Radiosurgery for Medial Temporal Lobe Epilepsy Resulting from Mesial Temporal Sclerosis

Thomas Gianaris, MD, Thomas Witt, MD, Nicholas M. Barbaro, MD*

KEYWORDS

• Mesial temporal sclerosis • Medial temporal lobe epilepsy • Radiosurgery • Epilepsy

KEY POINTS

- Radiosurgery for mesial temporal sclerosis (MTS)–associated medial temporal lobe epilepsy (MTLE) is an attractive option because it is relatively noninvasive, with lower morbidity than major surgery.
- Conventional open temporal lobectomy surgery may also be pursued if initial radiosurgical treatment is ineffective and after sufficient time has been permitted for the delayed radiosurgical antiepileptic effect after 3 years.
- The main known disadvantage of radiosurgery at present is the delayed response for seizure control, during which time patients continue to suffer from the sequelae of seizures.
- Future research into radiosurgery modality will ideally make individualized patient treatment more feasible and attainable, allowing the neurosurgical community to more effectively manage and treat medial temporal lobe epilepsy.

INTRODUCTION

Radiosurgery is the precise application of focused radiation to targeted brain with the aid of stereotactic guidance.[1–27] Radiosurgery is particularly well suited for treatment of MTS leading to medial temporal lobe epilepsy because MTS typically exhibits radiographic changes on MRI, allowing this focused radiation to be directed to a specific, small region of pathology, sparing the rest of the brain from harmful radiation.[24] Regis and colleagues[28] were able to demonstrate the safety of focused radiosurgery for medial temporal lobe epilepsy while still delivering doses effective enough to reduce seizure frequency, whereas a prospective multicenter European study using the Gamma Knife proprietary radiosurgery tools found similar efficacy rates for seizure reduction with a dose of 29 Gy, comparing radiosurgery to the gold standard of conventional microsurgery for epilepsy after 2 years with similar morbidity and mortality.

A similar multicenter trial studying a direct comparison of radiosurgery to resection for MTLE has shown in pilot studies that a dose of 24 Gy to the medial temporal lobe was able to eliminate seizures in 85% of patients at 2 years of follow-up as well.[29] In this pilot study, patients were treated with 2 different radiation doses (20 Gy or 24 Gy) and there was significant seizure remission in both groups at 12 months (58.8% and 76.9%, respectively), with no dose-based or seizure remission–based changes in headaches, visual field defects, and the use of steroids. Although these studies thus far only have time points at 1

Department of Neurological Surgery, Indiana University School of Medicine, 355 W. 16th St., Suite 5100, Indianapolis, IN 46202, USA
* Corresponding author.
E-mail address: Nbarbaro@iupui.edu

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and 2 years, recent research in France looking at outcomes of 5 and 8 years has demonstrated continued seizure reduction remission after radiosurgery, although at a lower rate, finding 47% remission at 5 years and 60% at 8 years.[30,31] In addition, there may be benefits with respect to memory and language preservation.

RISKS OF TREATMENT

Although these studies have shown that radiosurgery is effective with minimal morbidity and mortality at time points of greater than 1 year, radiosurgery, unlike open resection, has a lag time after treatment before patients begin to see the effects of therapy and, in the near term, patients are still exposed to the risks of continued seizures as well as the risks of radiation. Typically, patients treated with radiosurgery can achieve seizure reduction at 9 to 12 months and possible complete cessation of seizures between 18 and 24 months after radiosurgery treatment.[28] In addition, a transient increase in partial seizures (auras) can be noted at approximately the same time that complex seizures decrease with radiosurgery, and many of them require a transient period of steroid administration for the radiation-induced edema.[28] Srikijvilaikul and colleagues[32] found 2 deaths during this latency period in a small case series of 5 patients treated with 20 Gy before seizure remission, likely complications of ongoing seizures. Quigg and colleagues[33] found that language (Boston Naming Test), verbal memory (California Verbal Learning Test and Logical Memory Subtest of the Wechsler Memory Scale—Revised), cognitive efficiency and mental flexibility (Trail Making Test), and mood (Beck Depression Inventory) did not differ from baseline after radiosurgery, demonstrating long-term neurocognitive safety using established scoring scales, despite the increased potential for necrosis.

Radiosurgery for MTLE is not without risks and long-term effects; radiation necrosis has been demonstrated by several studies and case reports. Hensley-Judge and colleagues[34] found postoperative visual field deficits in 15 of 24 (62.5%) patients, all homonymous superior quadrantanopias, proportions similar to historical comparisons from open surgery for MTLE. Another case series demonstrated that 2 of 7 patients, status postradiosurgery for MTS presenting with symptomatic radiation necrosis, required resection after 5 and 10 years.[35] Additionally, there is some concern in the long term for radiosurgery-associated radiation-induced malignancies, although these reported cases are rare, and none has been reported after therapy for MTS.[36–39] Although it was initially studied as a primary modality for MTS treatment, radiosurgery is also being investigated as a treatment of refractory epilepsy after temporal lobe resection. Yen and colleagues[40] found significant seizure reduction in a case series of 4 patients who underwent radiosurgery after temporal lobe resection. There was reduction of seizure frequency at 6 months after radiosurgery for refractory epilepsy after temporal lobe resection as well as improved neuropsychological profiles, including memory function and quality of life, lasting up to the 2-year follow-up examination.

MECHANISM OF ACTION AND HISTOPATHOLOGY

Conversely, open resective surgery after radiosurgery has, as a side benefit, provided an opportunity to understand the mechanism of action of radiosurgery on a histopathologic level. In 2 separate studies, Kawai and colleagues[41] and Srikijvilaikul and colleagues[32] found histologic changes, including necrotic foci with vessel wall thickening and fibrinoid and hyaline degeneration, in a patient treated with 18 Gy, as well as perivascular sclerosis and macrophage infiltration on resection and evaluation of a patient treated with 20 Gy. Cmelak and colleagues[42] reported no radiation-induced histopathologic changes in tissues treated with 15 Gy of radiosurgery, suggesting that some histologic damage may be needed for effective seizure control.[43–45] Chang and colleagues[46] found vasogenic edema appeared approximately 9 to 12 months after radiosurgery on serial MRI scans and correlated with the onset of seizure remission, further corroborating this hypothesis. Barbaro and colleagues[29] suggested that the mechanisms may be some combination of neuromodulation and true neuronal destruction, with some animal studies demonstrating improvement in seizures without evidence of necrosis, whereas other investigators have shown direct structural, destructive lesions in the tissue zone to correlate better with outcome, perhaps because of some contribution from ischemic factors.[46,47] The concrete mechanism of radiosurgery, destructive or otherwise, warrants further study.

SUMMARY

In summary, radiosurgery for MTS-associated MTLE is an attractive option because it is relatively noninvasive, with lower morbidity than major surgery. Conventional open temporal lobectomy surgery may also be pursued if the initial radiosurgical treatment is ineffective and after sufficient time has been permitted for the delayed radiosurgical