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Breast Cancer Brain Metastases: Brain Metastasis Velocity and Outcomes After Gamma Knife Radiosurgery and Systemic Targeted Therapy

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Abstract
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Abstract

Objectives: To assess how systemic targeted therapy influences intracranial disease dynamics—specifically brain metastasis velocity (BMV)—and clinical outcomes in patients with brain metastases from breast cancer (BMBC) treated with Gamma Knife radiosurgery (GKRS), including those with extensive intracranial lesion burden.

Methods: A retrospective analysis of 230 BMBC patients treated with GKRS between 2014 and 2024 was performed. Patients were stratified by lesion count (≤4 vs. >4) and by BMV (< 4, 4–13, >13 new lesions/year). Outcomes included overall survival (OS), retreatment rates, and adverse radiation effects (AREs). Kaplan–Meier analysis, chi-square testing, and multivariable regression were used to evaluate factors associated with progression and survival.

Results: GKRS was safe and effective even for patients with high lesion counts (>4, >10, >20), showing no significant differences in OS (median 65.0 vs. 63.0 months), retreatment frequency, or AREs compared with patients with fewer lesions. Systemic targeted therapy was associated with significantly reduced BMV (7.9 vs. 11.4 lesions/year, p = 0.047) and delayed time to retreatment (21 vs. 12 months, p = 0.007), though survival was not improved. Higher BMV predicted increased retreatment and shorter survival post-GKRS (p = 0.005). Molecular subtype correlated with BMV group: 65% of HER2-positive patients were in the low-BMV group, while 75% of triple-negative patients were in the high-BMV group.

Conclusion(s): GKRS offers durable, safe intracranial control even in the setting of extensive metastatic burden. Systemic targeted therapy slows intracranial disease progression and delays retreatment, highlighting its biologic synergy with radiosurgery. BMV serves as a dynamic biomarker of progression kinetics and may guide risk-adapted, personalized management strategies in BMBC.