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Comparison of Local Control of Brain Metastasis with Stereotactic Radiosurgery versus Surgical Resection: A Secondary Analysis of EORTC 22952-26001

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#### Abstract

Objectives: There are no randomized trials comparing outcomes of stereotactic radiosurgery (SRS) versus neurosurgical resection in the management of limited brain metastases. We sought to evaluate local control of brain metastases among patients treated with SRS versus neurosurgical resection within EORTC 22952.

Methods: The EORTC 22952 trial randomized patients with 1-3 brain metastases to whole brain radiotherapy (WBRT) versus observation after complete surgical resection or prior to SRS. We performed an unplanned exploratory analysis to compare local control of patients treated with SRS versus surgical resection. We included patients treated per protocol who had 1-2 brain metastases and tumors < 4 cm (for generalizability). The primary endpoint was local recurrence (intracranial recurrence of a previously treated site) defined as time from randomization to recurrence. We compared local control according to modality by calculating cumulative incidence of local recurrence and used competing risk regression to adjust for prognostic factors and competing risk of death.

Results: A total of 268 patients were analyzed; 57.5% underwent SRS and 42.5% underwent surgical resection. Median follow-up was 13.5 months. Compared to SRS, patients undergoing surgery had larger tumors (median 20 mm vs. 28 mm, p < 0.001), more frequently presented with 1 brain metastasis (74 % vs. 98 %, p < 0.001), and differed in location (p < 0.001) with surgery more common among frontal and posterior fossa locations. Overall, SRS was associated with improved local control (p = 0.015) in unadjusted analyses, but absolute differences in local control decreased with time (p < 0.001 for interaction). Unadjusted cumulative incidence of local recurrence by modality in the SRS vs. surgery group, respectively, were as follows: 3 months (2.0% vs. 15.8%), 6 months (9.8% vs. 29.1%), 9 months (17.0% vs. 35.4%), 12 months (22.9% vs. 37.2%), and 24 months (28.5% vs. 40.2%). Rates of local control were similar by modality in the WBRT group (p = 0.398) while SRS exhibited improved local control than surgery

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in the non-WBRT group (p = 0.012).In adjusted models, surgical patients had a much higher early (0-3 months) risk of local recurrence compared to SRS patients HR [95% CI] = 5.94 [1.72-20.45], but their risk decreased with time: 3-6 months = 1.37 [0.64-2.90], 6-9 months = 0.75 [0.28-2.00]. At >= 9 months, local control appeared superior for surgery: 0.36 [0.14-0.93]. Increased risk of local recurrence was also associated with increasing tumor size (p = 0.031) and absence of macroscopic tumor outside of brain (p = 0.044).

Conclusions: In this exploratory analysis of phase III data, SRS appeared associated with improved early local control of treated lesions compared to patients treated surgically, although the relative benefit decreased with time. Differences in baseline patient characteristics between modalities limit this analysis warranting further prospective study.