Comparison of Quantitative Heterogeneity of Brain Tumors from Diffusion MR Versus Histological Tumour Grade: A Preliminary Study

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Target Audience
Radiologists, clinicians and researchers working in the area of neuro-oncology.

Purpose
Compared to existing methods for analyzing MR images (ROI analysis, histogram displays), "texture analysis" of images could potentially better capture the complex relationships between different regions within tumours, thereby providing deeper insights into biological properties such as tumour grade.
In this study, we report on the clinical testing of an image processing method (texture analysis) for quantifying spatial heterogeneity[1,2] in brain tumours from Apparent Diffusion Co-efficient (ADC) maps.

Method
Data Acquisition: 1.5 Tesla MR data from 10 patients with brain tumour was retrospectively analyzed. Necessary IRB and Ethics approvals were obtained. Routine anatomic imaging was performed using standard T1W, T2W, FLAIR and post-contrast T1W sequences. Diffusion images were acquired by standard EPI-based diffusion weighted imaging (b-values of 0 and 1000). ADC maps were generated using product software on the scanner console.

Heterogeneity Quantification: We have used a modified co-occurrence matrices[3] based method for quantifying the heterogeneity of the whole tumor in a slice (marked manually) in the ADC maps. The obtained heterogeneity value could be evaluated as a marker for tumour grade. Modified co-occurrence matrix is computed by *K* co-occurrence matrices at different spatial offsets. Neighbouring voxels in all the directions are used for creating *K* co-occurrences matrices. The co-occurrence matrices at different offsets are weighted by inverse of distance from the centre pixel i.e. $1/d^k$. Here we have used chessboard distance as a distance measure. All the co-occurrence matrices are concatenated along third dimension to get modified co-occurrence matrix of size *I*, *J*, *K*; where *I* and *J* are number of grey levels used for computing co-occurrence matrices and *K* represents number of neighbouring voxels or number of offsets.
From the co-occurrence matrix obtained above, a "contrast" feature is computed, which is the specific heterogeneity measure used in this study.
For each dataset, we compute a "Heterogeneity Index" as follows:

$$Heterogeneity\ Index = \frac{heterogeneity\ of\ tumour\ -\ heterogeneity\ of\ normal\ brain}{Heterogeneity\ of\ normal\ brain} * 100$$

We then compared heterogeneity index with the final tumour grade obtained by histological analysis after surgical resection. Heterogeneity index is also compared with "Mean ADC index", which is defined as the difference between mean ADC of tumour and normal tissue divided by mean ADC of normal tissue multiplied by 100. Wilcoxon rank test was used for statistical significance analysis.

Results
The heterogeneity ("contrast" value) of tumour was found to be statistically different compared to normal brain tissue (p-value < 0.01). The heterogeneity index of tumour(s) (derived from ADC maps) was compared with mean ADC index (figure 1). In five out of six patients with grade 4 tumours, the heterogeneity index was above 150. In one patient with grade 4 tumor the heterogeneity index was below 100. All four tumours with grades 1, 2 and 3 showed heterogeneity index below 150 (figure 2). Heterogeneity index yielded similar low values for edematous regions and normal brain.

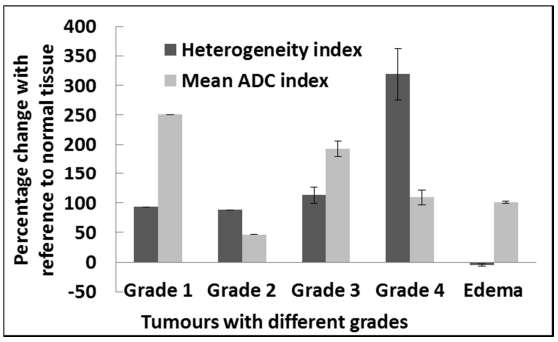

Figure 1: Heterogeneity index and mean ADC index of tumours with different grades (error bars show SE).

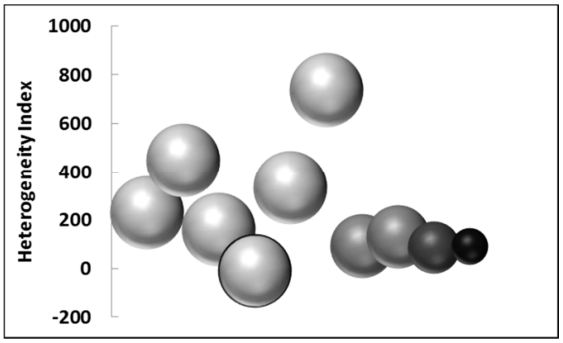

Figure 2. Graph demonstrates higher grade lesions (larger and brighter) associated with higher heterogeneity (y axis). One grade 4 tumor with low heterogeneity is encircled in black.

Discussion
There appears to be good correlation between higher heterogeneity index and grade 4 brain tumours. In one grade 4 tumour located in the corpus callosum, the heterogeneity index was low, possibly due to the dense structured white matter. For tumours of lower grade, in view of a small sample size, the assessment of correlation with heterogeneity index was not possible.
Heterogeneity index (calculated from ADC maps) could discriminate between grade 4 and lower grade tumours. However, while using ROI mean ADC values, there was significant overlap between grade 4 and lower grade tumours.

Conclusion
This preliminary study suggests that heterogeneity index could be a better marker for tumour grade than mean ADC index. In future, the study can be extended to include heterogeneity analysis of other MR parametric maps e.g. perfusion, permeability maps.

References
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