Probabilistic Tractography of Cerebellar-Cerebral Connections in Paediatric Brain Tumor Patients

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Introduction and Purpose: Treatment with cranial-spinal radiation (CRT) is often required for effective control of aggressive pediatric brain tumours, such as medulloblastoma. Unfortunately, this modality is consistently associated with adverse late effects. White matter damage is the most striking anatomical change following CRT. Clinically it is documented as T2 hyper-intensity. Based on recent studies, changes in normal appearing white matter are also evident in children treated with CRT, including decreases in white matter volume. Diffusion Tensor Imaging (DTI) indices of white matter integrity in this population typically show increased mean diffusivity and decreased anisotropy relative to normal control children. More recently, there has been investigation of potential regional effects of CRT on white matter. These studies have generally been limited to relatively diffuse regions of white matter (i.e., frontal regions) as opposed to defined white matter tracts. Examining the integrity of specific white matter pathways is important for delineating not only effects of CRT, but also the impact of the tumor and related surgical defects. The posterior fossa is the most common location of tumors in childhood. The impact of these tumors and their treatment may damage cerebellar-cerebral pathways important in mediating motor and cognitive function. We used probabilistic tractography to delineate the main white matter pathway from the cerebellum to cerebral cortex (via the red nucleus and ventro-lateral thalamus) bilaterally. We then examined differences in FA for children treated with CRT relative to control subjects within these tractography based regions of interest.

Subjects and Methods: Seven patients treated with CRT for medulloblastoma (mean age = 10.11; mean IQ = 88.57) and 7 control children (mean age = 9.27; mean IQ = 108.57) participated in the study. Data was acquired with a GE LX 1.5T MRI scanner using a single shot spin echo DTI sequence with an EPI readout (25-31 directions, TE/TR=100/6000ms, 128 x 128 matrix, FOV = 24 cm, rbw = 125 kHz): 42 contiguous axial slices (3 mm) were acquired from the base of the cerebellum to the top of the cerebrum. Using the b0, regions of interest that were manually placed bilaterally on the superior cerebellar peduncle and were subsequently used to seed probabilistic tractography of the cerebellar-cortical pathway on both the left and right side [1]: way-ward seed placement was based on existing models of cerebellar-cerebral connectivity and directed the pathway through the red nucleus and ventro-lateral thalamus on the contra-lateral side (Figure 1). Seed size was standardized across subjects. The resulting tracts were used as regions of interest to extract mean FA.

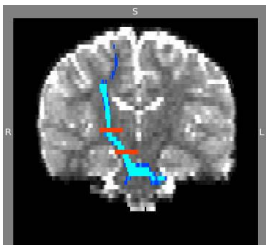

Figure 1: Wayward seeds placed at the red nucleus and ventro-lateral thalamus

Results: Tracts were produced that clearly replicated the cerebellar-cerebral pathway that has been delineated in prior models for both patients and normal controls (Figure 2). Notably, the tracts cross over to the contra-lateral side from the cerebellar seed in the expected location of the pontine decussation. Furthermore, the tracts extended from the ventro-lateral thalamus to cortex which is consistent with existing models. Mean FA was decreased in patients relative to controls for the tract seeded from the right cerebellum

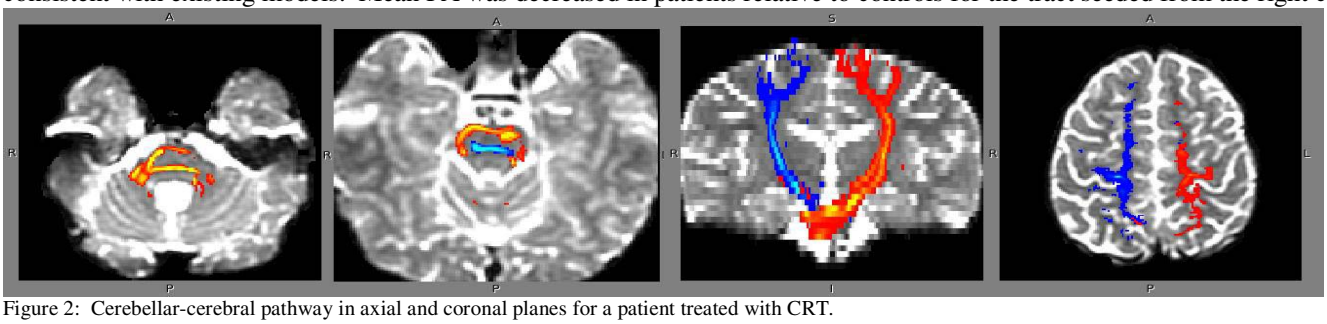

Figure 2: Cerebellar-cerebral pathway in axial and coronal planes for a patient treated with CRT.

and extending to left cerebral cortex (patients = .46, controls = .51, $p < .01$). Mean FA was also decreased for patients in the tract seeded from the left cerebellum extending to right cerebral cortex (patients = .47, controls = .50) but this effect was not statistically significant likely due to the small sample size.

Conclusions: Using a tractography-based region of interest methodology, we documented compromised white matter integrity for the cerebellar-cerebral pathway in patients treated with CRT relative to controls. The ability to identify differences in the integrity of white matter for specific pathways is an important first step in localizing the regional effects of posterior fossa tumors and CRT. Given the hypothesized relevance of cerebellar-cerebral connections for cognitive function, and that we have demonstrated that these connections are likely disrupted in PF patients treated with CRT, we plan to examine the relations between white matter integrity and cognitive function as we acquire a larger sample of participants.

Reference: [1] Behrens TEJ., *et al*. (2003) MRM. 50:1077