Conclusion: Analogous to HER2+ breast cancer BM patients, gene mutations profoundly influence survival (positively for EGFR and ALK, negatively for KRAS) in pts with lung adenocarcinoma and BM. Compared to prior reports, MS in this cohort was substantially longer. Transition to a DS晚期-GPA incorporating molecular variables will aid clinical decision making and stratification of future clinical trials.


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A Phase I/II Dose-Escalation Trial of 3-Fraction Stereotactic Radiosurgery (SRS) for Large Resection Cavities of Brain Metastases

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Purpose/Objective(s): RTOG 9005 provided data-based guidelines for single-fraction SRS dosing. No prospective data exist for multiple fraction SRS. We performed a dose-escalation trial to determine the maximum tolerated dose (MTD) of 3-Fraction SRS.

Materials/Methods: Initially designed for both intact and resected brain metastases, institutional practice patterns changed over time to preferentially resect large metastases; accrual to the intact tumor arms was closed. Metastases, institutional practice patterns changed over time to preferentially resect large metastases; accrual to the intact tumor arms was closed. Initially designed for both intact and resected brain metastases, institutional practice patterns changed over time to preferentially resect large metastases; accrual to the intact tumor arms was closed. Reoperation (n=2 patients died of progressive extracranial disease prior to 30 day follow-up, and thus, could not be evaluated for DLTs. As there were no acute DLTs, both arms were escalated to 33 Gy. Median GTV volume was 14 cm³ (range, 5 – 33). See Table for late CNS toxicity: Of 11 patients (22%) with radionecrosis diagnosed on imaging, 4 were resected and pathologically confirmed, 5 (10%) were asymptomatic, 6 (12%) were symptomatic: G2 requiring steroids; n = 1 at 24 Gy and n = 3 at 33 Gy; G4 – urgent surgery; n = 1 at 24 Gy (after both WBRT and SRS) and n = 1 at 30 Gy. With a median follow-up of 11.7 months (range, 2.5–59.5), median OS was 19.8 months. The 12-month cumulative incidence rates of failure were: LF 7.1% (95% CI = 1.8–17.6), DF 50% (95% CI = 35–63), LMD 15% (95% CI = 7–27).

Conclusion: Although the MTD was escalated to 33 Gy per protocol, given that 4 of 12 patients had late toxicity, we recommend a 3-fraction dose of 27 to 30 Gy for cavities of 2–4 cm. Whether these doses are applicable to intact metastases is unknown. Dosimetric analysis of predictors of necrosis is ongoing.


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Comparing Preoperative Stereotactic Radiosurgery (SRS) to Postoperative SRS for Resectable Brain Metastases


Purpose/Objective(s): Postoperative (Post) stereotactic radiosurgery (SRS) alone is an increasingly common treatment for resected brain metastases (BM). Preoperative (Pre) SRS has also been shown to be a viable approach. The goal of this multi-institutional retrospective study was to compare outcomes and toxicities of these two SRS paradigms.

Materials/Methods: We reviewed records of patients who underwent resection of BM and either Pre-SRS or Post-SRS alone from 2005–2013 at 2 institutions. Preoperative SRS consisted of dose-reduced SRS based on lesion size followed by planned resection within 48 hours. Overall Survival (OS) and radiation necrosis were calculated using the product limit method. Cumulative incidence with competing risk of death was used for all other intracranial outcomes. Multivariate analysis (MVA) was performed using the Cox and Fine and Gray models, respectively.

Results: One hundred eighty patients underwent surgical resection for 189 BM: 66 (36.7%) received Pre-SRS and 114 (63.3%) received Post-SRS. Patients were well balanced at baseline except for the pre-SRS cohort having higher rates of ECOG performance status 0 (62.1% vs 4.5%, P = .027) and number of BM (2.5 vs 3.5, P = .002). Several SRS parameters differed between cohorts: pre-SRS had lower median PTV margin (0 vs 1 mm) and peripheral dose (14.5 vs 18 Gy). Median GTV volume (8.3 vs 9.2 cm³, P = .85) and proportion with GTV volume >14 cm³ (33.3% vs 24.2%, P = .24) were similar between the pre-SRS and post-SRS cohorts, respectively. The median imaging follow-up period was 11.1 months for all patients and 24.6 months for alive patients. There was no difference in OS between groups in MVA adjusting for baseline characteristics (hazard ratio [HR] 0.61, P = .14). There was also no difference in local recurrence (LR) and distant brain recurrence (DBR) between cohorts (combined 1-year LR 15.7% and DBR 42.2%). Leptomeningeal disease (LMD) occurrence was higher with post-SRS (19.3% vs 4.5%, P = .01). Multivariate analysis for LMD demonstrated pre-SRS cohort (HR = 0.25, P = .027) and number of BM (HR = 1.3, P = .028) as independent significant factors. The occurrence

Oral Scientific Abstracts 84; Table 1.

<table>
<thead>
<tr>
<th>Arm</th>
<th>Toxicity Grade and Surgical Resection per Dose Level (6 patients per arm)</th>
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<tbody>
<tr>
<td>Arm 1: 4.2–14.1 cc</td>
<td>G1 = 1 G2 = 1 G4 = 1  No No Yes</td>
</tr>
<tr>
<td>Arm 2: 14.2–33.5 cc</td>
<td>G4 = 1  Yes</td>
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