DTI measures of white matter following cranial radiation for pediatric brain tumors

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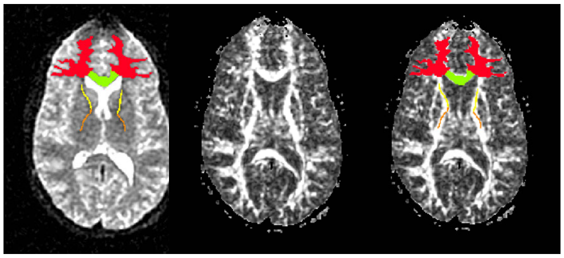
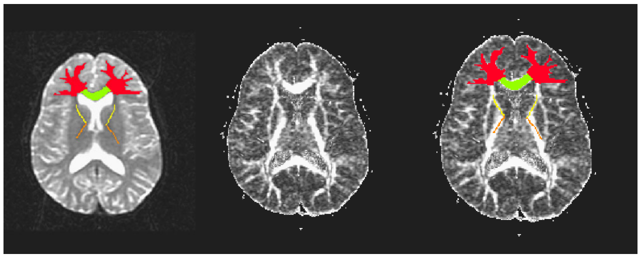
Introduction and Purpose: Treatment with cranial-spinal radiation (CRT) is often required for effective control of aggressive pediatric brain tumours, such as medulloblastoma. Unfortunately, this modality is consistently associated with adverse late effects. Demyelination is the most striking anatomical change following CRT, and has generally been documented as T2 hyper-intensity. Further, a progressive decline in intelligence has been noted following CRT and this decline has been related to white matter volume loss. Diffusion Tensor Imaging (DTI) has significant potential for studying white matter microstructure and axonal integrity following radiotherapy. We examined differences in Fractional Anisotropy for children treated with CRT relative to control subjects.

Subjects and Methods: Six patients treated with CRT for medulloblastoma and 7 control children participated in the study. Data were acquired with a GE LX 1.5T MRI scanner using a single shot spin echo DTI sequence with an EPI readout (25 directions, TE/TR=100/6000ms, 22 contiguous axial slices, 3 mm thick, 128 x 128 matrix, FOV = 24 cm, rbw = 125 kHz). Fractional Anisotropy (FA) was evaluated using a region of interest (ROI) approach in the genu of the corpus callosum (CC), the anterior and posterior limb of the internal capsule (ALIC and PLIC), and the inferior frontal white matter (IFWM). ROI's were drawn on the T2 image, which was registered with the FA map.

ROIs on the T2 and FA map for Control Subject



ROIs on the T2 and FA map for a subject treated with CRT



Mean FA was calculated for each ROI and a 2 (group) x 4 (ROI) analysis of variance with repeated measures on the last variable was conducted to compare overall FA for patients treated with CRT relative to the control sample across the 4 regions of interest. Further, one way analysis of variance was conducted to evaluate group differences within each ROI. Intra-rater reliability was calculated for the entire sample by computing the correlation between mean FA values for each ROI placed 2 different times by the same individual. Inter-rater reliability was calculated for the control sample only by computing the correlation between mean FA values for each ROI as placed by 2 different individuals.

Results: High intra- and inter-rater reliability of mean FA was observed for all ROIs (Table 1). Mean FA across ROIs was lower in the CRT group relative to controls (0.37 versus 0.49), $\underline{p} < 0.01$. Further, FA for the total sample was significantly higher in the CC relative to the ALIC, PLIC, and IFWM, $\underline{p} < 0.01$ (Table 1). Mean FA did not differ between the ALIC and PLIC, but was significantly higher in these areas, relative to the IFWM, $\underline{p} < 0.01$ (Table 1). Finally, mean FA was significantly lower in each ROI for patients treated with CRT relative to controls (Table 1).

Table 1

Group	*N*	Genu of Corpus Callosum		Anterior Limb of the Internal Capsule		Posterior Limb of the Internal Capsule		Inferior Frontal White Matter	
		FA	Reliability	FA	Reliability	FA	Reliability	FA	Reliability
Total	13	0.54	0.97	0.43	0.99	0.46	0.96	0.31	0.99
Control	7	0.58[a]	0.86	0.50[a]	0.88	0.52[a]	0.94	0.36[a]	0.88
CRT	6	0.49[b]	-	0.35[b]	-	0.39[b]	-	0.24[b]	-

FA values with different superscripts within a column differ at $\underline{p} < 0.01$

Conclusions: Values between the ROIs were consistent with the expected anatomical microstructure: for example highest FA was observed in the CC, a structure with substantial directionality in fiber orientation, and lowest FA was observed in the IFWM. FA appears to be sensitive to white matter and fiber damage following CRT for pediatric brain tumors. Lower FA values, indicating decreased directionality in water diffusion, were observed in the CC, ALIC, PLIC, and IFWM for patients treated with CRT relative to controls. These findings are consistent with compromised white matter microstructure and/or fiber integrity that is not visualised on typical clinical sequences. Quantitative measures of white matter integrity are essential for examining the relations between brain structure/function and neurobehavioral outcome in children treated with cranial radiation.