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Epileptologist's view: Laser interstitial thermal ablation for treatment of temporal lobe epilepsy

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A R T I C L E I N F O

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A B S T R A C T

A procedure called laser interstitial thermal ablation has been utilized to treat drug resistant epilepsy. With this technique, a probe is stereotactically inserted into a target structure responsible for seizures, such as mesial temporal lobe, hypothalamic hamartoma, or a small malformation of cortical development, and the tip is then heated by application of laser energy to ablate structures adjacent to the probe tip. This procedure has the advantage of selectively targeting small lesions responsible for seizures, and is far less invasive than open surgery with shorter hospitalization, less pain, and rapid return to normal activities. Initial results in mesial temporal lobe epilepsy are promising, with perhaps half of patients becoming free of seizures after the procedure. Neuropsychological deficits appear to be reduced because of the smaller volume of ablated cortex in contrast to large resections. More research must be done to establish optimal targeting of structures for ablation and selection of candidates for surgery, and more patients must be studied to better establish efficacy and adverse effect rates.

1. Introduction

Approximately 50 million people worldwide have epilepsy, making it one of the most common neurological diseases in the world (Anon, 2017a). About a third of individuals with epilepsy experience recurrent seizures despite appropriate treatment with antiepileptic drugs and may be considered to have drug-resistant epilepsy (Brodie et al., 2012). In these people, surgery is often an effective treatment, particularly for those with mesial temporal lobe epilepsy. Longitudinal studies demonstrate a 60–80% chance of attaining seizure freedom after surgery compared to a 3–4% chance of remission with continued medical therapy (Wiebe et al., 2001; Mittal et al., 2005). Despite these excellent results, only a small percentage of potential surgical candidates have epilepsy surgery, and this underutilization may be partly due to appropriate concerns and fears about the invasiveness and risks of brain surgery as well as the prolonged recovery time.

In the past few years, a significant advance has been made in the surgical treatment of drug resistant epilepsy. Compared to open resections, less invasive surgical techniques have been developed with less discomfort and temporary disability, and greater preservation of functional tissue compared to traditional open resections. One example of such procedure is laser thermal ablation (also known as laser interstitial thermal therapy, LiTT) (Fig. 1). This utilizes advances in imaging technology and surgical navigation techniques that make LiTT safer and easier to implement, offering an effective and less painful neurosurgical tool for patients with drug resistant epilepsy. There are several review articles written by our colleagues in neurosurgery, neuropsychology and neuroradiology on the use of laser interstitial thermal therapy (Gross et al., 2016; Waseem et al., 2017; Medvid et al., 2015b). This article will review the current clinical application of laser thermal ablation treating drug-resistant mesial temporal lobe epilepsy from epileptologist's perspective.

2. Overview of current applications

The United States (U.S.) Food and Drug Administration (FDA) first approved the use of MRI-guided LiTT system for ablating intracranial lesions in 2007. The procedure was first developed for treatment of small brain tumors and then adopted to treat epilepsy (Medvid et al., 2015a). The first report for treatment of refractory epilepsy appeared in 2012 (Curry et al., 2012); 5 children were treated, and the authors noted evidence for feasibility and efficacy of this novel procedure for drug-resistant epilepsy. Since 2012, laser thermal ablation has been used to target a variety of epileptogenic lesions including mesial temporal sclerosis (Curry et al., 2012; Kang et al., 2016; Willie et al., 2014; Lewis et al., 2015), hypothalamic hamartomas, periventricular nodular

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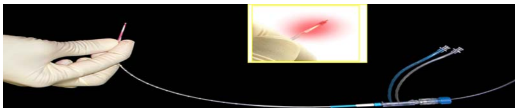

Fig. 1. Catheter with 10 mm diffusing tip as used in the Visualase system. This catheter is stereotactically inserted into the target area and the laser then heats the tip to create a thermal lesion. Lesion size depends upon total energy and time that the laser is left on (typically less than 3 min), and the lesion size can be calculated in advance. The laser is employed with the patient in the MRI machine for real-time imaging of the lesion. (Figure courtesy of Visualase).

heterotopia (Esquenazi et al., 2014), tuberous sclerosis (Curry et al., 2012), cortical dysplasia (Gross et al., 2016; Ellis et al., 2016), cavernous hemangiomas, and insular encephalomalacia (Hawasli et al., 2014) though the number of patients in some reports is small. This article will review its use in mesial temporal lobe epilepsy.

3. Laser interstitial thermal ablation in mesial temporal lobe epilepsy (mTLE)

Mesial temporal sclerosis (MTS) is a readily recognized, surgically amenable cause of intractable temporal lobe epilepsy. This relatively small and discrete pathological lesion makes MTS an ideal target for laser thermal ablation (Fig. 2). Outcome data is presently limited and the follow-up times are short (less than 3–4 years), but initial results suggest that laser thermal ablation is a promising alternative treatment to open procedures (see Table 1). Willie et al. (2014) reported successful outcome in about half of the 13 patients who underwent stereotactic laser amygdalohippocampotomy for medically intractable mesial temporal lobe epilepsy at a follow up of 5–26 months. They noted that patients whose MRI showed MTS had higher rates of seizure freedom than patients without MTS in the MRI, but the sample size was too small to draw firm conclusions. An updated review including the original 13 patients report stable seizure free rates at latest follow up (Gross et al., 2015). A recent article (Jermakowicz et al., 2017) reported slightly higher seizure free outcome in 23 patients that were followed for at least a year; 65% of the patients were free of disabling seizures. Our analysis of outcome in 20 patients at Thomas Jefferson University Hospital found that 40% of individuals with mesial temporal lobe epilepsy were free of disabling seizures after 2 years follow-up (Kang et al., 2016). The number of patients without MTS was small but only 1 out of 3 patients without MTS was seizure free after laser thermal ablation. Patients with persistent seizures often did not experience a substantial reduction in seizure frequency if thermal ablation failed to control seizures. Most who had a subsequent anterior temporal lobectomy (3/4 patients) became seizure free after the second procedure. We suggested that thermal ablation could be considered a reasonable first step, as those who failed to respond could still have an open procedure. It remains to be determined seizure freedom is attained at similar rates as anterior temporal lobectomy, and a clinical trial is now underway to better define outcomes after this procedure.

