A Comparison of Enhancing Fraction and DCE-MRI Parameters in Glioma of Various Grade

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Background: Dynamic contrast enhanced MRI (DCE-MRI) requires the use of tracer kinetic modelling to produce estimates of parameters which describe microvascular structure and function. As an alternative, a simpler measure of bulk tumour perfusion, the enhancing fraction or perfused proportion, has been proposed.[1, 2]. This has shown promise in differentiating stable from progressive disease and in predicting time to progression following first line chemotherapy in ovarian cancer [3]. Enhancing fraction is a measure of the proportion of voxels within a given tumour where there is evidence of enhancement following contrast agent administration. It does not quantify the amount of enhancement occurring in any single voxel but identifies the number of voxels where perfusion is seen. In low grade gliomas, vessel permeability is low and the blood brain barrier is intact, therefore contrast agent remains mostly within the vascular space. Conversely, in high grade gliomas there is local disruption of the blood brain barrier and marked leakage of contrast agent into the extravascular extracellular space. Given these properties, we hypothesised that enhancing fraction would relate differently to the DCE-MRI parameters of contrast transfer coefficient (K^{trans}, a measure of contrast passing from the intravascular space to the extravascular extracellular space), v_e (the extravascular extracellular volume) and v_p (the blood plasma volume) in different tumours and be dependent upon the integrity of the blood brain barrier and the ability of contrast agent to pass into the extravascular extracellular space.

Methods: 32 patients with glioma (11 grade II, 2 grade III, &19 grade IV) were imaged using a 3.0T Philips Achieva MR scanner (Philips Medical Systems, Best, NL), prior to surgery. Imaging included DCE-MRI & anatomical sequences. Tumour volumes of interest (VOIs) were defined on the anatomical images. The DCE-MRI protocol consisted of a baseline T_1 measurement using a variable flip angle 3D T_1-Fast Field Echo (T_1-FFE – RF-spoiled gradient echo) approach, followed by 3D T_1-FFE volumes acquired every 3.4s. Gadolinium-based contrast agent (Gd-DTPA-BMA; Omniscan, GE Healthcare, Oslo, Norway) was injected as a bolus of 3ml, at 15mls^{-1} (dose of 0.1mmol/kg of body weight) after acquisition of the 5th image volume. The FFE volumes were oriented in a sagittal-oblique plane to ensure that both the tumour and a carotid artery were included for arterial input function definition Post processing was performed with in-house software generating measurements of enhancing fraction and DCE-MRI parametric maps of K^{trans}, v_e, and v_p. Histological grade and median values of DCE-MRI parameters were compared with measurements of enhancing fraction. Voxels within a tumour were identified as enhancing if a measure of the initial area under the contrast agent concentration curve (*IAUC*) calculated over a 60s period was greater than zero, providing a sensitive measure of the presence of enhancement.

Results: Enhancing fraction did not differentiation between tumour grade. In grade II gliomas, enhancing fraction correlated with v_p (R^2=0.6158, p=0.004, Spearman's rho=0.782, Figure 1) but not K^{trans} (p=0.747) or v_e (p=0.631). In grade IV tumours enhancing fraction correlated with K^{trans} (R^2=0.3134, p=0.019, Spearman's rho=0.533, Figure 2) and v_p (R^2=0.1318, p=0.021, Spearman's rho =0.525) but not v_e (p=0.808). There were insufficient numbers in the grade III group (n=2) to perform an analysis.

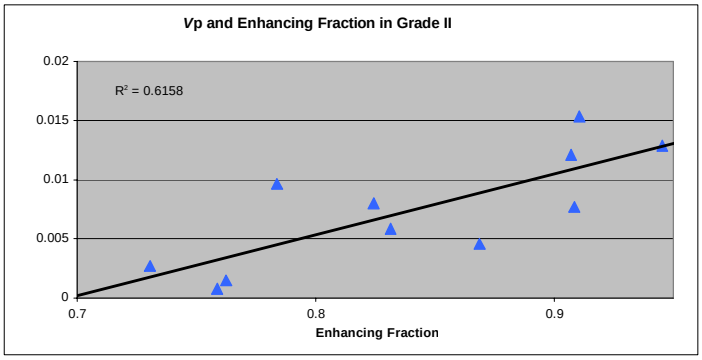

Figure 1. Scatter plot demonstrating the relationship between v_p and enhancing fraction in grade II gliomas (p=0.004, Spearman's rho correlation coefficient=0.782)

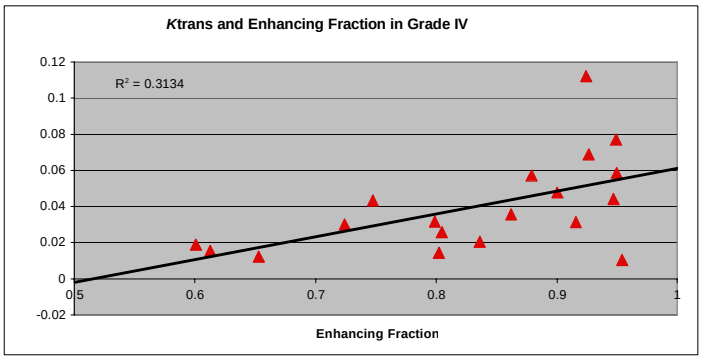

Figure 2. Scatter plot demonstrating the relationship between K^{trans} and enhancing fraction in grade IV gliomas (p=0.019, Spearman's rho correlation coefficient=0.533)

Conclusion: The failure of enhancing fraction to distinguish between tumour grades is likely to be due to the high sensitivity of the IAUC measure to the presence of contrast agent. Enhancing fraction does not relate the absolute amount of enhancement but instead identifies the proportion of the tumour in which any enhancement occurs. The sensitivity of this method is greater than that of a human observer using conventional radiological criteria, which are generally used to distinguish grade II (in conventional radiology terms, 'non-enhancing' tumours) from grade IV (classically 'enhancing' tumours) gliomas. Our results suggest that this simple measure, enhancing fraction, may, in fact, be a potential surrogate for these more complexly derived parameters in tumours. Enhancing fraction reflects v_p in grade II tumours and K^{trans} in grade IV gliomas. This may be of importance for both low and high grade tumours. In low grade tumours with an oligodendroglial component, v_p has previously been shown to distinguish between different genotypes of tumour (those with and without 1p/19q chromosomal loss, which is related to chemosensitivity) [4]. In high grade tumours, K^{trans} has been shown to convey important prognostic information [5]. Hence if enhancing fraction is a surrogate of these DCE-MRI parameters in high & low grade glioma it may carry similar genetic & prognostic information & has the advantage of been a more simply derived measure.

References

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