Evaluation of a new multimodality voxel-based imaging biomarker for therapeutic response assessment in GBM

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Introduction: Gliomas continue to be the most common form of brain malignancy in adult patients. Even with advancements in the clinical management for these patients, assessment of therapeutic induced response continues to be based on late or serial changes in tumor volume as measured by CT or MRI [1; 2]. The purpose of this study was to evaluate the diagnostic performance of MRI based T1 and rCBV maps analyzed a multi-modality voxel-based analysis referred to as multi-parametric response mapping for early chemoradiation response prediction in patients diagnosed with high-grade gliomas.

Materials/Methods: **Patient***:* Patients (n=23) with Grade III/IV glioma were recruited in a prospective imaging trial. Patients underwent MRI before RT, 1 and 3 weeks after RT. MRI scans were acquired on a 1.5T GE clinical scanner (GE Medical Systems, Milwaukee, WI) or a 3T Philips clinical scanner (Philips Medical Systems, Andover, MA). **MRI**: The MRI protocol included fluid-attenuated inversion recovery imaging (FLAIR), quantitative T1 mapping, dynamic contrast-susceptibility (DSC) T2*-weighted imaging and contrast-enhanced T1-weighted imaging. DCS-MRI was performed following an intravenous administration of a standard dose (0.1 mLxkg^{-1}) bolus of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA). The relative cerebral blood volume (rCBV) in the brain and tumor were computed as described previously [3]. **Data analysis**: All images were co-registered to Gd-enhanced T1-weighted images acquired before RT using a fully automated, affine, mutual information-based, simplex optimization algorithm. Following co-registration, the tumor VOIs were manually contoured either on the contrast-enhanced T1-weighted (CE-T1w) or on the FLAIR images by a neuroradiologist and applied to the rCBV and T1maps. For each patient, mid-treatment time point and VOI the percentage change, PRM and mPRM techniques were used to analyze data. Briefly, PRM was performed by calculating the difference in the rCBV values of each voxel within the tumor at mid-treatment values with respective pre-treatment values. A threshold (1.2 a.u.; [3]) was then applied to the absolute difference of the rCBV in a voxel and all like voxels were summed to obtain tumor volume fractions that showed significantly increasing (PRM_{rCBV+}: red), significantly decreasing (PRM_{rCBV-}: blue), and unchanged (PRM_{rCBV0}: green) rCBV values following therapy [3] (Fig. 1b). We used the same procedure for determining the PRM of T1 maps using a 266 ms threshold (Fig. 1a). mPRMs maps were computed by combining both PRMs (T1 and rCBV) in a single color map (Fig. 1c). **Statistics**: Receiver operator characteristic analysis (ROC), assessed for 12 month survival, was used to determine the optimal cutoff for each parameter. The patient population was then stratified based on the optimal cutoffs obtained from the ROC analysis. Overall survival for each parameter was determined using Kaplan-Meier curves and the log-rank test. Statistical significance was assessed at $p<0.05$.

Results: Standard PRM, using T1or rCBV maps (specifically PRM_{T1+} and PRM_{rCBV-} metrics) and percentage change methods were found to be predictive of survival only for specific time of acquisition and VOI used. $mPRM_{T1+/rCBV-}$ significantly identified patients resistant to therapy irrespective of tumor volume delineation on CE-T1w or FLAIR images (Fig. 1d-e) and the time point mid-treatment used (Fig. 1f-g).

Conclusions: Our results show that mPRM improves the sensitivity of quantitative T1 and rCBV maps to predict overall patient survival. This study introduces a new approach for analyzing and combining multi-parametric MR images into a single multi-parametric response map (mPRM). mPRM shows promise as an early and robust imaging biomarker of treatment response in patients diagnosed with high grade gliomas. This novel approach (mPRM) is a very sensitive tool for analysis of multiparametric and/or multimodal data with enhanced sensitivity for early detection of therapy response.

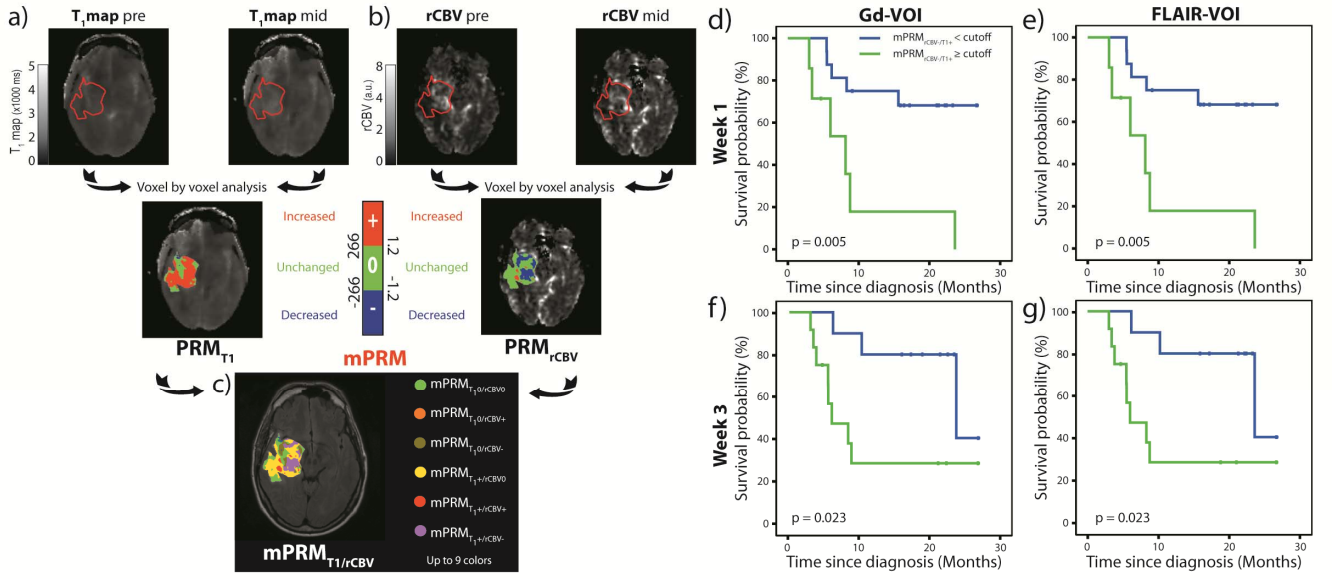

Figure 1: a) Schematic PRM technique used using a single MR map: a) PRM_{T1} or b) PRM_{rCBV}, or c) A combination of two PRMs: $mPRM_{T1/rCBV}$. d-g) Kaplan-Meier survival plots for overall survival, presented as stratified by $mPRM_{rCBV-/T1+}$ at (d, e) week 1 or (f, g) week 3 after treatment initiation and using either (d, f) Gd-VOI or (e, g) FLAIR-VOI. The cutoff of 0.7% was defined as the mean of the optimal cutoff calculated for each time interval post therapy and each VOI.

References:

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