to remove CSF was performed on T2* maps overlaid with T2w structural images reconstructed from 12-16 stacks and transformed to the space of T2* map. Frontal lobe WM ROIs were manually segmented using the same pairs of images. Mean values for the whole brain and WM for all 2E and 5E T2* maps were plotted against age and brain volume for all datasets.

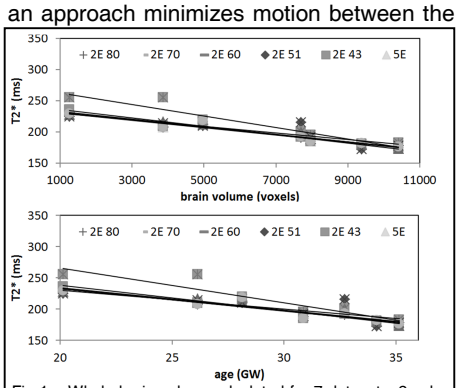

Fig 1. . Whole brain values calculated for 7 datasets, 2 echo (2E) TE2=~43, 51, 60, 70, 80 and 5 echo (5E) T2* maps plotted against age and brain volume, fitted straight line.

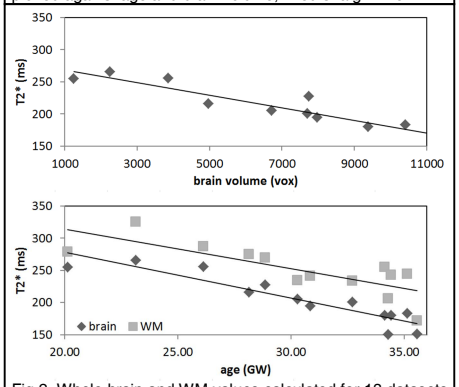

Fig 2. Whole brain and WM values calculated for 13 datasets on 2E T2* map (TE2=~43), with fitted straight line.

Results Fetal head motion from the slice transformations were: -0.3+/-1.4, 1.3+/-5.5, -2+/-4 mm in translation 4+/-12, 2.4+/-4.8 and 2.1 +/-3.2deg. of rotation in the x, y, z axes. Fig 1 and Tab 1 summarise T2* across all brain tissues 7 datasets with multiple echoes using 2E and 5E, plotted against age & brain volume. The results for all 13 scans with 2E as shown in Tab 2 and Fig 2. Fig 3 shows example T2* maps at 20 and 35GW, and highlights the high values in early gestation around the region of the sub-plate not observed in earlier studies limited to later gestation.

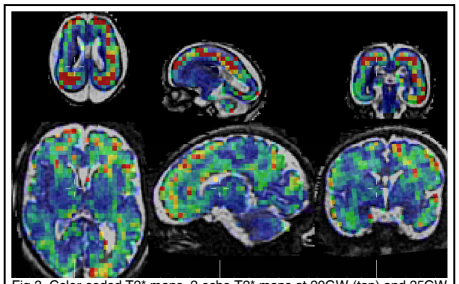
Fig 3. Color-coded T2* maps, 2 echo T2* maps at 20GW (top) and 35GW (bottom) overlaid in on corresponding high resolution T2W images.

Discussion In this work we shown feasibility of 3D T2* mapping in the fetal brain even in studies with head motion. Values derived from 2E and 5E T2* maps were comparable suggesting the practical use of a shorter 2E sequence. Mean T2* values within WM were similar to previously reported for healthy fetuses in late gestation (4), and the whole brain values were higher than the results acquired in preterm newborns of comparable age (1). The developmental trend for the T2* values to be higher in younger fetuses were confirmed and the results were extended to earlier (20-26GW) gestation relevant for clinical studies.

Conclusion This study includes first 3D maps of T2* relaxation in healthy fetuses down to 20GW revealing higher values, particularly in regions corresponding the sub-plate.

References 1. Rivikin at el. MRM, 2004. 2. Lee at el, 2012, DMCN. 3. Vasylechko et al., 2014, MRM. 4. Hutton et al. 2002, Neuroimage. 5. Seshamani et al., ISBI, 2013.

	2E 80	2E 70	2E 60	2E 51	2E ~43	5E
MEAN	198.21	199.31	199.73	200.95	212.07	198.86
SD	19.53	22.86	20.26	20.04	31.69	20.16
R age	0.94	0.89	0.87	0.63	0.85	0.85
R volume	0.96	0.94	0.96	0.75	0.90	0.92

Tab 1. Whole brain values calculated for 7 datasets, 2 echo (2E) with TE2=~43, 51, 60, 70, 80 and 5 echo (5E) T2* maps.

	WM	brain
MEAN	251.12	204.98
SD	38.21	37.77
R age	0.61	0.85
R volume		0.85

Tab 1. Whole brain and WM values calculated for 13 datasets on 2E T2* map