Evaluating the Impact of Cancer Therapy on the Developing Brain

W. E. Reddick[1], J. O. Glass[1], J. J. Jain[1], N. S. Phillips[1], Q. Ji[1], R. J. Ogg[1], T. E. Merchant[2], A. Gajjar[3]

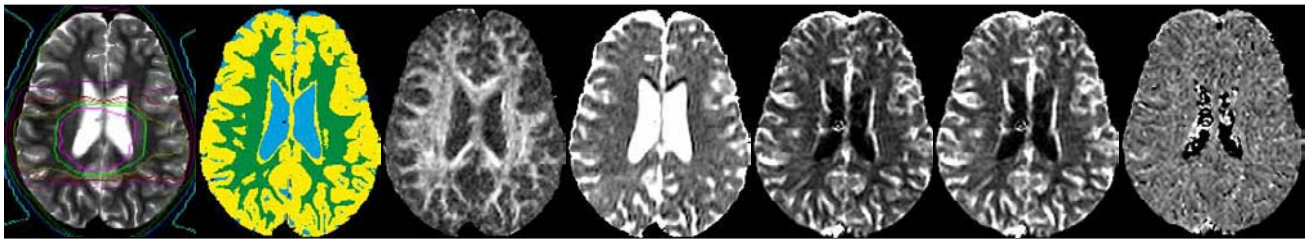
[1]Div Translational Imaging Research, St. Jude Children's Research Hospital, Memphis, TN, United States, [2]Div Radiation Oncology, St. Jude Children's Research Hospital, Memphis, TN, United States, [3]Dept Hematology / Oncology, St. Jude Children's Research Hospital, Memphis, TN, United States

PURPOSE

The combination of radiation and chemotherapy, although effective for long term survival of patients with tumors of the CNS, induce normal tissue effects that result in neurocognitive, endocrine and neurologic deficits. This study presents a comprehensive MR evaluation of the impact of cancer therapy on the developing brains of children treated for cancer.

METHODS

Conventional imaging for tissue segmentation, dynamic-susceptibility contrast imaging, and diffusion tensor imaging were all fused with composite radiation dosimetry to assess WM after craniospinal irradiation and chemotherapy. Comprehensive MR evaluations were conducted at baseline, post cranial irradiation, and at 12 month follow-up for five subjects and divided into anterior/posterior and left/right quadrants. A Kohonen Self Organizing Map (SOM) was used to segment conventional brain images into normal appearing white matter, gray matter, and CSF [1]. The dynamic-susceptibility contrast imaging was analyzed voxel-by-voxel using an automated technique to determine the local arterial input function by the selection of best-candidate arterial pixels using a Kohonen Self-Organizing Map (SOM). This AIF is used in subsequent SVD analyses to produce absolute quantification of cerebral blood flow (CBF), volume (CBV), and mean transit time (MTT). The diffusion images were processed using Diffusion Toolbox 2.0 [2] installed in SPM2 to generate fractional anisotropy (FA) and apparent diffusion coefficient (ADC) maps. The parametric values for the four regions were extracted from the registered maps and analyzed across the five subjects using a paired t-test. Figure 1 illustrates the T2 with composite dose overlay, SOM classified segmentation map, and the registered FA, ADC, CBV, CBF and MTT maps in that order.



RESULTS

Table 1 summarizes the mean values for each of the parameters in each of the four regions across the five subjects. Mean RT dose levels in the posterior regions were higher than those in the anterior regions. White matter volumes in all four regions increased immediately post irradiation but returned to baseline values by the 12 month follow-up. Diffusion measures of ADC in the posterior quadrants decreased significantly immediately post irradiation and were still depressed at the follow-up. CBV and CBF values were not significantly changed over this time period but MTT was significantly shorter at the 12 month follow-up compared to baseline.

ANT-R (36.85 Gy)							**POST-R** (41.66 Gy)					
Time Point	**NAWM**	**FA**	**ADC**	**CBV**	**CBF**	**MTT**	**NAWM**	**FA**	**ADC**	**CBV**	**CBF**	**MTT**
Baseline	34.54	0.32	0.79	3.1%	30.78	2.92	51.81	0.36	0.79	3.3%	29.94	3.17
Post RT	37.16	0.33	0.77	3.2%	31.86	3.03	56.27	0.38	0.77	3.3%	31.08	3.14
12 mo	33.37	0.35	0.73	3.1%	34.38	2.69	51.33	0.38	0.76	3.5%	36.6	2.80
Base vs Pre RT	0.007						0.004		0.048			
Base vs 12 mo			0.048						0.032			0.028
Pre RT vs 12 mo	0.001	0.046	0.055				0.015					
ANT-L (36.54 Gy)							**POST-L** (41.38 Gy)					
Time Point	**NAWM**	**FA**	**ADC**	**CBV**	**CBF**	**MTT**	**NAWM**	**FA**	**ADC**	**CBV**	**CBF**	**MTT**
Baseline	33.56	0.34	0.77	3.2%	31.56	3.01	53.00	0.36	0.79	3.3%	29.76	3.18
Post RT	35.45	0.33	0.77	3.1%	31.02	2.99	56.00	0.37	0.76	3.2%	30.78	3.12
12 mo	32.90	0.35	0.73	3.2%	35.34	2.71	53.27	0.36	0.76	3.6%	38.70	2.78
Base vs Pre RT	0.007						0.030		0.008			
Base vs 12 mo			0.066						0.055		0.052	0.028
Pre RT vs 12 mo	0.013									0.001		

CONCLUSIONS

A comprehensive and quantitative MR evaluation of the impact of cancer therapy on the developing brains of children treated for brain tumors will facilitate the development of early non-invasive markers of neurotoxicity and aid in treatment design. Future work focuses on understanding the physiological changes causing the observed.

REFERENCES 1. Reddick et al, *Neuro-oncol,* 7(1):12-9, 2005. 2. Basser et al., *J Magn Reson B*, 103(3):247-54, 1994.