

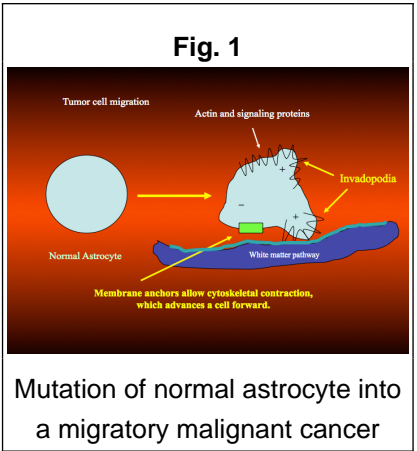
# Up-Front “Leading Edge” Gamma Knife Radiosurgery to Tumor Migration Pathways in 161 Patients with Glioblastoma Multiforme: A Novel Adjunctive Therapy

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**Learning Objectives**  
By the conclusion of this session, participants should be able to: 1) Define the "leading edge" of GBM, 2) Understand the concept of GBM tumor cell migration, 3) Understand the treatment protocol using "leading edge technique" (Patent pending)

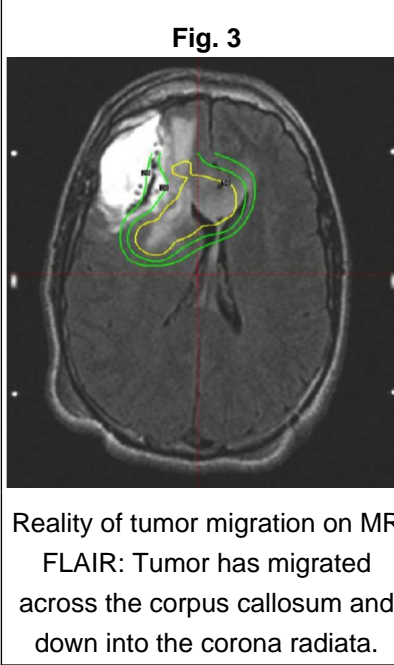
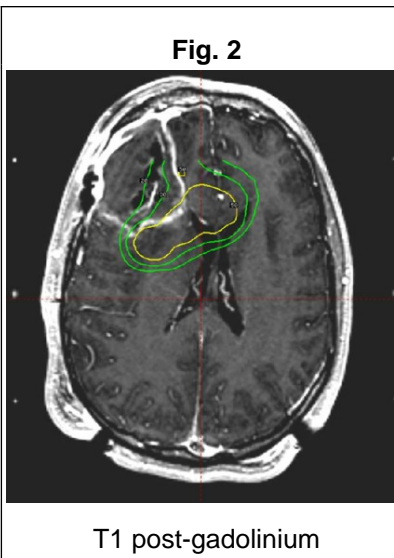
**Introduction**  
Glioblastoma multiforme (GBM) physically migrates along predictable white matter pathways (Fig. 1). This is why it evades complete surgical excision. Unfortunately, adjunctive treatments have done little to eradicate this disease. Targeting white matter pathways adjacent to, and leading away from, the original enhancing tumor site, as defined by MR-FLAIR-positive regions with stereotactic radiosurgery as a boost to standard therapy ("Leading Edge Gamma Knife Radiosurgery," (LEGKRS)) could blunt the spread of

glioma cells and improve survival for patients diagnosed with GBM. To date, the standard therapy of raditherapy plus temozolomide, offers only a 14.7 mo median survival (1)

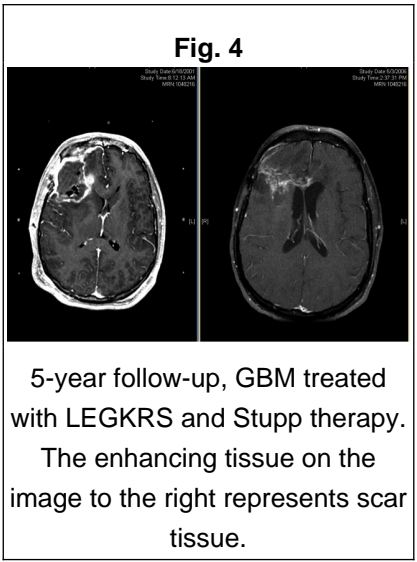


**Methods**  
Between December-1998 and March-2015, after an initial diagnosis of GBM, and prior to standard radiation therapy and chemotherapy only, 161 patients treated with radiosurgery to the “Leading Edge” (LE) of tumor cell migration were reviewed. The LE was defined as a region outside the enhancing, tumor nidus, defined by FLAIR MRI (Figs. 2 and 3). Spectroscopy was also used in some patients. The median age was 59 years (range: 22-87). Patients underwent LEGKRS a median of 18 days from original diagnosis.

The median target volume of 48.5 cm3 (range: 2.5-220.0) of LE tissue was targeted using 8 Gy (range: 6-14) at the 50% isodose line.



**Results**  
The median overall survival was 22.3 months (mean: 90.1 months) from diagnosis. The 2-, 3-, 5-, 7- and 10 -year overall survival rates post-LEGKRS were 40%, 26.7%, 15.5%, 9.3% and 3.7% respectively (Fig 4). Nine percent of patients developed edema or radiation necrosis, 4% required operative intervention for treatment related symptoms. Six percent had permanent complications related to this treatment.



**Conclusions**  
LEGKRS is a relatively safe and effective upfront adjunctive therapy for patients with newly diagnosed GBM. Compared to protracted treatments with chemotherapy it is relatively cost-effective. Limitations of this study include a single center experience and single investigator determination of the “leading edge”. A subset of patients did extraordinarily well speaking to “control” of the leading edge. A multicenter trial will further elucidate its value in the treatment of GBM.

**References**  
(1) Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma Stupp, R, et al. N Engl J Med 2005; 352:987-996