

## ABSTRACT

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Phase I/II Dose-Escalation Trial of 3-Fraction Stereotactic Radiosurgery for Resection Cavities From Large Brain Metastases: Health-related Quality of Life Outcomes.

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**OBJECTIVES:** We investigated differences in quality of life (QoL) in patients enrolled on a phase I/II dose-escalation study of 3-fraction resection cavity stereotactic radiosurgery (SRS) for large brain metastases.

**METHODS:** Eligible patients had 1 to 4 brain metastases, one of which was a resection cavity 4.2 to 33.5 cm<sup>3</sup>. European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaires core-30 (QLQ-30) and brain cancer specific module (QLQ-BN20) were obtained before SRS and at each follow-up. Nine scales were analyzed (global health status; physical, social, and emotional functioning; motor dysfunction, communication deficit, fatigue, insomnia, and future uncertainty). QoL was assessed with mixed effects models. Differences  $\geq 10$  points with q-value (adjusted P-value to account for multiplicity of testing)  $< 0.10$  were considered significant.

**RESULTS:** Between 2009 and 2014, 50 enrolled patients completed 277 QoL questionnaires. Median questionnaire follow-up was 11.8 months. After SRS, insomnia demonstrated significant improvement (q=0.032, -17.7 points at 15 mo post-SRS), and future uncertainty demonstrated significant worsening (q=0.018, +9.9 points at 15 mo post-SRS). Following intracranial progression and salvage SRS, there were no significant QoL changes. The impact of salvage whole brain radiotherapy could not be assessed because of limited data (n=4 patients). In the 28% of patients that had adverse radiation effect, QoL had significant worsening in 3 metrics (physical functioning, q=0.024, emotional functioning q=0.001, and future uncertainty, q=0.004).

**CONCLUSIONS:** For patients treated with 3-fraction SRS for large brain metastasis cavities, 8 of 9 QoL metrics were unchanged or improved after initial SRS. Intracranial tumor progression and salvage SRS did not impact QoL. Adverse radiation effect may be associated with at least short-term QoL impairments, but requires further investigation.

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