Purpose: To develop an image analysis framework to delineate the physiological imaging-defined subvolumes of a tumor in relating to treatment response and outcome.

Methods: Our proposed approach is designed to delineate subvolumes of a tumor based upon its heterogeneous distributions of physiological imaging parameters. The method assigns each voxel a probabilistic membership function belonging to the physiological parameter classes based upon a sample of tumors, and then calculates the related subvolumes for each tumor. We applied our approach to regional cerebral blood volume (rCBV) and Gd-DTAP transfer constant (Ktrans) images of patients who had brain metastases and were treated by whole brain radiation therapy (WBRT). Forty five lesions were included in the analysis. Changes in the rCBV (or Ktrans)-defined subvolumes of the tumors from pre RT to 2 weeks (2W) after the start of WBRT were evaluated for differentiation of responsive, stable and non-responsive tumors using Mann-Whitney U test. Performance of the newly developed metrics for predicting tumor response to WBRT was evaluated by Receiver Operating Characteristic (ROC) analysis.

Results: The percentage decrease in the high-CBV defined subvolumes of the tumors from pre-RT to 2W was significantly greater in the group of responsive tumors than in the group of stable and nonresponsive ones (p<0.007). The change in the high-CBV defined subvolumes of the tumors from pre-RT to 2W was a predictor for post-RT response significantly better than the change in gross tumor volume observed during the same time interval (p=0.0124), suggesting the physiological change occurs prior to the volumetric change. Also, Ktrans did not add significant discriminatory information for assessing response with respect to rCBV.

Conclusions: The physiological imaging-defined subvolumes of the tumors delineated by our method have the potential to be a new imaging response-predictor and a candidate for intensified treatment.

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