

State of the art: the evolving role of RT in combined modality therapy for GBM

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I have not yet begun to Fight!
-Captain John Paul Jones, September 23, 1779

This special issue of the *Journal of Neuro-oncology* includes a comprehensive review of the state of the art for glioblastoma (GBM), and the evolving role of radiation therapy (RT) in the management of this disease. In the first article by Corso et al., the history of RT in the management of GBM is summarized, followed by a review of modern RT approaches in the context of combined modality therapy. Kirkpatrick et al. address key concepts in RT delivery, including the optimal treatment volumes, total dose and fractionation schemes, and also new and emerging RT modalities, such as particle therapy. Ellingson et al. provide a timely review of the challenges in differentiating true disease progression from pseudoprogression and radionecrosis in GBM. Their discussion also highlights the effects and complex interplay of cytotoxic therapies and immunotherapies in imaging interpretation. With the emergence of combined modality therapy as standard of care for GBM, Ludwig and Kornblum review key

biomarkers in glioma, which are now informing selection and stratification of patients for clinical trials. Bindra et al. profile the landscape of radiosensitizers for GBM, and they ask the provocative question of whether these agents are “Dead in the Water...or just the beginning (of a new era)?” Howard et al. review the evolving role of re-irradiation in recurrent GBM, either as a stand-alone salvage treatment, or in combination with systemic therapies. Sahebjam et al. provide a detailed review of immunotherapy combined with RT in GBM, and they cover key topics related to immunity in the CNS, that are relevant for therapeutic efficacy. Braunstein et al. present the current molecular landscape of pediatric high-grade gliomas, along with a review of current treatment strategies and recommendations for these tumors. Finally, Kunos et al. review key aspects of radiation-agent combinations for GBM, with an eye on relevant molecular features and novel tools to better model therapeutic interactions and design innovative clinical strategies.

The quotation from John Paul Jones above perfectly captures the state of affairs for our war on GBM. As captain of the flagship *Bonhomme Richard*, Jones was engaged in heavy battle with the Royal Navy during the Battle of Flamborough Head, a famous revolutionary war battle in 1779. Outgunned and outmanned by the Royal Navy, the *Bonhomme Richard* caught fire and began to sink. When asked by the British commander to surrender, Jones quickly retorted his historic words of defiance: “I have not yet begun to fight!” He went on to surprise the Royal Navy by winning the battle, a victory that largely was attributed to the sheer determination and relentless efforts by Captain Jones and his fearless crew.

Our field has encountered myriad past failures and disappointments in our quest to conquer GBM. However, as described in this special issue, our understanding of this disease, along with a number of exciting new technologies and

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multidisciplinary therapeutic options that are now available, make us quite optimistic about the future. Indeed, we have not yet begun to fight!

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