Title: Evaluating changes during treatment of pediatric diffuse intrinsic pontine glioma using diffusion tensor imaging

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Abstract Category: Pediatrics

Purpose: Diagnosis and management of children with diffuse intrinsic pontine glioma (DIPG) is reliant upon MRI, as biopsy tissue is rarely obtained. Diffusion tensor imaging (DTI) provides non-invasive analysis of the tissue microstructure and has been shown to be useful in evaluating response to therapy in some cancers. Studies of DTI in DIPG have reported increased diffusivity compared to normal tissue and other brain tumors. The global diffusion metrics used in most studies provide a limited view of the tumor structure, whereas histogram analyses may provide more specific information of diffusion properties throughout the lesion. This study evaluated pediatric DIPGs over the course of treatment using global metrics and histogram analysis of DTI parameters.

Methods: DTI was acquired at 2.5mm isotropic voxels with 60 diffusion directions (b-value=1100 s/mm$^2$) in 10 pediatric patients (range = 4 – 8 yr, median = 5 yr) enrolled in a clinical study of Pegylated Interferon Alfa-2b (PEG-Intron®) for treatment of DIPG prior to disease progression, with a median of 18 weeks from the initial scan to progression (range = 5 – 59.9 wks). Scans were performed following radiation therapy at multiple time points over the course of treatment. Mean diffusivity (MD) was evaluated in a region of interest (ROI) that encompassed the entire tumor, as identified by signal abnormality on T2 fluid attenuated inversion recovery (FLAIR) images. Tumor histograms were calculated from MD values. Histogram characteristics including the mean, median, and kurtosis were evaluated with time to progression.

Results: As seen in Figure 1A, mean MD values at initial scan were higher than normal tissue (ranges = 0.89 – 1.15x10$^{-3}$ mm$^2$/s) and were found to significantly increase during treatment (p< 0.05). However, mean MD was not predictive of time to progression. The range of initial mean MD was quite broad, thus the histogram of ROI values was analyzed in an attempt to find common features. Shape of the MD histograms was heterogeneous (median kurtosis = 8, range 2.2 – 34.7) with no clear pattern of MD distribution (Figure 1B).

Conclusion: While global measures of MD showed increased tumor diffusivity in all patients, the range of values was large. MD histograms revealed diverse diffusion characteristics in DIPG. These findings illustrate the vastly heterogeneous structure of these tumors, which can confound evaluation of treatment response.