

Quantitative histogram analysis of Gd enhancement in low grade gliomas may predict malignant transformation

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Aims: i) investigate histograms of subtle Gd enhancement in low grade gliomas; ii) can histograms predict the time of malignant transformation?

Introduction: Adult supratentorial low grade gliomas (WHO grade II) are usually left untreated (in the UK) until they transform into high grade gliomas (WHO grade III and IV). We are scanning subjects with untreated low grade gliomas every 6 months, using a variety of MR techniques, to search for parameters which may predict transformation. Here we show histograms features for quantifying Gd enhancement, and study how they vary between transformers (T) and non-transformers (NT).

Methods:

Subjects: Subjects were scanned every 6 months, for periods of 1-4 years, ceasing if transformation took place. This was defined as clinical deterioration, or the appearance of new or increased enhancement, and confirmed by biopsy of the enhancing region or resection of the tumour. **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 T₁-w IR spoiled 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 scanner gain settings were manually kept fixed for most examinations. 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 high-resolution 3D T₁-w dataset. A tumour region of interest was defined on the interpolated FLAIR images, then copied to the %E images (1). Normal appearing white matter (NAWM) was monitored, and used to correct the peak location by small yet significant amounts.

Histograms of %E, normalised to a total tumour volume of 100%, were produced for each tumour in each scan, for a total of 9 subjects, of whom 4 were clear non-transformers (NT), and 5 were clear transformers (T). This categorisation was carried out blinded to the histograms. The following 6 features were extracted from histograms: %vol (the tumour volume fraction that enhanced ≥10 percent units pu); V_{enh} (the absolute volume of tumour that enhanced ≥10pu), PH (peak height), mean (mean enhancement in the tumour), PL (peak location after NAWM correction), and skew. **Statistical analysis:** Features from the last scan before transformation (T-) and the scan after transformation (T+) were compared to those from NT's (using the penultimate scan NT-, since the last NT scan could be a T- if the subject was subsequently shown to transform).

Results:

- i) Histograms from NT's and T's showed clear differences (fig 1). Typical T histograms showed reduced peak height and increased right-hand tails, as the volume of enhancing tissue increased
- ii) T+ scans differed from NT- in 4 parameters (table 1)
- iii) T- scans differed from NT- in 2 parameters (%vol, V_{enh})
- iv) using the V_{enh} feature from NT- and T- scans to predict subsequent transformation in the following 6 month period, by setting a threshold of 6ml, would be completely accurate (figure 1).
- v) the first (baseline) T scans were significantly different from the baseline NT scans (V_{enh}, p=0.009)
- vi) in gain controlled scans, NAWM PL shifted (mean=0.3pu, range -2.3 to +6.6), suggesting a residual poorly-understood source of scanner variation.
- vii) normal appearing white matter (n=3 in NT) had %vol=1.4 to 4.7%vol, below that of all but one tumour.

Discussion and Conclusions

1. Clear histogram differences between NT and T are apparent, giving objective quantification of abnormal subtle enhancement, even before formal transformation.
2. Transformation could be predicted with complete accuracy, in this small sample.
3. Even the first scans showed T/NT differences, suggesting that malignant transformation is a long process.
4. Subtle multi-parametric statistical modelling, to include rate of change and other MR parameters (e.g. diffusion and volume), may improve prediction.
5. Equivocal subjects may be better understood using histogram features trained from these unequivocal subjects.

(1) Tofts PS et al. ISMRM 2004: 1987

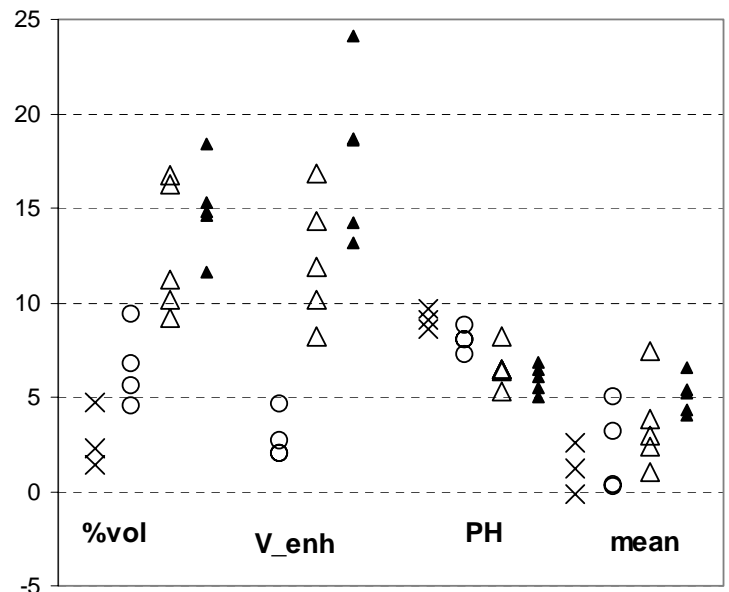


fig 1: NAWM (X), NT- (open circle); T- (open triangle); T+ (solid triangle)

feature	NT-	T-	T- vs NT-	T+	T+ vs NT-
	mean (sd)	mean (sd)	p	mean (sd)	p
%vol	6.6 (2.1)	12.7 (3.6)	0.02	14.9 (2.4)	0.001
V _{enh} (ml)	2.8 (1.2)	12.3 (3.4)	0.001	17.8 (4.4)	0.0003
PH (%vol/pu)	8.0 (0.7)	6.6 (1.0)	0.05	6.0 (0.7)	0.004
Mean (pu)	2.2 (2.3)	3.5 (2.4)	p>0.1	5.1 (1.0)	0.04
PL (pu)	0.6 (0.6)	1.5 (1.3)	p>0.1	2.3 (1.7)	p>0.1
skew	2.3 (1.0)	1.9 (1.3)	p>0.1	2.5 (0.8)	p>0.1

Table 1: histogram features