

# Apparent Diffusion Coefficient Histograms of Low-Grade Gliomas may aid in Differentiation of Tumour Type and Show Changes on Malignant Transformation

A. D. Waldman<sup>1,2</sup>, N. Danchaivijitr<sup>1</sup>, D. J. Tozer<sup>2</sup>, C. E. Benton<sup>2</sup>, R. Ramachandran<sup>2</sup>, P. S. Tofts<sup>2</sup>, J. H. Rees<sup>2</sup>, H. R. Jager<sup>2</sup>

<sup>1</sup>Imaging, Charing Cross Hospital, London, England, United Kingdom, <sup>2</sup>Institute of Neurology, University College London, London, England, United Kingdom

## Background

The majority of low grade gliomas (LGGs) grow slowly for years then, unpredictably, undergo malignant transformation. The clinical management of LGGs is controversial; there is no proven benefit to intervention prior to malignant transformation. After transformation, different histological subtypes (oligodendroglioma, oligoastrocytoma and astrocytoma) show differing response to chemotherapy. Non-invasive indicators of histology and early markers of malignant transformation are therefore desirable. Previous apparent diffusion coefficient (ADC) studies in brain tumours demonstrated an inverse correlation with cellularity, and suggest a role for diffusion imaging in tumour evaluation (1,2,3). We hypothesise that cellular proliferation occurs early in malignant transformation and ADC changes may provide an early surrogate marker.

## Purpose

To evaluate the distribution of ADC values within different subtypes of untreated LGGs, and correlate changes in ADC with malignant transformation in a longitudinal study. Specifically, to assess whether ADC histograms are useful for classifying histological type, monitoring changes in LGGs, and predicting malignant transformation. We have used a histogram approach to represent ADC values as it provides an objective index of heterogeneity, and is more sensitive to regional changes in components or cell populations within the whole tumour.

## Methods

17 patients with untreated LGGs were imaged at 6 monthly intervals (11M, 6 F, age range 26-69, 11 biopsy proven; 3 oligodendrogliomas (OD), 3 oligoastrocytomas (OA) and 5 astrocytomas (AC)). Malignant transformation was defined clinically (new focal neurological deficit or raised intracranial pressure) or radiologically (new pathological contrast enhancement); and patients classified as transformers (Ts) and non-transformers (NTs). Imaging was on a 1.5T MRI system (LX, GEMS, Milwaukee), and included EPI diffusion-weighted imaging ( $b=0$ ,  $b=1000$  s/mm<sup>2</sup>). ADC maps and  $b=0$  images were analysed off-line and ROI's selected from tumour boundaries defined by signal abnormality on  $b=0$  images on multiple slices using the dispimage software (Plummer, UCL, UK). Histograms were generated from ADC values within the whole tumour (the area under which were normalised to total tumour volume). Histograms were compared between subjects and serially within-subjects. Histogram morphology was evaluated visually, and using a range of quantitative indices including peak amplitude, mean ADC, skew, and 10-75<sup>th</sup> centiles.

## Results

8 of 17 patients underwent malignant transformation during during the study. 1. ADC measured from normal appearing white matter was longitudinally stable (3% variation over time) 2. At baseline, ADC patterns varied within the histological groups; the OD group generally showed less heterogeneity of ADC values within each tumour than the AC and OA groups (Figure 1a). There was a trend toward higher peak amplitude and lower mean ADC in the OD group ( $p=0.1$ ). 3. ADC was generally more stable with time in NTs compared to Ts. 4. Peak amplitude was significantly lower in Ts (which had transformed) than NTs ( $p=0.02$ ). No significant difference was shown in the ADC histogram prior to transformation compared to the baseline histogram. 5. The transforming group showed diverse changes with transformation; e.g. some developed low ADC populations (see Figure 1b for example), and some developed high ADC components.

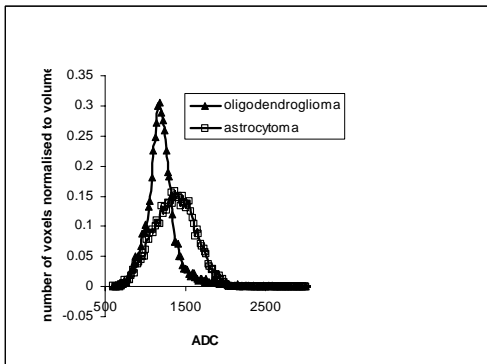


Figure 1a  
Conclusion

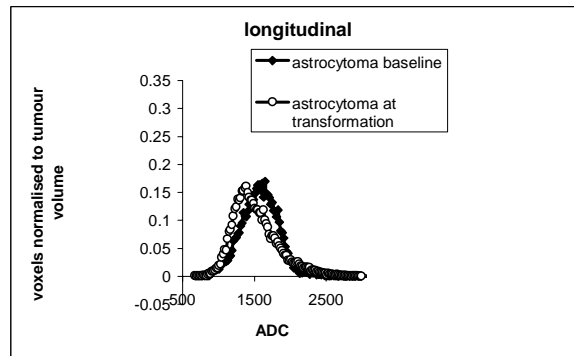


Figure 1b

ADC histograms are temporally stable, allowing longitudinal measurements of diffusion heterogeneity within tumours. ADC values within low grade ODs were generally lower and more homogeneous than in ACs, which may reflect the greater cellular homogeneity which characterises ODs histologically. These results suggest that ADC may help to differentiate OD from AC, which has important implications for subsequent chemotherapy decisions. Alterations in histogram morphology occur more frequently with malignant transformation than stable tumour growth, and in some cases precede transformation defined by standard criteria. They may provide early markers of transformation, but no consistent pattern of change was apparent in this small sample. Further study is warranted.

## References

(1) Guo AC *et al* Radiology 2002; 224:177-183 (2) Kono K *et al* AJNR 2001; 22:1081-1088 (3) Castillo M *et al* AJNR 2001; 22:60-6