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Demonstration of differential clinical radiosensitivity based upon mutation profile in metastatic melanoma

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Abstract

Objectives: Metastatic melanoma tends to involve the brain, impacting length and quality of life. Radiotherapy is an important treatment of melanoma brain metastases, although melanoma radiosensitivity is considered heterogeneous. Thus, identifying patient subsets with differential radiosensitivity is integral to improving outcomes.

Methods: Patients with metastatic melanoma were identified in a prospective Gamma Knife stereotactic radiosurgery (GKRS) database. Tumor samples were tested for alterations in B-RAF, N-RAS, and KIT. Standardized imaging following GKRS was reviewed to identify local recurrence of treated lesions and the development of new brain metastases (distant failure). Differences in local and distant failure based upon demographics, treatment details, and mutation profile were determined using modified Cox proportional hazards models.

Results: 102 patients treated for 1,028 brain metastases were included. B-RAF, N-RAS, and KIT mutation was identified in 45 (44.1%), 9 (8.8%), and 4 (3.9%) patients, respectively, while 44 (43.2%) were wild type. Median radiographic follow-up for local recurrence was 6.0 months (range 1-79 months). N-RAS mutated patients were significantly less likely to develop local recurrence after GKRS than wild type patients (HR 0.17, 95% CI 0.04-0.72, p=0.017). B-RAF and KIT mutations were not associated with altered rates of local recurrence. Lower local recurrence rates for N-RAS mutated tumors persisted on multivariate analysis (HR 0.18, 95% CI 0.04-0.84p=0.029).

Conclusions: N-RAS mutation is associated with improved local control following GKRS. Local recurrence is more common in wild type patients and those with B-RAF or KIT mutations. Further research is needed to validate these findings and integrate these observations into clinical practice.

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