Pre- and post-chemotherapy comparisons of calculated rBV and rBF with signal intensity drop on T_2* dynamic contrast-enhanced MRI of breast cancers

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Introduction: Quantitative flow parameters such as relative blood flow, relative blood volume and mean transit time, measured using dynamic contrast-enhanced T_2*-weighted MRI (T_2*w DCE-MRI) have to date been acquired mainly in brain tumours. This is partially due to the difficulty of performing the high time resolution scans in motion artefact-prone areas, and partially because of high first pass extraction of low molecular weight contrast media in visceral tumours. Calculating the parameters also requires the use of a complex gamma-variate fitting algorithm. A simpler and more widely implementable method for analysing brain T_2*w DCE-MRI tumour data has been suggested by Liu *et al.*[1] who calculated the relative maximal signal drop (rMSD: Figure 1) and compared it with a fully calculated relative cerebral blood flow (rCBF), relative cerebral blood volume (rCBV) and mean transit time (MTT). They noted that rMSD provided equivalent information to rCBV in leaky brain tumours provided that MTT was not substantially prolonged. In this study, we compare rMSD with gamma-variate based quantitative analysis in breast cancer patients[2], both before and after 2 courses of FEC (5-Fluorouracil, Epirubicin and Cyclophosphamide) chemotherapy.

Methods: 29 patients with invasive breast cancers were imaged pre- and post-FEC chemotherapy using a single slice T_2*w DCE-MRI protocol (TE 20ms, TR 30ms, flip angle 40°) with 0.2 mmol/kg bw Gd-DTPA being administered after the first 10 of 60 images, time resolution 2s. Fifteen minutes before this was done, they had undergone a T_1w DCE-MRI examination with 0.1mmol/kg Gd-DTPA. Pixel-by-pixel analysis to calculate rBV, rBF and MTT via a gamma variate fit was performed using MRIW software (Institute of Cancer Research, London). In-house software was used to calculate the normalised relative maximal signal drop (rMSD) from baseline ($=100*(S_o-S_{min})/S_o$), also on a pixel-by-pixel basis. Regions of interest (ROIs) on the whole tumour outline were drawn. rBV and rBF were plotted for all tumour pixels in each patient and linear regressions performed to evaluate the spread of MTT. A similar analysis was performed on a patient-by-patient basis correlating rBV/rBF with median rMSD values both pre- and post-chemotherapy.

Results: Figure 1 shows a T_2*w signal intensity-time curve for invasive ductal breast cancer with a gamma-variate fit and relative maximal signal drop. Pre-treatment rBF/rBV regression gave a mean R^2 of 0.916 ± 0.146 and post-treatment regression gave a mean R^2 of 0.938 ± 0.071 for all patients. When patients were split into responders (r) and non-responders (nr), the pre-treatment R^2 values were 0.992 (r) and 0.936 (nr) (Figure 2a), and post-treatment R^2 values were 0.948 (r) and 0.995 (nr). Figures 2b and 2c show the patient-by-patient correlation comparing median rMSD with (b) pre-chemo rBV (R^2=0.867) and (c) post-chemo rBV (R^2=0.315). Pre-chemo rBF had R^2=0.894 and post-chemo rBF R^2=0.405.

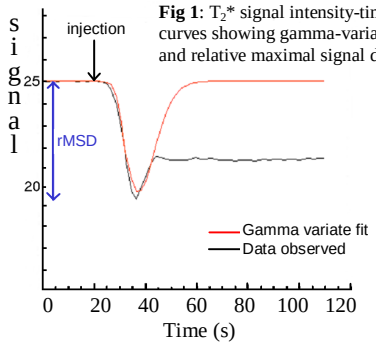

Fig 1: T_2* signal intensity-time curves showing gamma-variate fit and relative maximal signal drop

Discussion: The signal intensity (SI) for the breast patients (Figure 1) does not return to baseline, in common with extra-cranial tumours. This is due primarily to susceptibility effects induced by contrast medium pooling in the extravascular extracellular space (EES), and recirculating in the vasculature[3]. Since rBV is the integral of the contrast/time curve (assuming a return to baseline), a gamma variate is fitted to the data to compensate for the non-return, and the integration carried out on the fit[4]. Any effects of T_1 enhancement caused by contrast medium in the EES were minimised by 'pre-loading' the EES with contrast medium from a prior T_1w DCE-MRI measurement (with 0.1mmol/kg Gd-DTPA dose).

There is little difference between the rBF and rBV correlations for both pre- and post-FEC chemotherapy, and between responders and non-responders. This indicates that the MTTs are not significantly prolonged. For pre-treatment tumours, the relative maximal signal drop in susceptibility-weighted DCE-MRI can be used to indicate the perfusion status of breast cancers and could be used as an alternative to more complex gamma-variate perfusion calculations. However, in the post-treatment setting, rMSD is not as good an indicator of blood volume or flow, irrespective of response category.

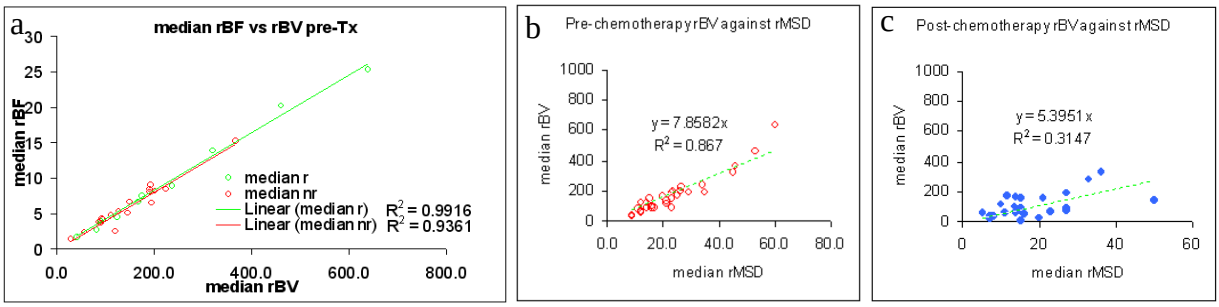

Figure 2a: median rBF vs rBV pre-therapy. **2b, 2c**: Pre- and post relative blood volume, plotted against relative maximal signal drop.

References

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