Logistic regression of multiparametric MR for glioma grading

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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 T_2 FLAIR and T_1 contrast imaging was acquired along with diffusion tensor imaging (directions=32), T_1 dynamics (tdel=5sec), multi-flip angle T_1 volumes (3°,5°,10°,20°,40° flip angles) and EPI T_2* 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 FSL[1]. 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 (λ_L) and radial diffusivity (λ_R). 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 T_1 values calculated from the multi-flip angle data (R_1). DSC-MRI was processed using gamma variate and Boxerman[2] models. Cerebral blood volume (CBV_{GVF}, CBV_{BOX}) maps were then normalised to global white matter ($rCBV_{GVF}$, $rCBV_{BOX}$). T_1 and T_2* dominant leakage rate (K_2) was also measured. Parametric volumes were created by registering the FLAIR, T_1 post contrast, ADC, FA, q, RA, λ_L, λ_R, R_1, K_{trans}, v_e, v_b, $rCBV_{GVF}$, $rCBV_{BOX}$, and K_2 into a single 4D [x, y, z, parameter] volume[3]. Whole tumour volumes of interest (VOI) were manually contoured using morphological imaging (T_2 abnormality + T_1 post contrast abnormality – necrosis/cyst – haemorrhage).

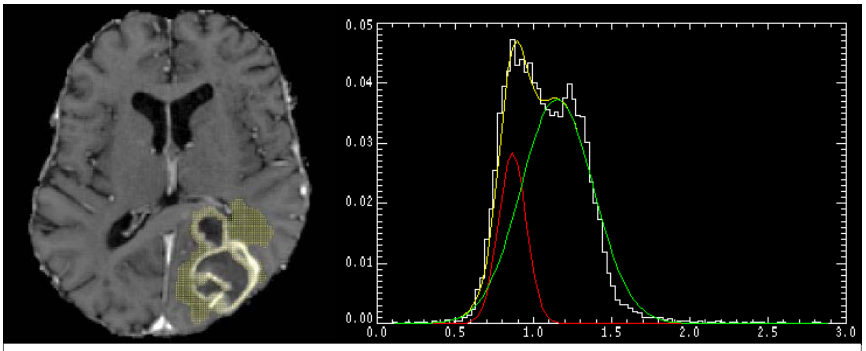

Figure 1 – Single slice from whole abnormality VOI in GBM patient. (left). Two population Gaussian mixture model of ADC values from the VOI (right).

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, λ_R, K_{trans} and v_e, whilst ADC was used for the distinction between grade II and III tumours.

PARAM.	VOI	2 (10)	3 (12)	4 (33)	Sig. P=
		Med	Med	Med	
ADC	Pop 0	1.206	1.061	1.003	0.017
FA	Comb.	0.165	0.186	0.206	0.003
q	Comb.	0.295	0.285	0.341	0.002
RA	Pop 0	0.099	0.111	0.138	0.002
λ_R	Pop 0	1.067	0.982	0.891	0.004
R_1	Pop 0	0.600	0.654	0.753	0.012
K_{trans}	Comb.	0.028	0.036	0.087	<0.001
V_e	Comb.	0.039	0.051	0.158	<0.001
V	Pop 0	0.020	0.019	0.034	<0.001
CBV_{GVF}	Pop 1	2.573	2.801	3.629	0.002
$CBVB_{OX}$	Pop 1	2.432	2.795	3.244	0.013
K_2	Pop 0	-1.010	-1.379	-1.956	0.001

Observed Grade	Predicted Grade 2+3	Predicted Grade 4	% Correct
2+3	20	2	90.9
4	2	31	93.9
Overall %			92.7

Observed Grade	Predicted Grade 2	Predicted Grade 3	% Correct
2	7	3	70.0
3	3	9	75.0
Overall %			72.7

Grade			Predicted Group Membership 2	3	4	Total
Original	Count	2	8	2	0	10
		3	5	6	1	12
		4	1	1	31	33
	%	2	80%	20%	0%	100%
		3	42%	50%	8%	100%
		4	3%	3%	94%	100%

82.8% of original grouped cases correctly classified.

Equation 1. - Grade 2+3 vs. 4 with 0.5 cut-off = -1.223 + (19.291*q_comb) + (-6.887* λ_R_pop0) + (-163.500*Ktrans_comb) + (124.824*ve_comb)

Equation 2. - Grade 2 vs. 3 with 0.5 cut-off = 8.009 + (-7.034*ADC_pop0)

Figure 2 – Kruskal-Wallis tests correlating tumour grade with MR parameter (left). Logistic regression model 1, split grade IV lesions from lower grade tumours. (top middle). Logistic regression model 2, split grade II lesions from grade III tumours (bottom middle). Using both models in combination, the right table was generated which used both steps to classify lesions. The full equations for the models can be seen in the bottom right.

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.

References: 1. Jenkinson *et al*. Medical Image Analysis. (2001) **5**: 143-156. **2**. Boxerman *et al*. Am J Neuroradiol. (2006) **27**: 859-67. **3.** Kenning *et al.* Proc. 21st ISMRM. (2013). 0975.