

## Comparison of central nervous system toxicity profiles following radiosurgery versus whole brain radiation

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## Abstract

**Objectives:** Immunotherapy is increasingly used for patients with advanced malignancies, many of whom will also require treatment for brain metastases at some point. However, the safety of brain radiation after immunotherapy is unknown. We therefore sought to compare the toxicity profiles of GammaKnife radiosurgery (GKRS) vs. whole brain radiation (WBRT) among patients treated with immunotherapy.

**Methods:** Patients treated with checkpoint inhibitor immunotherapy at our institution that also received GKRS or WBRT before or after the initiation of immunotherapy were identified. Toxicity data were obtained and classified according to CTCAE v5.0. Fisher's exact test was used to compare occurrence of acute grade 3+ toxicity between courses of GKRS vs. WBRT, as well as within GKRS and WBRT groups based upon relative timing of radiation and the initiation of immunotherapy.

**Results:** 94 courses were identified, consisting of 71 GKRS (33 before and 38 after immunotherapy) and 23 WBRT courses (8 before and 15 after immunotherapy). Grade 3+ toxicity occurred in 3 (9.4%) of GKRS courses before and 4 (10.8%) of courses after immunotherapy ( $p=0.58$ ). WBRT after immunotherapy was associated with a non-statistically significant increase in grade 3+ toxicity (42.9% vs. 12.5%, respectively,  $p=0.19$ ). Rates of grade 3+ toxicity of either GKRS or WBRT before immunotherapy did not differ (9.4% vs. 12.5%,  $p=0.99$ ). Grade 3+ toxicity was significantly higher with WBRT vs. GKRS when delivered after immunotherapy (42.9% vs. 10.8%,  $p=0.02$ ). Acute grade 4 cerebral edema occurred in 4 WBRT courses following immunotherapy (26.7%).

**Conclusions:** GKRS appears safe whether delivered before or after checkpoint inhibitor immunotherapy. Conversely, WBRT delivered after immunotherapy is associated with heightened rates of grade 3+ toxicity, including life-threatening cerebral edema in approximately one quarter of courses in this sample. These results provide an early assessment of the safety of integrating immunotherapy and brain radiation, and require further validation.

### Open Access

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