Challenges for the functional diffusion map in paediatric brain tumours with different grades

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Target Audience: Clinicians and researchers interested in cancer treatment.

Purpose: The functional diffusion map (fDM), or parametric response map, has been suggested as a tool for early detection of tumour treatment efficacy, and has been shown to work well in higher grade tumours[1–3]. The method consists of a voxel-wise comparison of pre- and post-treatment apparent diffusion coefficient (ADC) maps in tumour areas. An increase in ADC reflects a decrease in tumour cellularity and positive treatment response. A decrease in ADC reflects an increase in tumour cellularity and poor treatment response. We have previously shown how areas of necrosis confound results in the fDM[4]. We have now extended the previous work in order to study the fDM in tumours of varying grades. In this study, we analyse the fDM in high, mid- and low-grade tumours. High grade tumours tend to be more cellular and have a lower ADC value than average. Hence the standard fDM approach of an increase in ADC implying a good prognosis, and a decrease in ADC implying a poor prognosis, applies. In low grade tumours however, the ADC value is already high, and an increase in ADC is expected to imply tumour becoming necrotic/cystic. Conversely, a decrease in ADC in low grade tumours is expected to be representative of positive treatment response, as the sparsely cellular tumour area returns to more cellular healthy tissue. We therefore hypothesize that fDM changes need to be interpreted in accordance to the tumour grade.

Methods: 27 patients (14 male, 13 female, ages 4 months to 13.7 years, mean 7 years) with brain tumours and who had diffusion-weighted imaging (DWI) as part of their clinical imaging, were enrolled in a retrospective study that examined the fDM. The fDM implemented in MATLAB (MathWorks), was used to compare sequential imaging in 3 high-grade glioblastoma multiforme (GBM) patients (WHO grade 4), 18 mid-grade diffuse intrinsic pontine glioma (DIPG) patients (WHO grade 2 & 3) and 6 low grade optic nerve glioma (ONG) patients (WHO grade 1). A comparison was made between results of the fDM and clinical reports at the time of the imaging.

Results: Patients with GBM showed an increase in ADC at treatment response (red) and a decrease in ADC at progression (blue) in agreement with previous literature[1]. However, patients with DIPG and ONG showed areas of increased ADC at tumour progression and areas of decreased ADC at treatment response (Figure 1). Furthermore, in the lower grade tumours, with therefore a higher mean ADC, an increase in ADC was mostly associated with an increase in necrotic/cystic components of the tumour.

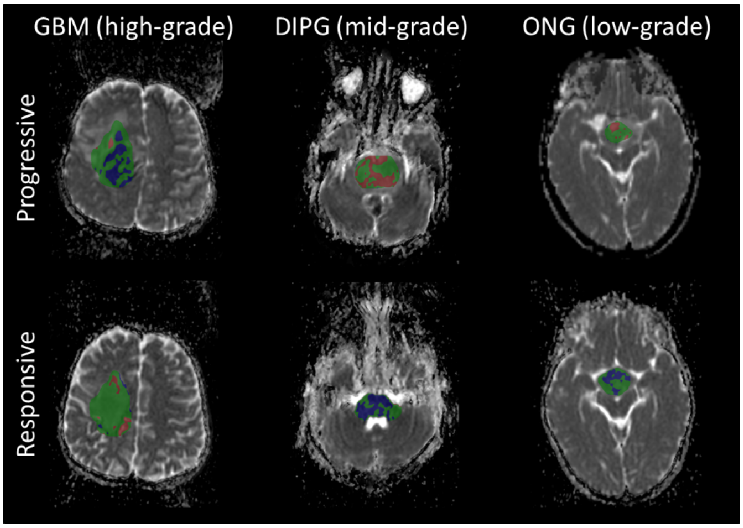

Figure 1: Comparison of the fDM in GBM (left), DIPG (centre) and ONG (right) in the case of progression (top row) and positive response to therapy (bottom row). Whereas in high grade tumours a decrease in ADC is indicative of an increase in cellularity and progression, in low grade tumours a decrease in ADC is indicative of treatment response. In the images, red implies an increase in ADC, green implies no change in ADC and blue implies a decrease in ADC.

Discussion: The fDM has been presented as a tool for treatment response. It has been shown that a decrease in ADC should be representative of an increase in cellularity and poor treatment response. However, we have shown that in cases of lower grade tumours, a decrease in ADC is more likely to represent good treatment response as the higher ADC tumour areas are replaced by lower ADC in normal brain tissue. This indicates the importance of accounting for the tumour type and grade prior to interpreting results in the fDM. The increase in ADC in low grade tumours reflected an increase in necrotic/cystic components, which we have previously shown to be a confounder in the fDM[4].

Conclusion: The fDM has been shown to be a useful tool in evaluating tumour treatment response; however, results need to be interpreted in light of the tumour type and tumour biology.

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