Vessel Size Imaging in the Brainstem
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Introduction
Imaging biomarkers are increasingly being used to evaluate novel therapeutics and targets in oncology. One such biomarker that shows promising results is MRI measurement of vessel size. A number of pre-clinical studies1-3 have shown a strong correlation with histological measurements and response to treatment. In recent years, a variant of vessel size imaging (VSI) that uses an evoked BOLD response (using gas challenges) has been demonstrated in the human brain4.5. This new technique offers a completely non-invasive method of evaluating disease and treatment in a clinical setting. Here we investigate the possibility of acquiring BOLD-VSI data in the brainstem, which is the location of 10% of childhood brain tumors6. As with standard fMRI studies, data from the brainstem is highly influenced by capillary artifacts. Two different data acquisition methodologies: dual-echo EPI (gradient/segment) and multi-echo single-shot-sampling of spin-echo refocusing (MESSER), are compared with and without cardiac gating. The initial results demonstrate an increase in performance for both gated acquisitions (against their respective continuous acquisitions), each demonstrating a significant reduction in chi-square fitting residuals. While the dual-echo readout demonstrably outperforms the MESSER acquisition both with and without cardiac gating.

Theory
VSI is based on the vessel size dependence of T2 and T2* - weighted acquisitions. Changes in susceptibility during breathing challenges result in differential changes in T2 and T2*-weighted signals, from which estimates of mean vessel radius can be made up a priori against appropriate biological models2. During data acquisition the brainstem is subject to cardiac artefacts due to the basilar artery and natural elongation and contraction of the whole brainstem. Gated acquisitions have been shown to significantly reduce this noise2, but result in temporal fluctuations in signal due to the changing repetition time (TR). Fitting to multi-echo acquisitions can overcome these fluctuations, creating purely T2 or T2*-weighted images. In this study a MESSER acquisition is used with 3 EPI readouts either side of a refocusing pulse. The first three echoes (free-induction decay) are used to calculate R2*, while the second set of echoes (spin-echo re-phasing) are used to calculate R2, as per Jochimsen et al7, where R2 = -ΔΔI/2ΔT. Alternatively, single echo data can be corrected for the temporal signal changes with a T2 map. Here we estimate T2 from the GE readout according to the method outlined by Guimaraes et al8, minimising the function S2 = [1-exp (TR/T2)] during signal plateau periods (where S2 is the measured signal and TR is the repetition time for each readout).

Methods
Two healthy volunteers were scanned on a 3 Tesla Siemens Verio with a 32-channel head coil. For each subject a diffusion weighted scan (3 orthogonal directions with two b values (0 and 1000mm2/s)) and four VSI scans were acquired. The VSI data was acquired using a dual GE-SE EPI readout (TR=2s, TE=30/90ms) and a MESSER EPI readout (TR=2s, TE=13,31,49,78,95,113ms Spin Echo time=125ms). A GRAPPA factor of 2 was used for both readouts. Thirteen axial slices (3.1x3.1x4mm voxels, 1.0mm inter-slice gap) were acquired with and without cardiac gating. Each VSI imaging paradigm consisted of one 18-minute session, comprised of 3x3minute hyperoxic periods interleaved with 3x3minute periods of normal air. During periods of hyperoxia, 100% oxygen was delivered to the volunteers via a non-rebreathing mask. All individual echoes were motion corrected and spatially smoothed (8mm FWHM) with FSL. A 2nd order time domain filter was then used to further reduce noise (this was applied to the MESSER data after relaxation rate calculation to maintain any baseline drift and T2 dependence between echoes). Dual-echo data was high-pass filtered to remove baseline changes. The MESSER data was fit with a linear regression to produce ΔR2 and ΔR2* data. Relaxation rate changes for the dual echo data were calculated as ΔR2* = log(S2/(S2+SE))/TESE and ΔR2 = -log(S2/(S2+SE))/TESE. The plateau periods from the triggered GE data (with TR times calculated from DICOM headers) were used to estimate T2 maps, and correct for variations in TR. A weighted total least squares regression was used to calculate q, the ratio of ΔR2* and ΔR2, q values were masked, limited to a range of 1 to 25 and converted to mean vessel radii via a polynomial fit to Monte-Carlo model data (using the group mean ADC value of 0.753μm2/mm and an assumed susceptibility change of 0.2ppm).

Results
The figure shows example vessel size maps calculated with each acquisition method. The group averaged brainstem values and fitting residuals are given in the table below. The dual-echo gated sequence appears to produce robust fits produced by the gated dual-echo acquisitions suggest that this methodology can become a useful tool for assessing vascular changes in the brainstem.

Discussion and Conclusions
The increased performance of the gated acquisitions is consistent with previous results in brainstem fMRI and further demonstrates the robustness of T2 estimates from gated EPI data. The inability for the MESSER sequence to make robust vessel size estimates in the Pons is likely due to the large susceptibility gradient in the anterior aspect of the brainstem, the short T2* in this region causing considerable attenuation of the signal in the 4th echo readout. The noise associated with fitting R2* is also the likely cause of the poor performance of the multi-echo data. The robust fits produced by the gated dual-echo acquisitions suggest that this methodology can become a useful tool for assessing vascular changes in the brainstem.

References
6. cancer.net/cancer-types/brain-stem-glioma-childhood/statistics (05/11/2012)