Response Assessment to Immune Checkpoint Inhibitors in Recurrent Glioblastomas using Multiparametric MRI based Prediction Model

Sanjeev Chawla[1], Laiz Laura de Godoy[1], Archith Rajan[1], Arati Desai[2,3], Suyash Mohan[1]

Department of Radiology[1], Abramson Cancer Center[2], and Glioblastoma Translational Center of Excellence[3], Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA.

Introduction: Immune checkpoint inhibitor (ICI)–based immunotherapy has emerged as an alternative treatment modality for recurrent glioblastomas (GBMs). However, it often induces inflammation at the tumor site, known as pseudoprogression (PsP), complicating post-treatment imaging assessment. Standard MRI techniques are frequently inadequate for reliably distinguishing PsP from true progression (TP) following immunotherapy.[1,2] The purpose of this study was to evaluate the performance of our previously established multiparametric MRI–based predictive model[3] in assessing treatment response in GBM patients receiving ICIs.

Methods: Six patients with recurrent GBM treated with ICIs, 4 with pembrolizumab (200mg IV every 3 weeks) and 2 with nivolumab (240mg IV every 2 weeks) were included. All patients underwent 3T MRI at baseline (prior to initiation of ICI) and follow-up periods (post-ICI). Tumor progression was determined based on a combination of clinical status and mRANO criteria. In our previous study, a prediction model was developed based on the histological analyses of tumor specimens collected after repeat surgery from GBM patients receiving standard therapy and had an accuracy of over 90% in determining TP and PsP cases. This multiparametric model consisted of predictive probabilities (PP) of tumor progression computed from diffusion and perfusion MRI-derived parameters (fractional anisotropy, coefficient of linear anisotropy and maximum cerebral blood volume) from contrast-enhancing regions of neoplasms. We used prediction model[3] to compute the PPs of tumor progression at each time point. Lesions were considered TP if PP was ≥ 50% and PsP if PP was < 50%.[4] The PP values were validated using overall survival, clinical status, and mRANO criteria.

Results: Cases 1, 5, and 6 were classified as TP at baseline, and the PP values stayed high at all time points, suggesting true TP. Cases 2 and 3 were classified as TP at baseline and showed decreased PP after immunotherapy. But case 3 was still classified as TP at the 2-month follow-up. Case 4 had low PP at baseline and demonstrated increased PP consistent with TP after immunotherapy 1 and 2 months later. In summary, 4 patients were classified as TP and 1 patient as PsP by our multiparametric model. Overall, the TP patients showed marked increased tumor volume compared to the baseline in the 3-month MRI follow-up, confirming true TP by the mRANO criteria. Although case 2 showed a continued increase in tumor volume in the first 2 months, the tumor volume decreased to baseline level 3 months after the initiation of the trial, suggesting treatment response (**Table 1**).

Conclusion: Our preliminary findings demonstrate that multiparametric MRI based prediction model may be used as a potential surrogate endpoint for assessment of treatment response in patients with recurrent GBM receiving ICIs.

Table 1. Characteristics of GBM patients treated with anti-PD1 therapy.

Patient	PP-Baseline MRI	Baseline MRI vol.	1st MRI PP	1st MRI vol.	2st MRI PP	2st MRI vol.	3rd MRI PP	3rd MRI vol.	PP Results	mRANO Results	OS from Trial (days)	OS from Diagnosis (days)
1	93%	3.4	99%	6.3	90%	13	98%	20	TP	TP	356	697
2	99%	6	38%	9.2	49.3%	10.9	45.2%	6.3	PsP	PsP	307	738
3	97%	132.7	83%	197.5	80%	140.1			TP	TP	118	479
4	26%	13.4	96%	15.7	98%	23.8			TP	TP	97	634
5	99%	0.9	96%	3.5	99%	10.2	100%	14	TP	TP	240	570
6	99%	14.6	99%	5	98%	10.8	94%	14.9	TP	TP	90	600

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