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A neurosurgeon`s view: Laser interstitial thermal therapy of mesial temporal lobe structures

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A B S T R A C T

Stereotactic laser ablation of mesial temporal structures is a promising new surgical intervention for patients with mesial temporal lobe epilepsy (MTLE). Since this procedure was first used to treat MTLE in 2010, the literature contains reports of 37 patients that underwent MR-guided stereotactic laser amygdalohippocampotomy (SLAH) using Laser Interstitial Thermal Therapy (LITT) with at least 1 year of follow-up. This early body of data suggests that SLAH is a safe and effective treatment for MTLE in properly selected patients. Moreover, SLAH is substantially less invasive when compared with open surgical procedures including standard anterior temporal lobectomy and its more selective variants, results in immediate destruction of tissue in contrast to radiosurgical treatments for MTLE, and can more readily ablate larger volumes of tissue than is possible with techniques employing radiofrequency ablation. Finally, evidence is accruing that SLAH is associated with lower overall risk of neuropsychological deficits compared to open surgery. Thus, LITT constitutes a novel minimally invasive tool in the neurosurgeon's armamentarium for managing medically refractory seizures that may draw eligible patients to consider surgical interventions to manage their seizures.

1. Introduction

1.1. Historical overview

Epilepsy is a serious neurological condition affecting 0.5–1% of the world's population (Engel et al., 2003). While the mainstay of treatment remains medical management with antiepileptic drugs (AEDs), approximately one-third of patients continue to have seizures that are resistant to medications (Kwan and Brodie, 2000), defined by the International League Against Epilepsy epilepsy as lack of seizure freedom despite adequate trials of two separate antiepileptic drug regimens (Kwan et al., 2010). Mesial temporal lobe epilepsy (MTLE), or epilepsy originating in the hippocampus and/or amygdala, is the most common epilepsy syndrome, occurring in approximately 27% of all patients with epilepsy or ~1.9 cases per 1000 people (Asadi-Pooya et al., 2016). Mesial temporal lobe sclerosis is frequently associated with MTLE, with up to 70% of surgical patients demonstrating some evidence of this pathology on magnetic resonance imaging (MRI; (Engel et al., 2012)). Despite the prevalence of MTLE, it remains particularly resistant to medical management (Wiebe and Jette, 2012). However, an ample body of evidence including two randomized controlled trials (Engel et al., 2012; Wiebe et al., 2001) suggests that early surgical intervention may prevent or reverse disabling psychosocial consequences of uncontrolled seizures and decrease the risk of untimely death (Sperling, 2004). With this in mind, Clinical Practice Guidelines published by the American Academy of Neurology in 2003 recommend early referral for surgery after AEDs have failed to achieve seizure freedom (Engel et al., 2003).

1.2. Surgery for mesial temporal epilepsy

Surgery for MTLE entails the resection of the mesial temporal lobe, including the amygdala and hippocampus, along with varying proportions of the anterior temporal lobe. The standard surgical procedure was initially described by Penfield and Baldwin, in 1952. This procedure was further refined by a series of neurosurgeons into the modern anterior temporal lobectomy (ATL). The outcomes of this surgery are well-established, with a randomized-controlled trial demonstrating that 64% of patients undergoing this procedure were free from seizures impairing awareness at 1 year post-operatively (58% by intention-to-treat), compared to 8% of patients treated with best medical management (Wiebe et al., 2001). This was associated with improved quality of life as well. Similarly, a more recent trial of early surgery for epilepsy (within 2 years of drug resistance having been established) found that 73% of patients undergoing ATL were seizure free at 1 year, compared to 0% of those treated medically, although this study was halted early

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due to slow accrual (Engel et al., 2012). Finally, a meta-analysis of 11 trials found that ATL leads to seizure freedom in some 75% of patients at 1-year (Josephson et al., 2013).

More selective open procedures have also been used, in part to ostensibly minimize the neuropsychological sequelae of resecting the anterolateral temporal lobe, with Niemeyer being one of the first to report on selective amygdalohippocampectomy (SAH) via the middle temporal gyrus in 1958 (Niemeyer, 1958), and Weiser and Yasargil describing a trans-Sylvian approach to the same structures in 1982 (Wieser and Yasargil, 1982). Selective procedures are slightly less effective than ATL, with 67% of patients remaining seizure free at 1 year post-operatively (Josephson et al., 2013). The risk difference of 8% (95% CI 3%-14%) means that 13 (95% CI 7–33) patients needed to be treated to encounter 1 that would be seizure free after ATL but not SAH. While this meta-analysis, and another similar one (Hu et al., 2013), for the first time suggested decreased effectiveness of SAH, in general they suggest that surgeons, and ostensibly patients and treating neurologists, are willing to trade decreased effectiveness for the potential preservation of cognitive functions at risk from surgery.

Despite the preponderance of evidence and recommendations for early surgery in patients with drug-resistant MTLE, appropriate candidates for these procedures continue to be under-referred to epilepsy surgery programs, and when referrals do occur they are typically delayed by ~22 years from disease onset (Berg et al., 2003). The reasons for this are myriad, and include difficulty in establishing drug resistance and remission of seizures in some patients (Wiebe and Jette, 2012). Fear of surgery, ignorance of the various treatment options, and the tolerability of symptoms have also been identified as important factors (Dewar and Pieters, 2015). The latter group of factors suggests that less daunting surgical interventions associated with a lower risk of perioperative complications, promulgated appropriately, may increase the proportion of patients referred for surgical intervention. MR-guided stereotactic laser amygdalohippocampotomy (SLAH) using Laser Interstitial Thermal Therapy (LITT) is a promising new approach in meeting this goal.

