

**“Leading Edge” Gamma Knife Radiosurgery for Primary
Malignant Brain Tumors, Using MR Spectroscopy**

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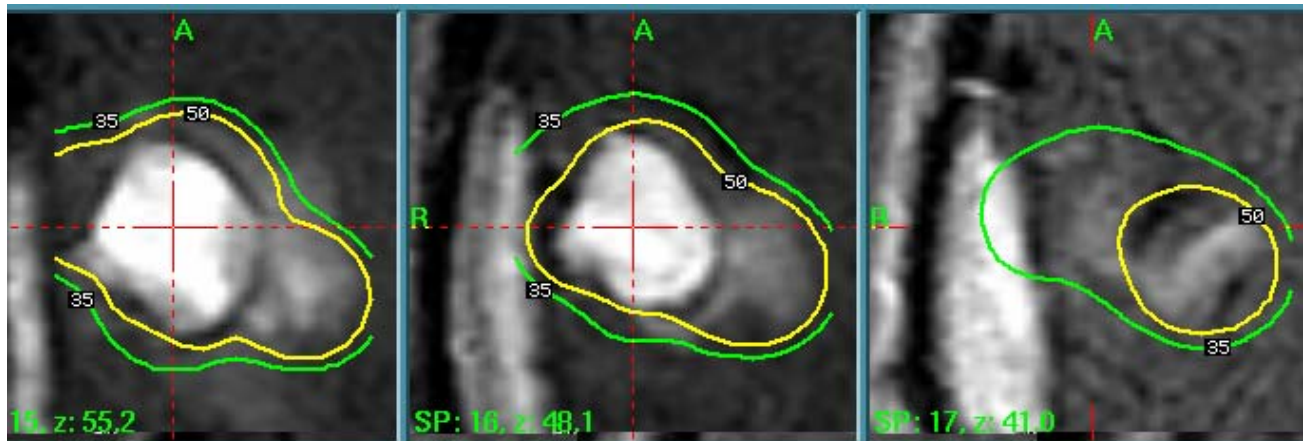
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Glioblastoma multiforme (GBM) is among the most common and devastating brain tumors affecting adults. The most successful treatment regimens for GBMs and Anaplastic Astrocytomas include surgical resection, radiation therapy and chemotherapy, followed by stereotactic radiosurgical boost (Gamma Knife radiosurgery) and immunotherapy. Despite aggressive therapies, the malignant nature of GBMs and Anaplastic Astrocytomas often results in tumor recurrence. 90% of GBMs and Anaplastic Astrocytomas recur at the site of the original tumor. In addition to local recurrence, malignant gliomas frequently spread in predictable patterns along the white matter pathways in the brain. It is via this mechanism that long-fought battles against GBMs and Anaplastic Astrocytomas are often lost.

