Clinical Outcomes of Gamma Knife Lightning for Brain Metastases: Consistent Local Control but Size-Dependent Radionecrosis, Influenced by Dosimetric Shifts and Clinician Planning Priorities

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Objectives: To evaluate local control (LC) and radionecrosis (RN) in brain metastases before and after adoption of Gamma Knife Lightning inverse planning, and assess whether treatment era-related dosimetric shifts and clinician plan-selection priorities translated into clinically meaningful changes.

Methods: Retrospective cohort at a single high-volume Gamma Knife center, analyzing consecutive intact brain metastases from lung or breast primaries treated 2020–2024. Patients with < 9 months follow-up were excluded. Lesions were categorized as pre-Lightning (before Jan 1, 2022) or Lightning-era (on/after Jan 1, 2022). Lesions were stratified by volume: small (< 1 cc) and large (≥1 cc). Primary endpoints were LC and RN. RN was compared by chi-square. Cox models assessed LC and RN over time with covariates era and lesion size. Kaplan–Meier curves were generated for LC and RN-free survival, stratified by era and size.

Results: The study cohort included 198 brain metastases (pre-Lightning: 106; Lightning: 92) with comparable primary tumor types (Breast: pre 20, Lightning 7; Lung: pre 86, Lightning 85) and size distributions (pre: 74 small, 32 large; Lightning: 67 small, 25 large) between eras.

Local Control (LC): LC was excellent across both eras. Pooled 12-month LC was 100.0% for small lesions and 91.2% for large lesions. Cox analysis showed no association between era and LC (HR=0.746, p=0.679), whereas lesion size was significantly associated with LC (small vs large: HR=5.792, p=0.013).

Radionecrosis (RN): Overall RN rates were low and not significantly different following Lightning implementation (p=0.299) though crude proportions suggested higher RN in the Lightning era (pre 8.5% [9/106] vs Lightning 13.0% [12/92]). Twelve-month RN-free rates were 98.0% pre-Lightning and 86.6% post-Lightning. Lesion size was significantly associated with RN risk (small vs large: HR=4.033, p=0.003). When stratified by size, RN risk showed a non-significant trend toward higher incidence for small lesions following Lightning implementation (HR=4.615, p=0.062), but no significant difference for larger lesions across eras (HR=1.232, p=0.731). Joint era-size stratification showed 12-month RN-free rates of 100.0% (small) and 93.1% (large) pre-Lightning versus 88.9% (small) and 80.0% (large) in the Lightning era.

Conclusion(s): The adoption of Lightning inverse planning into treatment planning workflow did not impact LC, which remained excellent across eras. This continued excellent LC is particularly reassuring given our previous dosimetric work showing increased selectivity in Lightning-era plans, which could theoretically increase the risk of marginal failure. RN rates were very low overall, a factor

that likely limited the statistical power of this single-institution study to detect significant differences in these rates. Nevertheless, a concerning non-significant trend toward increased RN was observed specifically for small lesions in the Lightning era. This aligns with our prior dosimetric findings of a statistically worse gradient index for small targets in Lightning-era plans. These findings suggest that when selecting Lightning-era plans, careful consideration of gradient index in small lesions may be important to reduce the risk of RN without compromising LC. Larger, prospective studies with standardized dosimetric reporting and explicit documentation of clinician optimization priorities are needed to confirm whether this observed trend is statistically real and clinically relevant.