Logistic regression of multiparametric MR for glioma grading

Lawrence Kenning1, Martin Lowry2, Martin Pickles2, Christopher Roland-Hill3, Shailendra Achawal3, Chittoor Rajaraman3, and Lindsay W Turnbull2,3

1Centre for Magnetic Resonance Investigations, University of Hull, Hull, East Riding of Yorkshire, United Kingdom, 2Centre for Magnetic Resonance Investigations, Hull York Medical School at the University of Hull, Hull, East Riding of Yorkshire, United Kingdom, 3Hull and East Yorkshire Hospitals NHS Trust, East Riding of Yorkshire, United Kingdom

Introduction: Pre-operative glioma grading using MR has the potential to influence patient management and future treatment. This is particularly important for non-resectable lesions, or tumours located in eloquent regions of the brain. This study investigates the role of functional MR parameters to determine glioma grade, which may be of interest to clinicians and clinical scientists.

Methods: Multi-parametric MR data was acquired from 55 patients with histologically proven gliomas. Patients were scanned using a 3.0T GE 750 Discovery system with an eight channel phased array head coil. Morphological imaging in the form of T2 FLAIR and T1 contrast imaging was acquired along with diffusion tensor imaging (directions=32), T1 dynamics (tdel=5sec), multi-flip angle T1 volumes (3°,5°,10°,20°,40° flip angles) and EPI T2* dynamics (tdel=2sec). DCE-MRI preceded DSC-MRI to preload the tissue, reducing leakage effects. Motion within and between sequences was minimised by applying a series of motion correcting registrations using FSL1. All data was processed using in-house software. DTI parameters were: apparent diffusion coefficient (ADC), fractional anisotropy (FA), anisotropic component of diffusion (q), relative anisotropy (RA), longitudinal diffusivity (λL) and radial diffusivity (λR). Pharmacokinetic modelling using a two compartment Tofts-Kety model and a population AIF was applied to the DCE-MRI data transformed to contrast concentration using T1 values calculated from the multi-flip angle data (Ri). DSC-MRI was processed using gamma variate and Boxerman2 models. Cerebral blood volume (CBVGVF, CBVBOX) maps were then normalised to global white matter (rCBVGVF, rCBVBOX). T1 and T2* dominant leakage rate (K2) was also measured. Parametric volumes were created by registering the FLAIR, T1 post contrast, ADC, FA, q, RA, λL, λR, Ktrans, vD, vO, rCBVGVF, CBVBOX, and K2 into a single 4D [x, y, z, parameter] volume. Whole tumour volumes of interest (VOI) were manually contoured using morphological imaging (T2 abnormality + T1 post contrast abnormality – necrosis/cyst – haemorrhage).

Mean parameter values were generated for the VOI of each lesion. Gaussian mixture modelling (limited to 2 populations) was also applied to the VOI of each parameter, generating a further two means for each parametric volume. These two additional values were sorted in ascending order and labelled Population 0 and 1 respectively. Patients were categorised according to the WHO grade as defined by histology. Non-parametric T-tests (Kruskal-Wallis) were used to examine relationships between grade and MR parameter. Bonferroni (P=0.05/39) and non-corrected p values (P<0.05) were both calculated. The most significant results for each parameter were then the input for logistic regression models using a backward Wald methodology. A two-step decision tree was used to predict lesion classification. The first logistic regression model was to split grade IV lesions from lower grade tumours. Following this, a second logistic regression model was used to split grade II and III lesions. The most significant VOI for each parameter (combined, pop0 or pop1) was input into each model.

Results: Following non-parametric T-tests, 29/39 parameter means significantly correlated with grade. Of these only 11/29 results retained significance following Bonferroni correction. Figure 2 shows the list of parameters and the volume of interests (VOI), that served as input to the logistic regression model. Using multi-parametric MR, 82.8% of cases were correctly classified using the two-step logistic regression model decision tree. Key parameters for the first logistic regression model, which split grade IV lesions from grade II and III lesions were q, λL, Ktrans, and vD, whilst ADC was used for the direction between grade II and III tumours.

Discussion: Multiparametric MR can be used to classify lesion grade. Parameters derived from DTI and DCE appeared to be the most useful for this cohort of patients. DSC parameters may have been too similar to DCE parameters to be used in the final model. A greater number of grade II and III lesions may improve the model for separating the two pathologies. Higher values of q, the anisotropic component of diffusion possibly relate to the greater volume of oedema associated with higher grade lesions. The ability to identify grade IV lesions using multiparametric MR appearing to be excellent (93%). This work demonstrates that multiparametric MR could be used to grade lesions where tissue samples are unavailable. This work could also be used to identify transforming lower grade lesions.

Conclusions: Pre-operative glioma grading using multiparametric MR should be considered and may improve patient management.