



Patterns of Recurrence and Toxicity for Pre-operative versus Post-operative Stereotactic Radiosurgery (SRS) for Resected Brain Metastases: A Multi-Institutional Analysis

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Introduction

Post-operative (Post) stereotactic radiosurgery (SRS) after resection of brain metastases (BM) is an increasingly accepted regimen. However, pre-operative (Pre) SRS has also been shown to be a viable approach. The goal of this multi-institutional retrospective study was to compare the patterns of failure and toxicities of these two SRS paradigms.

Methods

The records of patients who underwent resection of BM and either Pre-SRS or Post-SRS alone between 2005-2013 at 2 institutions were retrospectively reviewed. Pre-SRS used an approximate 20% dose reduction strategy based on tumor size, followed by planned resection within 48 hours. Cumulative incidence with competing risk of death was used to determine estimated rates.

Results

180 consecutive patients underwent resection of 189 BM, with 66 (36.7%) receiving Pre-SRS and 114 (63.3%) receiving Post-SRS. Median margin (0 vs. 2 mm) and peripheral dose (14.5 vs. 18Gy) differed between cohorts (Pre vs. Post-SRS). However, median GTV volume (8.3 vs. 9.2 cc, p=0.85) and proportion with GTV volume >14cc (33.3% vs. 24.2%, p=0.24) were similar. The median imaging follow-up period was 24.6 months for alive patients. The 2-year rates (Pre-SRS vs. Post-SRS) of cavity local recurrence (LR), distant brain recurrence (DBR), leptomeningeal disease (LMD), radiation necrosis (RN), and symptomatic RN (SRN) were: 22.8% vs. 15.4% (p=0.33), 48% vs. 44.6% (p=0.84), 3.2% vs. 16.6% (p=0.01), 8.2% vs. 28.5% (p=0.001), and 4.9% vs. 16.4% (p=0.01). The composite endpoint of LR, LMD, or SRN occurrence favored the pre-SRS cohort (27.9% vs. 39.3%, p=0.02). Multivariable analyses revealed no difference between groups for overall survival (OS) (p=.1), LR (p=.24), or DBR (p=.75).

Conclusions

Pre-SRS and Post-SRS for resected BM provide similarly favorable rates of cavity local control, DBR, and OS, but with significantly higher rates of RN, symptomatic RN, and LMD occurrence in the post-SRS cohort in both univariate and adjusted analyses. A prospective clinical trial comparing these treatment approaches is warranted.

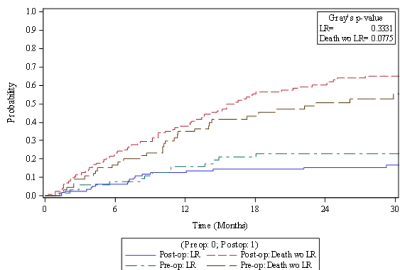
Learning Objectives

By the conclusion of this session, participants should be able to: 1) describe the pre-operative and post-operative SRS paradigms for resected brain metastases, 2) Understand the rates and similarities in local cavity control between strategies, and 3) discuss the differences in toxicity (primarily radiation necrosis) and patterns of recurrence (primarily leptomeningeal disease) between strategies.

References

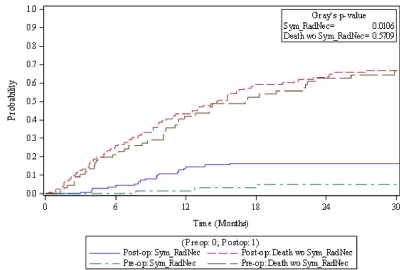
Asher AL, Burri SH, Wiggins WF, et al. A new treatment paradigm: neoadjuvant radiosurgery before surgical resection of brain metastases with analysis of local tumor recurrence. International journal of radiation oncology, biology, physics. Mar 15 2014;88(4):899-906.

Cumulative Incidence of Local Recurrence.



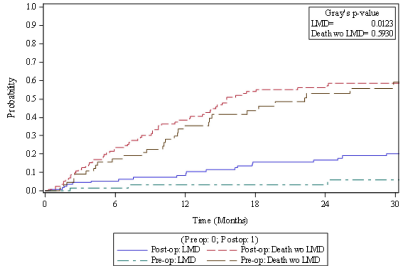
LR = local recurrence. Curves truncated at 30 months.

Cumulative Incidence of Symptomatic Radiation Necrosis.



Sym_RadNec = symptomatic radiation necrosis. Curves truncated at 30 months.

Cumulative Incidence of Leptomeningeal Disease.



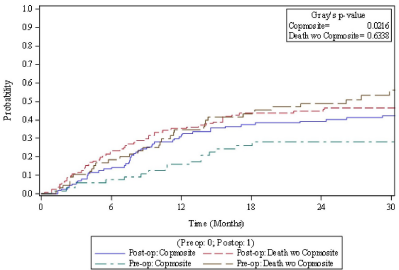
LMD = leptomeningeal disease. Curves truncated at 30 months.

Patient and Treatment Characteristics

	Pre-SRS (n=66 patients or 71 lesions)	Post-SRS (n=114 patients or 118 lesions)	
Median Age	58.2 years	56 years	p=3.7
Institution			
Emory University	0 (0%)	113 (99.1%)	p<.001
Levine Cancer Institute	66 (100%)	1 (0.9%)	
Primary Histology			p=.006
Breast	18 (27.2%)	12 (10.5%)	
NSCLC	24 (36.5%)	45 (42.1%)	
Melanoma	11 (16.6%)	23 (20.2%)	
Other	13 (19.7%)	31 (27.2%)	
ECOG performance status			p<.001
0	41 (62.1%)	32 (28.1%)	
1	15 (22.7%)	64 (56.1%)	
≥2	10 (15.1%)	18 (15.8%)	
Active Systemic Disease			p=.16
Yes	27 (38.5%)	60 (47.4%)	
No	38 (42.5%)	54 (52.6%)	
Number of BM			p=.88
1	43 (65.2%)	78 (68.4%)	
2	18 (27.3%)	23 (21.9%)	
3	4 (6.1%)	9 (7.9%)	
≥4	1 (1.5%)	2 (1.8%)	
BM Location			p=.359
Frontal	23 (35.2%)	51 (43.2%)	
Parietal	19 (28.8%)	28 (23.7%)	
Temporal	11 (15.5%)	9 (7.6%)	
Occipital	2 (2.8%)	7 (5.9%)	
Cerebellum	14 (19.7%)	23 (19.5%)	
Median GTV (cc) (range)	8.3 (0.89-46.8)	9.24 (0.68-54.6)	p=.85
GTV > 14 cc ¹			p=.24
yes	22 (33.3%)	28 (24.5%)	
no	44 (66.6%)	88 (75.5%)	
Median Dose	14.5 Gy	18 Gy	p<.001
Median Margin	0 mm	2 mm	p<.001
Hypofractionated (3.5 fractions)/regimen	0 (0%)	16 (13.6%)	p<.001

NSCLC = non-small cell lung cancer. BM = brain metastases. GTV = gross tumor volume

Cumulative Incidence of Composite Outcome (defined as LR, LMD, or symptomatic RN).



Curves truncated at 30 months.