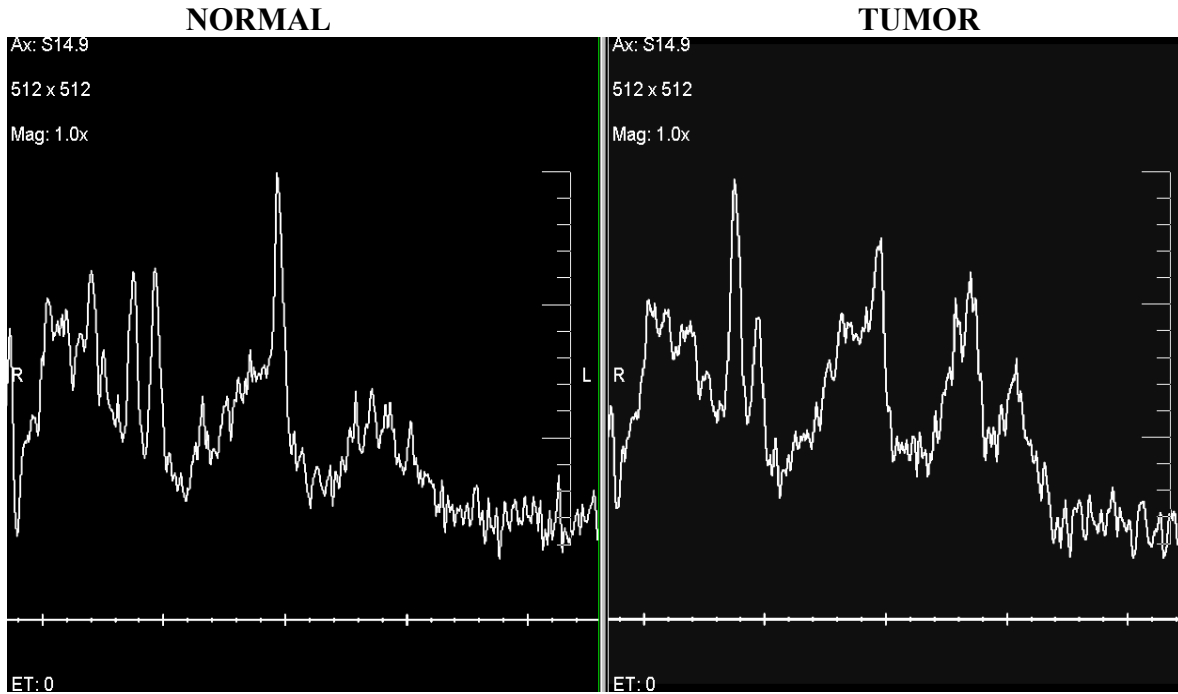


PREDICTABLE PATTERNS OF SPREAD IN MALIGNANT GLIOMAS

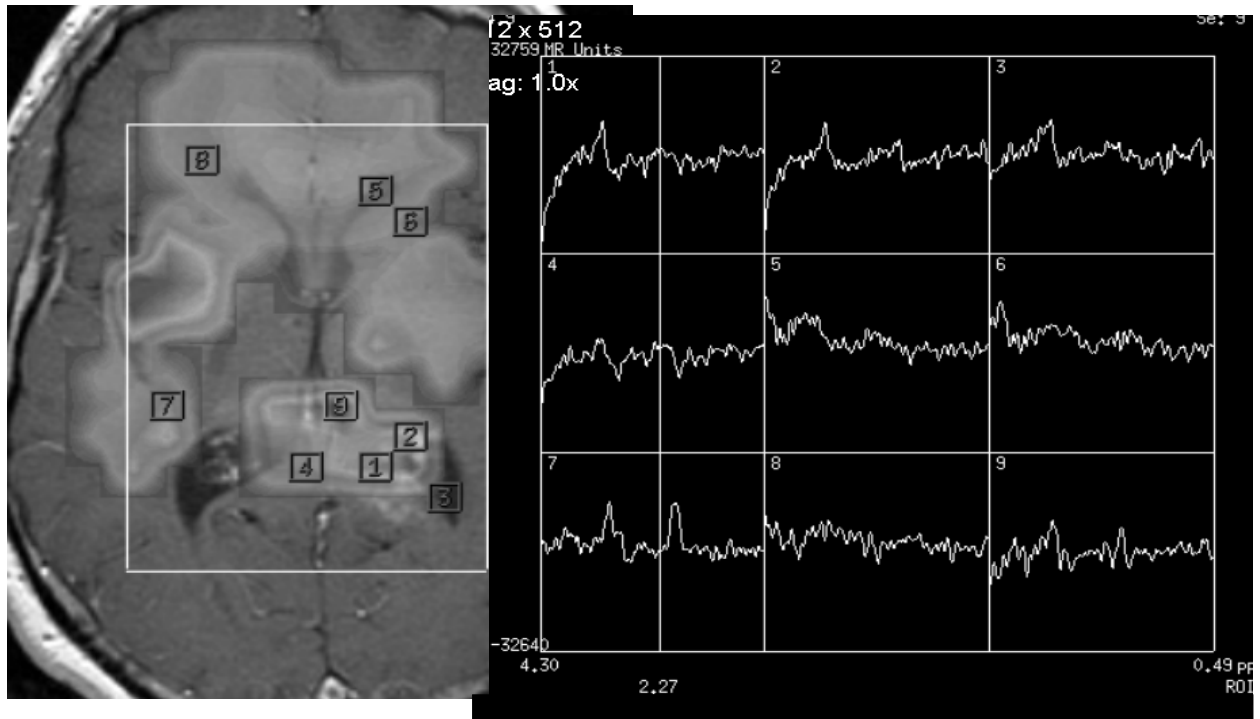
Traditional radiosurgical techniques have focused solely on local tumor margins, as determined by gadolinium enhancement on MRI. However, recent data suggests that by targeting the “leading edge” of these tumors, their spread along white matter pathways can be more effectively halted. FLAIR sequences and Multivoxel MR-Spect scans can be utilized to define positive areas outside of the gadolinium T1-weighted enhancing zones. Targeting these zones with gamma knife is proving to be a successful method of blocking the path of malignant gliomas.



