Quantitative analysis of Gd enhancement histogram tails predicts transformation in low grade gliomas

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Aim: To determine and optimise the ability of histograms of subtle Gd enhancement to predict transformation in low grade gliomas

Introduction::Adult supratentorial low grade gliomas (WHO grade II) are usually left untreated until they transform into high grade gliomas (grade III and IV). We have been imaging subjects with untreated low grade gliomas every 6 months, using a variety of MR techniques[1], including double-dose Gd enhancement. Previously we have reported[2] that enhancement histograms may have predictive power for the time of transformation.

Methods:
Subjects: A subset of 21 subjects (8 non-transformers NT, 13 transformers T) that had been scanned every 6 months, for periods of 2-5 years, until transformation occurred, was analysed. Transformation was defined as clinical deterioration due to tumour growth or the appearance of a new area of enhancement, and confirmed by biopsy of the enhancing region.
MRI: FSE FLAIR images (TR/TI/TE=8774/2192/161; pixel 0.94 x 0.94 mm; slice thickness 5 mm; gap 1.5 mm) were used to define tumour boundaries. 3D T_1-w IR spoilt gradient echo images (TR/TI/TE/FA = 14.4/650/6.4/20°; voxel 0.94 x 0.70 x 1.5 mm) were collected before and 10 min after injection of double dose Gd (0.2 mM/kg). The 3D image datasets were spatially registered, subtracted, and normalised to the contralateral normal-appearing white matter (NAWM) to provide %enhancement (%E) maps in pu (percent units). The low-resolution 2D FLAIR images were interpolated and registered to the pre-Gd 3D T_1-w dataset, in order to define a tumour region of interest which was then copied to the %E maps. *Histogram*s of %E, normalised to a total tumour volume of 100%, were produced for each tumour in each scan. Peak location was fixed at 0pu (since its raw value varied, almost certainly due to imager instability). We focussed on features derived from the right and left hand tails (%E>10pu or <-10pu). The *left tail* was sometimes abnormally high. Genuine negative enhancement is unlikely, and signal decreases were related to pulsation artefacts, particularly in the temporal lobe. Such artefacts would probably affect both tails equally. Thus the *corrected enhancing volume* V_{enh}^* = (right_tail - left_tail)* (tumour volume) was a strong candidate feature, as was *uncorrected enhancing volume* V_{enh} = right_tail * (tumour volume)
Statistical analysis: Features from the immediately pre-T scan (T-) were compared to the penultimate scan from NT's (NT-1). Classification using a threshold, and t-tests, were used. Time-to-transformation Kaplan-Meier ('survival') curves were plotted, based on the baseline exams.

Results: i) for the (NT-1 vs T-) comparison, the most discriminatory feature was the corrected volume of enhancing tissue V_{enh}^* (p=.011)
ii) A threshold V_{enh}^* > 3.0 ml detected all of those who would transform in the next 6 months (sensitivity=100%, specificity=87% - fig 1).
iii) time-to-transformation curves for V_{enh} (fig 2) showed dramatic differences (threshold at V_{enh} > 4.0ml gave p<0.04 at 5 years).

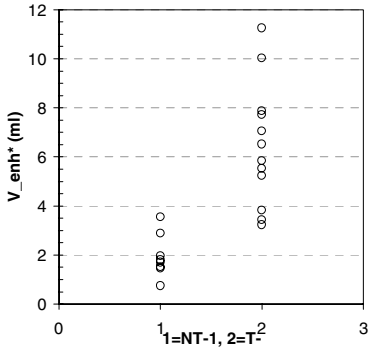

Fig 1: scatter plot for V_{enh}^* = corrected volume of enhancing tissue

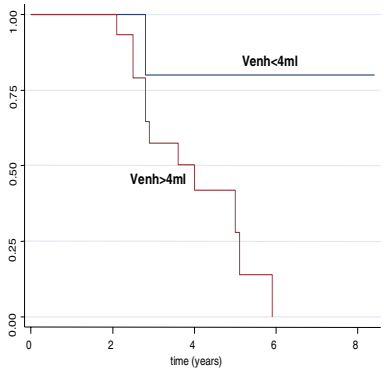

fig 2: time-to-transformation curves for V_{enh} from baseline exam

Discussion and Conclusions
1. Clear histogram differences between NT and T are apparent at presentation, suggesting the process of transformation starts very early.
2. Prognosis and patient management could be influenced by quantification of the volume of subtly enhancing tumour tissue.
3. More subtle statistical analysis may allow continuous updating of the probability of transformation, based on using all the imaging exams

References: 1. Jager AJNR 2005; 26:274 2. Tofts ISMRM 2005; 754