A Comparison of DCE-MRI Derived Measure of Extracellular Volume and ADC in Glioblastoma Multiforme

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Background: Pharmacokinetic modelling methods for the analysis of DCE-MRI data provide information about both the vascular structure and function and information regarding the volume of the extravascular extracellular space (v_e). Diffusion weighted imaging allows quantification of the degree of motion of free water molecules, resulting from Brownian motion. Apparent diffusion coefficients (ADC) maps can be generated which represent the amount of diffusion of water molecules which have been shown to be sensitive in identifying changes of water diffusion which may reflect changes in cellular structure due to apoptosis and/or necrosis [1, 2] that occur in early response to treatment [1-4]. A number of groups have shown ADC to have an inverse linear relationship with cell density in cerebral tumours [2, 5-7]. This generated the hypothesis that areas of increased cellularity, and therefore low ADC, would be expected to have small extravascular extracellular volumes (low v_e) and ADC would correlate with v_e in cerebral tumours.

Methods: 19 patients with glioblastoma multiforme (GBM) were recruited. All were treated with corticosteroids for a minimum of 48 hours prior to imaging and all imaging was performed prior to surgery. All imaging was performed on a 3 Tesla Philips Achieva system, using a SENSE head coil. Imaging included diffusion imaging (6 direction, b value=1000smm^{-2}, Δ=33.5ms), T_1-weighted DCE-MRI, and anatomical sequences. Tumour volumes of interest (VOIs) were defined on the anatomical images and modified to contain only voxels which showed significant changes in T1 value following administration of contrast. Parametric maps of ADC and v_e were generated. Images were co-registered using FSL, FLIRT linear registration package [8]. Statistical analysis of ADC and v_e were performed on both a voxel-by-voxel basis and by comparison of median values.

Results: No significant relationship was demonstrated between ADC and v_e in the voxel-by-voxel scatter plot (Figure 1). In addition, no significant relationship was identified when the median values obtained from the whole tumour were compared (p=0.124) (Figure 2).

Discussion: Voxel-by-voxel analysis and a comparison of median values failed to demonstrate the hypothesised relationship between ADC and v_e in GBM. There may be methodological reasons for this lack of correlation – for example, co-registration of datasets was required. Alternatively, there may be problems with partial volume effects that could mask the expected relationship; GBM are structurally extremely heterogenous tumours characterised by varying degrees of hypercellularity, cytoplasmic and nuclear pleopmorphism, mitoses, endothelial proliferation and necrosis within any given tumour. This marked heterogeneity may mean under-perfused areas of tissue, which exhibit cystic necrosis, will have low measured values of v_e (due to the hypo-perfusion) but high ADC (due to the cystic necrosis), thus resulting in a lack of correlation between the two parameters. Another explanation is that the diffusion of water observed using DTI is not strongly coupled to the compartmentalisation of the tissue. If this is indeed the case, then the pathological changes observed in diffusion may be dictated more by changes in membrane permeability than by changes in the ratio between intracellular and extracellular volume.

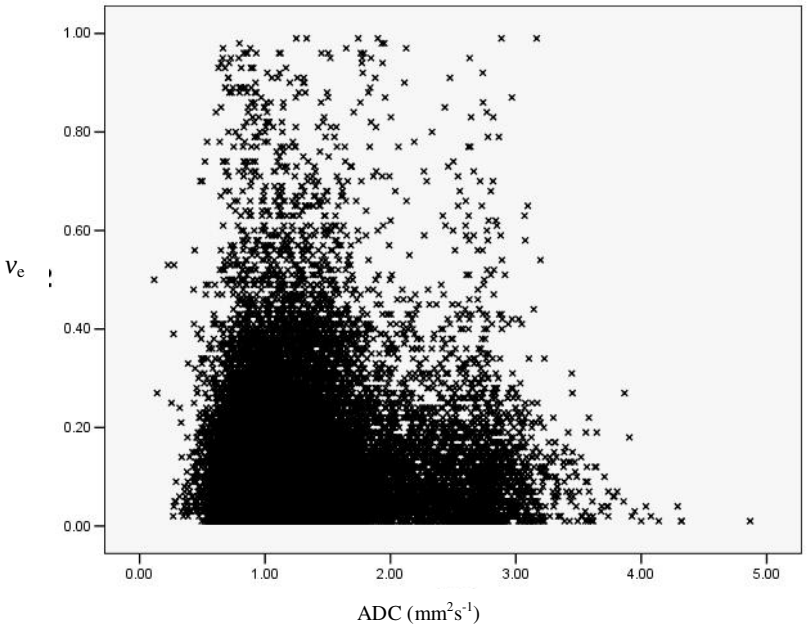

Figure 1. Scatter plot depicting voxel-by-voxel comparison of ADC and v_e.

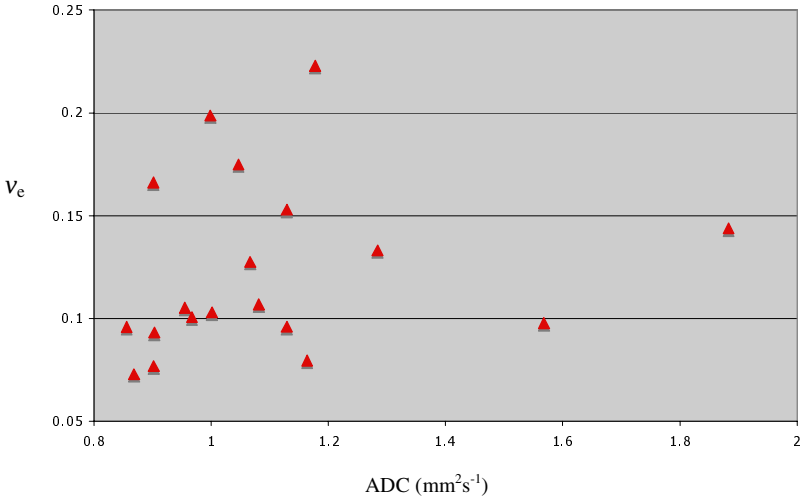

Figure 2. Scatter plot depicting comparison of median values of ADC and v_e (p=0.124)

References

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