TARGETING OF MR-SPECT POSITIVE ZONES OUTSIDE OF GADOLINIUM T1-WEIGHTED ENHANCING ZONES

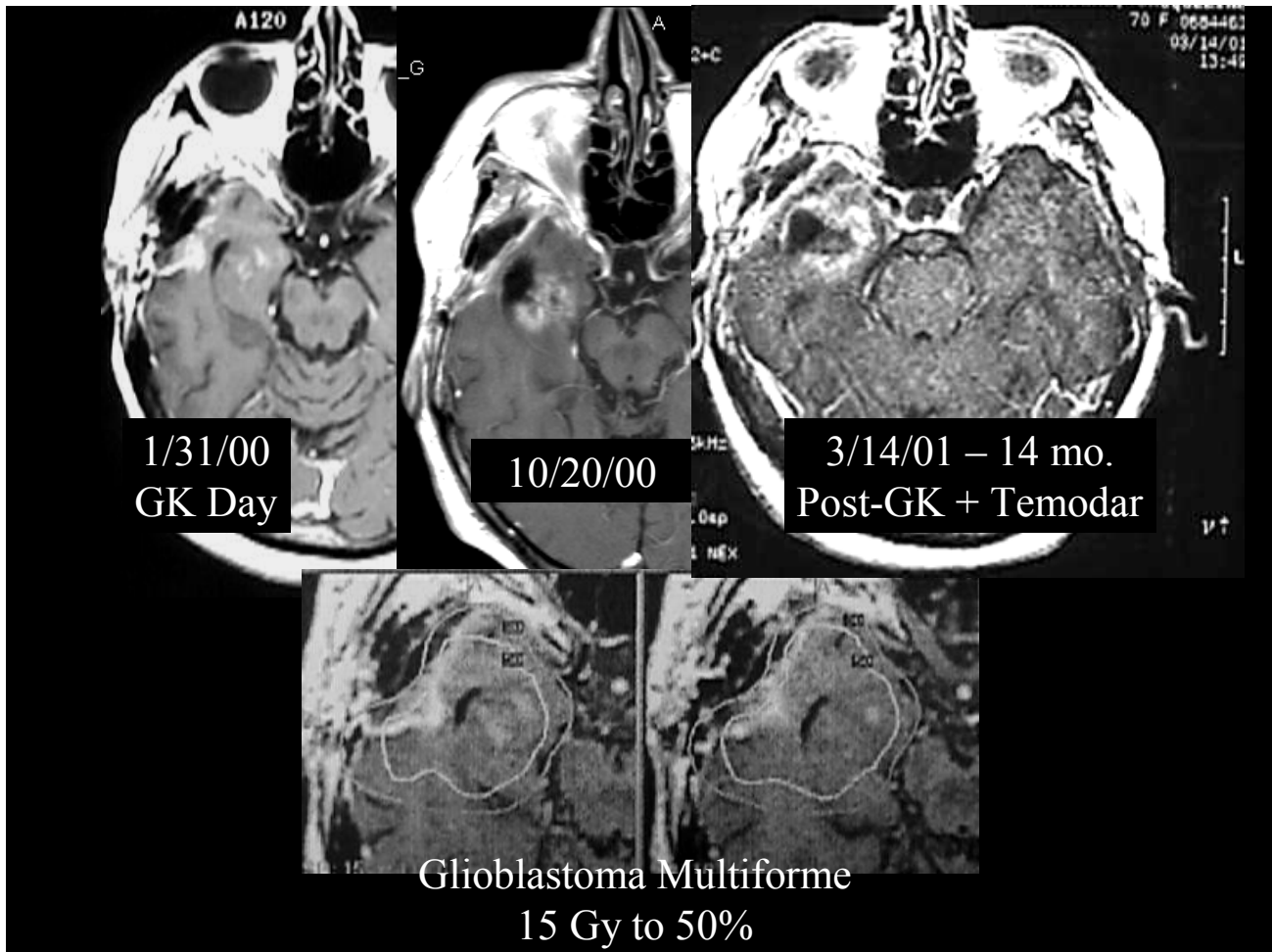


MR-SPECTROGRAPHY OF NORMAL AND NEOPLASTIC BRAIN REGIONS



MULTIVOXEL MRS CAN DISTINGUISH NORMAL AREAS FROM TUMOR

In our series, 18 consecutive patients with amenable tumors (i.e. lobar, polar locations) were treated with “leading edge” gamma knife radiosurgery. Ages ranged from 21 to 72 years (median = 49). Eight of the 18 patients were being treated for recurrent disease. Most had received some form of prior treatment, including LAK cell therapy (6), chemotherapy (8) and prior GK treatments (3). Complications were comparable to those seen with traditional radiosurgical targeting, and included a 44% mild edema rate requiring short-term steroid therapy, and 5% admission rate for mannitol and IV steroids for severe edema and radiation necrosis.



Initial results are optimistic, with a mean follow-up from diagnosis of 14.4 months (range = 2 to 58 months), and mean follow-up from the time of radiosurgery of 8.4 months (range = 1 to 24 months). Median projected Kaplan-Meier survival was 22 months for patients receiving leading edge therapy as their primary treatment, 15.5 months for patients with recurrent disease, and 23 months from the time of diagnosis for all patients.

Longer follow-up is necessary to determine the overall efficacy of “leading edge” radiosurgery. But these data suggest that targeting the white matter pathways along which GBMs and Anaplastic Astrocytomas are known to spread results in a survival advantage for patients with these aggressive, malignant gliomas.