Serial ADC measurements in low grade gliomas as a predictor of malignant transformation

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Aim: To measure the apparent diffusion coefficient (ADC) of low-grade gliomas longitudinally and to compare the changes in ADC histograms of stable tumours with those who underwent malignant transformation.

Introduction: Adult supratentorial low-grade gliomas (WHO grade II) transform into high grade gliomas (WHO grade III and IV) at an unpredictable point in their natural history. Early surgery and radiotherapy does not prolong survival (1) and there is now a tendency to withhold aggressive therapy until transformation occurs. We are scanning subjects with untreated low-grade gliomas every 6 months, using a variety of MR techniques, to search for parameters which may indicate transformation. ADC measurements have an inverse correlation with tumour cellularity (2) and have been used to differentiate between low- and high-grade gliomas (2-4). Here we demonstrate differences in longitudinal ADC measurements between transformers (T's) and non-transformers (NT's).

Methods: *MRI*: Diffusion weighted images were obtained using a SE EPI sequence (TR/TE=10000/98.6; FOV 26 cm; 96x128 matrix; slice thickness 5 mm without gap; b= 1000 s/mm^2). ADC maps were generated using FUNCTOOL 1.9m (GE Medical Systems). Tumour boundaries were defined on the b=0 images of the DWI sequence using a semi-automated contouring method in DISPIMAGE (5). Tumour volumes of interest were copied onto the ADC maps and histograms of ADC measurements of the entire tumour volume were generated with DISPIMAGE (5) using a bin width of 20 mm^2/s. The *ADC Histograms* were normalised to a total tumour volume of 100%. We measured peak location (PL), peak height (PH) and calculated tumour growth and the fractional volume with ADC values below 1000 x 10^{-6} mm^2/s ($FV_{<1000}$)
Subjects had MR scanning at approximately 6 months intervals up to the point of transformation into a high-grade gliomas. Malignant transformation was defined by clinical and standard radiological criteria, such as tumour enhancement, and confirmed by brain biopsy. We present data of the baseline (BSL) and most up-to-date follow-up (FU) MR scans of 4 patients who had biopsy proven malignant transformation and of 5 non-transformers.

Results. The follow-up period was 6-24 months (mean 18) for T's and 18-31 months (mean 23) for NT's. An increase in tumour volume was observed in both groups, on average by 30% in T's and by 16% in NT's. All T's showed a left-shift of the PL (Fig.1), on FU indicating a decrease in ADC whereas NT's showed a small right-shift of the PL (Fig.2). The average difference in PL (FU-BSL) in the group of T's was - 148 x 10^{-6} mm^2/s (range –27 to –409). PH did not differ significantly between the groups. There were, however, marked differences in $FV_{<1000}$ between BSL and FU (Figure 3). The $FV_{<1000}$ increased in T's by 9.2% (range 6-14.5%) and decreased in NT's by 4% (range 0.7-10.6%).

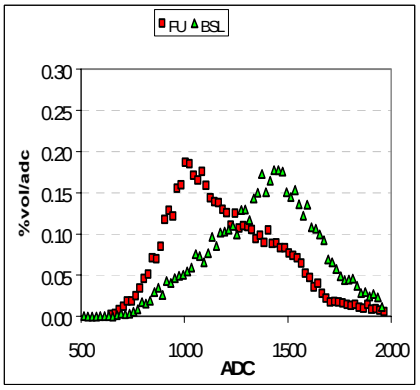


Fig 1: ADC histograms of T (BSL green; FU red)

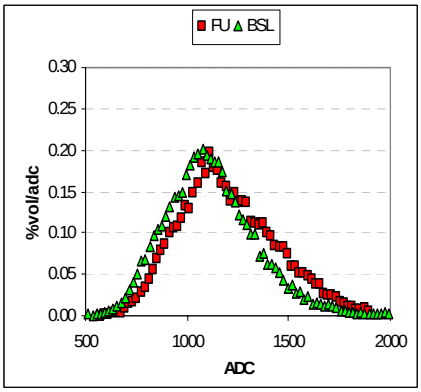
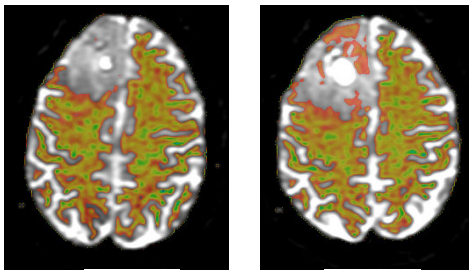


Fig 2: ADC histogram of NT (BSL green; FU red)



BSL FU

Fig.3 Colour overlay images.
Tissue with ADC values< 1000 x 10^{-6} mm^2/s are shown in colour. There is an increase in $FV_{<1000}$ on the FU

Discussion and Conclusions

1. Tumour growth occurs in T's and NT's.
2. The evolution of whole tumour ADC values differs between T's and NT's.
3. Malignant transformation is associated with a left shift of the PL on FU histograms and also with an increase in the proportion of the tumour exhibiting ADC values below 1000x10^{-6} mm^2/s.
4. NT's show small changes of PL and $FV_{<1000}$ in the opposite direction of T's.
5. Malignant transformation is associated with increased cellular density and the ADC changes can be explained by the previously described inverse correlation of cellular density and ADC measurements (2).

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