A Composite Model of the Parametric Response Map Predicts Survival Independent of Radiographic Response in Patients with High Grade Glioma


1Radiology, University of Michigan, Ann Arbor, MI, United States, 2Radiation Oncology, University of Michigan, Ann Arbor, MI, United States, 3Biostatistics, University of Michigan, Ann Arbor, MI, United States

Introduction: Assessment of radiographic response (RR) is critical in the management of patients with high-grade glioma. We recently developed the parametric response map (PRM), a method to quantify regional changes in tumor diffusion (apparent diffusion coefficient (ADC)) and perfusion (relative cerebral blood flow (rCBF)) MRI parameters, as an early response metric [1]. Here we evaluated if the combination of PRM_ADC and PRM_CBF would increase their prognostic value.

Methods and Materials:

Patient

Patients (n=44) with Grade III/IV glioma were recruited for this trial. Patients underwent MRI 1-2 weeks before RT and at weeks 3-4 during RT. When MRI was performed at weeks 1-2 during RT, the patients had received a median dose of 12 Gy (range, 5-6). At Weeks 3-4, the median dose was 32 Gy (range, 26-40). 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).

Dynamic Contrast Susceptibility- Magnetic Resonance Imaging

Dynamic contrast-susceptibility (DCS) T2*-weighted imaging with intravenous administration of a standard dose (0.1 mL/kg) bolus of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA), and post contrast T1-weighted images were acquired by a gradient-echo echo-planar imaging pulse sequence (TR=2s, T2=60ms, field of view 220x220 mm², matrix 128x128, flip angle 60°, and 14 interleaved slices with 6mm thickness and 0mm gap). The relative cerebral blood flow (rCBF) in the brain and tumor were computed as described by Ostergaard [2].

Diffusion Weighted Imaging

Diffusion weighted images were acquired using a single-shot, spin-echo, diffusion-sensitized, echo-planar sequence. Sequence parameters were: TR/TE=10000/100ms; FOV=22cm; matrix=128x128; 24 slices; and slice thickness = 6mm thick. Slices were contiguous with the slice package axial-oblique. Diffusion-weighting was performed with gradients applied along all orthogonal directions with b values of 0 and 1000 s/mm² (b0 and b1, respectively). Scan time was approximately 40 s. The DWIs for the three orthogonal directions and b0 image were used for calculating an ADC map.

Parametric Response Map (PRM)

All images were co-registered to Gd-enhanced T1-weighted images acquired before RT using an automated mutual information and simplex optimization module [3]. Following co-registration, brain tumors were manually contoured on the Gd-enhanced T1-weighted image pre-radiotherapy.

Statistics

Receiver operator characteristic analysis, assessed for 12 month survival, was used to determine the optimal cutoff for V1 and V0 generated individually from PRM_ADC and PRM_CBF. For each PRM analysis, the parameter (V1 or V0) that generated the largest area under the curve was used to determine the optimal cutoff. Patient population was then stratified based on these optimal cutoffs. The composite model comprised of information from both PRM_ADC at week 3 and PRM_CBF at week 1: 1) patients found to be non-responders by both methods, 2) patients found to be responders by both methods and 3) patients where both methods conflict. PRM_ADC at week 3 and PRM_CBF at week 1 were empirically determined to be the 95% confidence intervals calculated from normal contralateral brain tissue.

Results: The differences between PRM_CBF and PRM_ADC are highlighted in Fig. 1. In this figure, a representative slice is provided showing (A) contrast enhancement on a T1-weighted image, (B) PRM_CBF and (C) PRM_ADC color-encoded ROI superimposed onto a Gd-enhanced T1-weighted MR image pre-radiotherapy.

Discussion:

Compared to conventional RR both PRM_ADC and PRM_CBF provided earlier assessments of treatment response that were similarly predictive of overall survival. In addition, the combination of PRM parameters provided the best predictor of overall survival and was independent of RR.

References: