

# Imaging Glioblastoma Posttreatment Progression, Pseudoprogression, Pseudoresponse, Radiation Necrosis



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## KEYWORDS

• Glioblastoma • Pseudoprogression • Pseudoresponse • Radiation necrosis

## KEY POINTS

- Various assessment guidelines for tumor progression, primarily designed for the purpose of phase 2 clinical trials, have been used over the course of the past several decades, with changes over time reflecting evolution in the approach to treatment and technological advances in imaging.
- Radiation necrosis and pseudoprogression are often thought of as 2 opposite extremes on the spectrum of radiation-induced injury, and imaging features may mimic disease progression.
- Pseudoresponse occurs in the setting of antiangiogenic therapy, and imaging findings include decreased contrast enhancement, edema, and permeability as early as 1 day after initiation of therapy.
- A multimodality approach to treatment response coupled with an understanding of the strengths and limitations of various imaging techniques is essential to accurate assessment of treatment response.

## INTRODUCTION

Eighty percent of all malignant primary brain tumors diagnosed in the United States are gliomas.<sup>1</sup> The current treatment paradigm for high-grade gliomas (grades III and IV) includes maximal surgical resection followed by concurrent adjuvant radiation and chemotherapy. The relatively recent addition of adjuvant chemotherapy with an oral alkylating agent, temozolomide, is based on pivotal data published in 2005 by Stupp and colleagues,<sup>2</sup> which demonstrated a clinically meaningful and statistically significant overall survival benefit with minimal additional toxicity.

For patients with primary treatment failure or recurrence, the Food and Drug Administration

approved the use of bevacizumab, an anti-vascular endothelial growth factor (VEGF) monoclonal antibody, in 2009.<sup>3</sup> In addition, there are many experimental therapies currently under active investigation for patients with recurrent glioblastoma. These include immunomodulatory approaches, such as immune checkpoint inhibitors, tumor vaccines, chimeric antigen receptor (CAR)-modified T-cell therapy, and oncolytic virotherapy. Recently developed immune checkpoint inhibitors such as anti-CTLA-4 (ipilimumab) and anti-PD-1 (pembrolizumab and nivolumab) antibodies have demonstrated clinical efficacy in several solid tumors, with clinical trials for glioblastoma ongoing. Examples of viruses currently under investigation in patients with recurrent glioblastoma include an

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