

EMERGING SURGICAL TREATMENTS FOR MEDICALLY REFRACTORY FOCAL EPILEPSY

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In the treatment of medically refractory focal epilepsy, minimally and non-invasive techniques have seen both revolutionary and evolutionary changes over the past twenty years. This presentation will discuss recent developments in MRI-guided laser interstitial therapy (also known as stereotactic laser thermal ablation, radiosurgery, and focused ultrasound for the treatment of medically refractory epilepsy.

The development of more precise stereotactic ablation techniques and advances in imaging modalities have provided improved guidance and targeting, while MRI thermometry revolutionized intraoperative monitoring of ablation (LaReviere and Gross, 2016). The more recent introduction of MR-guided laser interstitial thermal therapy (MRg-LITT) offers tighter thermal control, and the combination with thermal MRI imaging allows the surgeon to protect critical structures from damage. The use of laser ablation for treating focal epilepsy is only in its early stages, but its superior targeting and intraoperative feedback control makes it an exciting candidate for further investigation. Data from case reports and small series suggest that MRg-LITT may be effective and safe in treating seizures associated with cortical dysplasia (Devine et al., 2016), hypothalamic hamatomas and mesial temporal lobe sclerosis. One of the advantages of MRg-LITT compared to craniotomy-based respective surgery is the short duration of post-operative hospitalization.

Radiosurgery is the precise application of focused radiation to targeted brain with the aid of stereotactic guidance. Radiosurgery is particularly well suited for treatment of mesial temporal sclerosis (MTS) leading to medial temporal lobe epilepsy (Gianaris et al., 2016) 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. Regis and colleagues (2004) 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 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. Radiosurgery for MTS-associated epilepsy 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 antiepileptic effect after 3 years. Its main known disadvantage at present is the delayed response for seizure control, during which time patients continue to suffer from the sequelae of seizures. Future research into this treatment modality will ideally make individualized patient treatment more feasible and attainable, allowing the neuro-surgical community to more effectively manage and treat medial temporal lobe epilepsy.

Focused ultrasound (FUS) is an incision-less intervention that is a Food and Drug Association (FDA) approved surgical treatment for various pathologies including uterine fibroids and bone metastases. Recent advances in magnetic resonance imaging thermometry and ability to use FUS across the intact calvarium have re-opened interest in the use of FUS in the treatment of neurological diseases, including epilepsy (Piper et al., 2016). FUS currently has a European CE mark for use in movement disorders. However, it shows potential in the treatment of other neuropathologies including tumours and as a lesional tool in epilepsy. FUS may exert its therapeutic effect through thermal or mechanical fragmentation of intracranial lesions, or by enhancing delivery of pharmaceutical agents across the blood-brain barrier. Current literature reports pre-clinical work exploring utility in epilepsy, neurodegenerative conditions (such as Alzheimer's disease) and thrombolysis. Magnetic resonance-guided

focused ultrasound (MRgFUS) thermal ablation of the mesial temporal lobe structures relevant in temporal lobe epilepsy is feasible in a laboratory model (Monteith et al., 2016). Safety and early efficacy data are now emerging, suggesting that transcalvarial FUS is a feasible and safe intervention. Further evidence is required to determine whether FUS is an effective alternative in comparison to current neurosurgical interventions.

References:

Stereotactic Laser Ablation for Medically Intractable Epilepsy: The Next Generation of Minimally Invasive Epilepsy Surgery.

LaRiviere MJ, Gross RE. *Front Surg*. 2016 Dec 5;3:64. Review. PMID: 27995127

Curative laser thermoablation of epilepsy secondary to bottom-of-sulcus dysplasia near eloquent cortex.

Devine IM, Burrell CJ, Shih JJ. *Seizure*. 2016 Jan;34:35-7. doi: 10.1016/j.seizure.2015.11.006. PMID: 26684982

Radiosurgery for Medial Temporal Lobe Epilepsy Resulting from Mesial Temporal Sclerosis.

Gianaris T, Witt T, Barbaro NM. *Neurosurg Clin N Am*. 2016 Jan;27(1):79-82. doi: 10.1016/j.nec.2015.08.011. Epub 2015 Oct 24.

Gamma knife surgery in mesial temporal lobe epilepsy: a prospective multicenter study.

Régis J, Rey M, Bartolomei F, Vladyka V, Liscak R, Schröttner O, Pendl G. *Epilepsia*. 2004 May;45(5):504-15. PMID: 15101832

Focused ultrasound as a non-invasive intervention for neurological disease: a review.

Piper RJ, Hughes MA, Moran CM, Kandasamy J. *Br J Neurosurg*. 2016 Jun;30(3):286-93. doi: 10.3109/02688697.2016.1173189. Epub 2016 Apr 22.

Transcranial magnetic resonance-guided focused ultrasound for temporal lobe epilepsy: a laboratory feasibility study.

Monteith S, Snell J, Eames M, Kassell NF, Kelly E, Gwinn R. *J Neurosurg*. 2016 Dec;125(6):1557-1564. Epub 2016 Feb 12.