AbstractID: 8764 Title: Early Blood-Brain-Barrier Disruption in Response to RT as a Biomarker for Neurotoxicity

Purpose: Studies of neurocognitive dysfunction after radiation in animals suggest that vascular injury plays a key role. We hypothesized that blood-brain-barrier (BBB) disruption in normal appearing cerebral tissue of patients early in the course of fractionated radiation therapy (RT) is a biomarker for delayed neurocognitive dysfunction. Methods: Ten patients with low-grade glioma, or suprasellar lesion and underwent 3D conformal cranial RT (28-33 fx of 1.8 Gy) participated in a prospective MRI study. Dynamic-contrast enhanced (DEC) MRI was acquired before, at week 3 and week 6 during the course of, and at 1, 6 and 18 months after the completion of RT. Using the modified Toft model, the contrast transfer constant (K) from the intravascular space to the extravascular extracellular space was estimated. A battery of standardized neuropsychological tests was performed at the same times as the pre- and post-RT MRI. The relationship between the temporal changes in K and the dosimetric parameters was analyzed by a linear mixed model. Correlations between the changes in K and early delayed changes in the neurocognitve functions were analyzed by linear regression. Results: The K values increased significantly in normal appearing tissue regions that received >40 Gy at week 6 during RT ($p<0.05$), suggesting BBB opening. The elevated K values decreased gradually after RT. The changes in K both during and after RT were significantly correlated with the doses received at the time but the significance decreased from $p = 0.0001$ at week 3 during RT to 0.03 at 6 months after RT. The changes in K of left frontal lobe at week 3 during RT were significantly negatively correlated with the changes in verbal learning scores at 6 months after RT ($p<0.02$). Conclusion: Our data suggest early BBB disruption could be a biomarker for delayed neurocognitve function deterioration.

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