Diffusion Tensor Imaging Study of Patterns of Tract Involvement in Diffuse Pontine Gliomas

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Introduction: Diffuse pontine gliomas (DPG) are a heterogeneous group of lesions that account for 15% of all pediatric central nervous system tumors. Prognosis is generally poor for patients with DPG, and there has been little progress in development of effective therapy for these tumors. Conventional MR imaging allows for the assessment of tumor location, focality, and response to therapy, but does little in terms of assessing tumor involvement in the major white matter tracts in the pons. We have shown previously that diffusion tensor imaging (DTI) is useful for qualitative and quantitative characterization of tumor involvement in brain stem tracts[1,2]. Here we report initial results of longitudinal analysis of DTI parameters of the major tracts in the pons in patients being treated for DPG.

Methods: Patients were imaged in the context of an IRB-approved therapeutic protocol and all patients gave informed consent to participate. Therapy includes anti-angiogenesis therapy (vandetanib) and concurrent RT. So far, 21 patients [10 male and 11 female. median age: 7.60 ± 4.16] have been enrolled and imaged as follows: baseline, 1 week into RT, 3 weeks into RT, at the end of RT, and then every 8 weeks until they are taken off protocol. Currently, there are 122 exams. MR imaging was acquired with Siemens 3T Trio and 1.5T Avanto scanners (Siemens Medical Solutions, Malvern, Pa). Conventional imaging included T2 anatomical images. Diffusion-weighted echo-planar images were acquired with a double spin-echo sequence (FOV 192 mm × 192 mm, matrix 128 × 128, slice thickness 3 mm, 40 slice, TR/TE, 6600/120 ms, 4 acquisitions per series). Diffusion encoding was applied along 12 noncollinear directions (b = 1000), and 1 image was acquired without diffusion encoding. Image acquisitions were realigned by using the realignment tools within Statistical Parametric Mapping (SPM2, Welcome Institute of Neurology, London, UK). Diffusion tensors were calculated by using the SPM diffusion toolbox software developed for SPM2 software. FA, ADC, and eigenvector maps were calculated. To aid in the visualization of the fiber tracts, we used an RGB-orientation color map to demonstrate fiber shape and direction. FA and ADC were evaluated in 3 regions of interest. The regions of interest were drawn around the bilateral corticospinal tracts and transverse pontine fibers at the level of the middle cerebellar peduncles.

Results and Discussion: Figure 1 shows representative examples of different patterns of tract involvement and tumor progression. Each column depicts a T2 image and the corresponding RGB color map of one patient at a certain time point while on study (black arrows). The graph depicts the change in ADC values measured in the tracts over the course of the treatment (up to 50 weeks).

The bilateral corticospinal tracts (white arrows) are apparent on the color maps. Posterior to these tracts are the transverse pontine fibers (yellow arrows). The ADC graphs at the bottom show the values from the right corticospinal tract (blue), the left corticospinal tract (red), and the transverse pontine fibers (green). The left column shows data from a patient that currently has a stable tumor. Hyperintense regions in T2 clearly outline the tumor. The color map however shows how the relatively focalized tumor has pushed the corticospinal tracts laterally, rather than infiltrating. The ADC graphs show that ADC decreased in all 3 tracts as the tumor responded to treatment FA values increased after the onset of therapy and demonstrated a trend similar to ADC [not shown]. The middle column shows the data from a currently deceased patient at a mid point of treatment. The tumor responded to treatment, as demonstrated by the reduced tumor size on T2 weighted imaging, but subsequently progressed after 5.5 months. The tumor response time course clearly seen in the ADC graph as the value dips when the treatment is working and then rebounds when the treatment fails. The T2 image and color map from 7 weeks into the treatment show clearly defined tracts and transverse fibers showing the effectiveness of the treatment as the tracts return to their normal position and size. The right column shows a patient who did not show imaging evidence of response to treatment, but was clinically stable over the study period. This is the first study. We saw tumor involvement in tracts. Tract involvement, FA, and ADC values seem to correlate

Fig.1: T2, RGB color map, and ADC curve of three patients at a certain time point (black arrows).

with treatment course. FA and ADC values respond to the start of treatment and when treatment is not effective. This is an ongoing trial and we are in the process of acquiring and analyzing a larger number of patient exams in order to further assess the relationship of treatment effectiveness and tract involvement in pediatric pontine tumors. Further studies could show the importance of tract involvement, ADC, and FA analysis in treatment optimization.
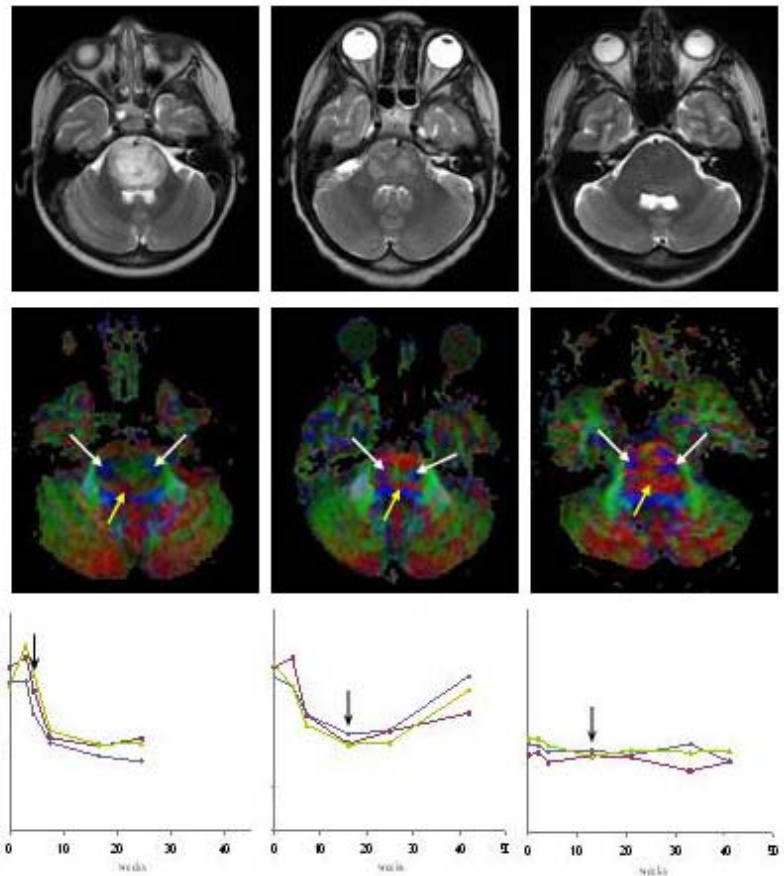
References: [1] K.J. Helton et al. *AJNR* 2006; 786-793. [2] N.S. Phillips et al. J Neurosurg 103:557–562, 2005