Quantitative Metrics derived from DCE MRI as a Biomarker for Early Response to Radiation Therapy in Brain Metastases

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Introduction: The response of metastatic lesions to whole brain radiation therapy (WBRT) is markedly heterogeneous. Changes in cerebral blood volume (CBV) and blood flow (CBF) of primary brain tumors during RT have been shown to correlate with treatment outcome. Based on these observations, a prospective study was conducted to evaluate quantitative metrics derived from dynamic contrast enhanced (DCE) MRI as early biomarkers of response of brain metastases to WBRT. We hypothesize that changes in CBV and CBF in metastatic lesions are better predictors of response than conventional MRI-derived metrics.

Methods and Materials: DCE MRI was acquired in 20 patients treated with WBRT for brain metastases prior to, at the end of, and 1 month after the completion of therapy. Histology included melanoma (12), NSCLC (6), renal cell (1), and squamous cell carcinoma of the head and neck (1). 3D volumetric DCE MRI covered the whole brain with isotropic voxels (2x2x2 mm^3), TR/TE=5.1/1.0 ms, and flip angle=20^o. A total of 40 dynamic phases were acquired during a single dose injection of Gd-DTPA. The general Toft model was used to derive K^{trans} and vascular volume (Vp). A perfusion index (PI), the ratio of the maximum slope of contrast uptake to the maximum of the artery input function, was estimated. Changes in K^{trans}, Vp and PI following WBRT were evaluated for association with response (tumor volumetric reduction greater 25% 1-3 months after WBRT).

Results: 21 of 47 analyzed lesions (45%) were responsive. At the end of WBRT as compared to pre therapy, the mean Vp decreased in the responsive lesions (-0.57$\pm$0.31 mL/100g) but increased in the non-responsive lesions (0.51$\pm$0.18), with significant differences between these two groups ($p<0.005$). This difference was more robust for the lesions with a volume > 1cc than those smaller than 1 cc. Similar findings were observed for the PI. For tumor volume > 1cc pre therapy, the mean PI decreased by -20.3%$\pm$7.6% in the responsive lesions but increased by 19.4%$\pm$8.1% in the non-responsive lesions at the end of RT, and this difference was significant ($p<0.002$). Changes in K^{trans} at the end of WBRT did not differentiate responsive lesions from non-responsive ones.

Conclusion: In this study we demonstrate that quantitative metrics derived from DCE MRI are potential biomarkers for early assessment of treatment response in brain metastases to WBRT. This requires further validation, but may provide a means for individualizing therapy in patients with brain metastases by selecting patients requiring treatment intensification with stereotactic RT.

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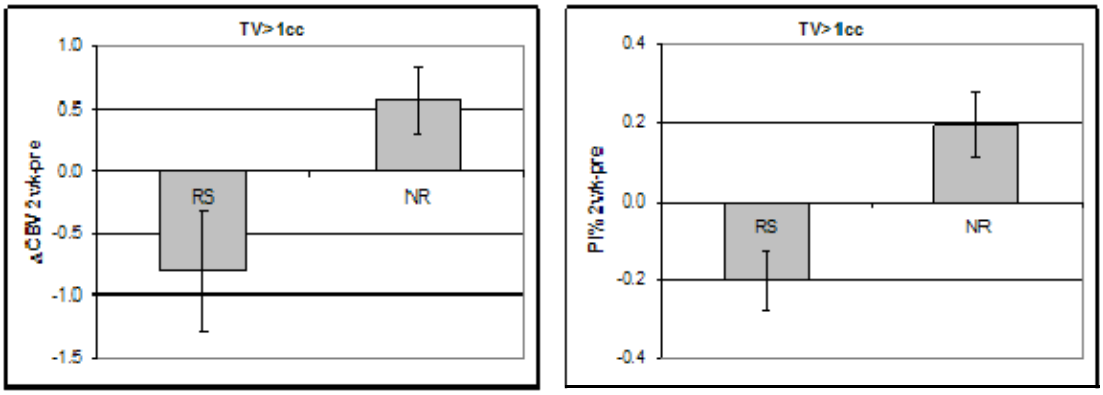

RS: responsive lesions; NR: non-responsive lesions.