Laser interstitial thermal ablation offers significant advantages over ATL is that the less invasive approach minimizes collateral damage to functional tissue. Drane et al. (2015) noted that the pre-operative verbal fluency and object naming scores were preserved in all of the patients who underwent laser ablation (10 dominant, 9 non-dominant). Other standard neuropsychological outcome measures (ie: verbal memory) were not reported in their study. In the Jefferson series, we reported that in the 5 patients who underwent laser thermal ablation, 3 patients experienced significant decline in total verbal memory scores as assessed by CVLT (California Verbal Learning Test) after laser thermal ablation (Kang et al., 2016). Dredla et al. (2016) reported similar findings in 2 patients with normal MRI but PET positive temporal lobe epilepsy; there was clinical meaningful decline in memory but other non-memory neurocognitive abilities (ie: visuo-spatial, attention) were preserved after SLAH. As decline in neuropsychological performance, particularly in verbal fluency and verbal memory, occurs in over half of the patients after dominant hemisphere resection (Ives-Deliperi and Butler, 2012; Tanriverdi et al., 2010), a targeted approach sparing the anterior and lateral temporal cortex with laser thermal ablation may offer benefit in preserving these skills.

The evidence thus far seems to suggest that the SLAH is a well-tolerated procedure with milder adverse effects compared to ATL. The most common complaint after surgery is headache, which is usually quite mild and responds to a 1 week steroid taper or over the counter analgesics such as acetaminophen. Patients usually stay in the hospital for only 1 day and are discharged the day after surgery without need for postoperative intensive care. After discharge, patients return to normal activities within 3-7 days. Complication rates still need to be determined; visual field deficits (quadrantanopia and less frequently homonymous hemianopia), intracranial hemorrhage (intraparenchymal, epidural, intraventricular), cranial nerve palsy (Cranial nerve 3 and 4), scalp numbness and worsening mood symptoms have been reported (Waseem et al., 2017; Medvid et al., 2015b; Curry et al., 2012; Kang et al., 2016; Willie et al., 2014; Pruitt et al., 2016). In theory, complications rates should be less than those observed after open anterior temporal lobectomy, and the period of postoperative pain and disability is certainly far less. As with temporal lobectomy, adverse events rarely result in permanent neurological disability (Pruitt et al., 2016). Pruitt and colleagues (Pruitt et al., 2016) highlight three occasions during the procedure when complications may arise: during catheter placement, during hyperthermia, and from technical malfunctioning of the cooling system. Sub-optimal catheter placement is the most common issue with this procedure; it is associated with increased risk of hemorrhage and directly effects the volumes ablated. To reduce the risk of hemorrhage, some centers fuse CT angiography to the MRI to verify and avoid vascular landmarks during device insertion. The risk of hemorrhage can be further reduced by using a sharp instrument for dural puncture and avoiding entry into the ventricles, when possible. Accurate positioning of the catheter is crucial; positioning the trajectory too laterally may result in incomplete ablation of the mesial portion of the hippocampal head, which may be factor in poor outcome (Jermakowicz et al., 2017). Even with accurate catheter placement, care must be taken to avoid thermal injury to other structures. The blood vessels and the ventricles surrounding the mesial temporal lobe are thought to function as heat sinks because of fluid flow within these structures, and critical structures (such as the brainstem) are thought to be protected from thermal injury by these features. In their early paper, Willie and colleagues placed temperature markers on the anterior and lateral mesencephalon to demonstrate that there is no increase in brainstem temperature during the procedure (Willie et al., 2014). Complications such as visual field deficits and cranial nerve injuries demonstrate that heat conduction can occur during the procedure, possibly due to by inaccurate catheter placement and/or excessive heating (Waseem et al., 2017). Commercial systems utilize catheter cooling methods during the procedure and have safety protocols that shut off the system to prevent overheating of the laser probe and catheter. However, technical malfunction involving the catheter cooling system has been reported and caution should be used when targeting structures with critical areas that are not separated by CSF or vasculature (Pruitt et al., 2016).

Our experience with laser thermal ablation is that there is an initial learning curve, as with most procedures. Physicians must learn about optimal patient selection, determining trajectory of probe insertion, and how to lesion mesial temporal structures so that anatomic targets are adequately ablated. Who are the “appropriate” candidates for mesial temporal laser ablation? We believe that patients with the semiology, EEG and imaging findings suggestive of mesial temporal lobe epilepsy will have the best chance of success. Whether patients without mesial temporal sclerosis on scan are also reasonable candidates must be determined. For example, whether mesial temporal thermal ablation should be offered to patients whose intracranial EEG shows