2. MR-guided stereotactic laser amygdalohippocampotomy

2.1. Overview

LITT consists of the focused application of thermal energy in the form of intense light to tissue anywhere within the intracranial space, in conjunction with real-time MR-thermography which is used to monitor the delivery of this energy. This combination allows for the precise delivery of titratable heat based on real-time feedback as to the extent of the ablation, which is modeled based on thermal thresholds of various tissues as well as the tissue penetration of the energy. The application of LITT in SLAH entails a minimally invasive procedure involving a small twist-drill craniostomy in the parieto-occipital region, through which a catheter containing an optical fiber is inserted stereotactically along a trajectory planned to target the amygdala and the head and body of the hippocampus as far back as the tectal plate (for a detailed description of this technique, please see Gross and colleagues (Gross et al., 2016)). The optical fiber may be placed via various stereotactic techniques including traditional frames, frameless systems, or direct MR-guidance with a skull-mounted miniframe that affords the surgeon the opportunity to revise the placement of the optical fiber as needed without returning to the operating room. This latter technique affords a significant advantage, as accurate placement of the laser fiber determines the success of the procedure.

2.2. Outcomes

We performed our first LITT procedure for MTLE in 2011, and the first paper on the use of LITT for epilepsy, published in 2012 by Curry et al., included one pediatric patient with MTLE. Given the novelty of LITT, there have only been six studies reporting outcomes of LITT in patients with MTLE published to date (Curry et al., 2012; Drane et al., 2015; Gross et al., 2016; Kang et al., 2016; Lewis et al., 2015; Waseem et al., 2015; Willie et al., 2014). By pooling the seizure outcomes at one year post-operatively across these studies, an Engel class I outcome (freedom from the most disabling seizures) was attained in 20/37 or 54.1% of patients at 1 year (see Table 1). For patients with mesial temporal sclerosis (Gross et al., 2016; Kang et al., 2016; Lewis et al., 2015; Waseem et al., 2015; Willie et al., 2014), 13/23, or 56.5% of patients remained free of disabling seizures 1 year post-operatively. All these series are retrospective and non-controlled, thus limiting the strength of conclusions that can be drawn from this as yet relatively limited experience.

Table 1
Seizure outcomes at 1 year in patients with MTLE undergoing SLAH.

Study	Patients with MTLE/MTS at 1 yr F/U	MTLE/MTS patients with Engel 1 outcomes
Curry et al. (2012)	1/1	1 (100%)/1 (100%)
Willie et al. (2014); Gross et al. (2016)	13/7	7 (53.8%)/4 (57.1%)
Drane et al. (2015)	19/10 (includes all patients in Willie et al., 2014)	11 (57.9%)/not specified
Lewis et al. (2015)	1/0	0
Waseem et al. (2015)	5/5	4 (80%)/4 (80%)
Kang et al. (2016)	11/10	4 (36.4%)/4 (40%)
Overall	37/26	20 (54.1%)/13 (56.5%)*

* 13/26, as the proportion of patients with MTS who had 1 year follow-up in Drane et al. (2015) was not defined.

The desire to limit the postoperative neuropsychological sequelae of epilepsy surgery has led to efforts to spare the anterolateral portions of the temporal lobe in surgeries for MTLE. However, all open surgical techniques entail the necessary disruption of some amount of lateral neocortical tissue to access the mesial temporal structures. SLAH is particularly attractive in this regard as it spares these structures entirely, and we have observed better outcomes in naming and recognition in patients undergoing SLAH – whether in the dominant or non-dominant hemisphere – compared to those undergoing open resection (for a detailed discussion, see Drane in this issue) (Drane et al., 2015). Indeed, no patients experienced a decline in these measures after SLAH, and improvements were seen in some patients.

2.3. Complications

The safety of SLAH is being evaluated in ongoing series and reviews, but given its relative novelty is in evolution. In our published surgical series, we observed a low risk of hemorrhage, including one case of a small acute subdural hematoma which was identified intraoperatively and subsequently evacuated without deficit. In addition, one patient had a homonymous hemianopia, which may have resulted from a deviation of the optical fiber (Willie et al., 2014) or thermal injury to the thalamus in a patient undergoing repeat laser ablation. No other patients in our extended series experienced this complication (Gross et al., 2016 and R.E. Gross, J.W. Willie, unpublished observations). Other publications report similar complications. A recent systematic review of 74 procedures found a 16.2% risk of serious complications per procedure, with the majority of these procedures (49) being from our own report (Gross et al., 2016). They consisted of the following. There were 7 visual field cuts (9.5%), two of which were ours: one the above noted homonymous hemianopia, another a transient quadrantanopsia resulting from a hemorrhage. The remaining 5 were quadrantanopsias as well, likely non-disabling (Waseem et al., 2016). In addition to the two non-disabling hemorrhages we reported (Willie et al., 2014; Gross et al., 2016), Waseem et al. (2016) reported one additional (4.1% overall). Finally, the 2 cranial nerve palsies reported in Waseem et al. (2016)

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