

Case Report

Stereotactic laser ablation of the splenium for intractable epilepsy[☆]Allen L. Ho^a, Kai J. Miller^a, Sam Cartmell^a, Katherine Inoyama^b, Robert S. Fisher^{a,b}, Casey H. Halpern^{a,b,c,*}^a Department of Neurosurgery, Stanford University, Stanford, CA, USA^b Department of Neurology and Neurological Sciences, Stanford University, Stanford, CA, USA^c Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA

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ABSTRACT

Partial or complete corpus callosotomies have been applied, traditionally via open surgical or radiosurgical approaches, for the treatment of epilepsy in patients with multifocal tonic, atonic, or myoclonic seizures. Minimally invasive methods, such as MRI-guided laser interstitial thermal ablation (MTLA), are being employed to functionally remove or ablate seizure foci in the treatment of epilepsy. This therapy can achieve effectiveness similar to that of traditional resection, but with reduced morbidity compared with open surgery. Here, we present a patient with a history of prior partial corpus callosotomy who continued to suffer from medically refractory epilepsy with bisynchronous onset. We report on the utilization of laser ablation of the splenium in this patient to achieve full corpus callosotomy. Adequate ablation of the splenial remnant was confirmed by postoperative MRI imaging, and at four-month follow-up, the patient's seizure frequency had dropped more than 50%. This is the first reported instance of laser ablation of the splenium to achieve full corpus callosotomy following a previous unsuccessful anterior callosotomy in a patient with intractable generalized epilepsy.

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1. Introduction

Surgical intervention is an option for a subset of the 30% of people with epilepsy whose seizures are resistant to antiseizure drugs [1]. Some patients with multifocal tonic, atonic, or myoclonic seizures may benefit from partial or complete corpus callosotomy [2,3]. Partial callosotomy involves sectioning the anterior half to two-thirds of the corpus callosum. Complete callosotomy also includes the splenium (Fig. 1). When reduction in symptoms has been unsatisfactory following partial callosal resection, complete callosotomy can be beneficial [4].

Minimally invasive methods, such as MRI-guided laser interstitial thermal ablation (MTLA), are being employed to functionally remove or ablate seizure foci. This therapy can achieve effectiveness similar to that of traditional resection [5], but with reduced morbidity compared with open surgery. Laser ablation for epilepsy has been applied to the periventricular region for heterotopia [6] and the hypothalamus for removal of seizure-inducing hamartomas [7]. Here, we present the first reported instance of laser ablation of the splenium following a

previous unsuccessful anterior callosotomy in a patient with intractable generalized epilepsy.

2. Case presentation

2.1. Case history

The patient is a 30-year-old ambidextrous male with a history of developmental delay, hypothyroidism, and symptomatic generalized epilepsy. Onset of poor feeding and limb jerking episodes began at 9 months in an otherwise normal infancy. Electroencephalogram monitoring at two years showed myoclonic seizures. Seizures worsened throughout childhood and adolescence, despite the introduction of numerous antiseizure medications, including carbamazepine, vigabatrin, gabapentin, lamotrigine, clobazam, clonazepam, diazepam, pyridoxine, valproate, corticosteroids, and topiramate. Magnetic resonance imaging in 2004 was unable to identify any structural correlate of the seizures. Electroencephalogram monitoring in January of 2005 demonstrated multifocal epileptiform discharges and slow spike-waves emanating from the right frontal lobe. A subsequent routine EEG captured a seizure with clonic activity beginning over the left hemisphere. In June of 2005, at another hospital, the patient underwent an anterior two-thirds corpus callosotomy via a right anterior craniotomy. This procedure provided roughly three months of seizure freedom before the patient relapsed with atonic seizures.

Upon first presentation to our institution in 2006, the patient was experiencing roughly 4-5 generalized tonic-clonic and 1-2 myoclonic

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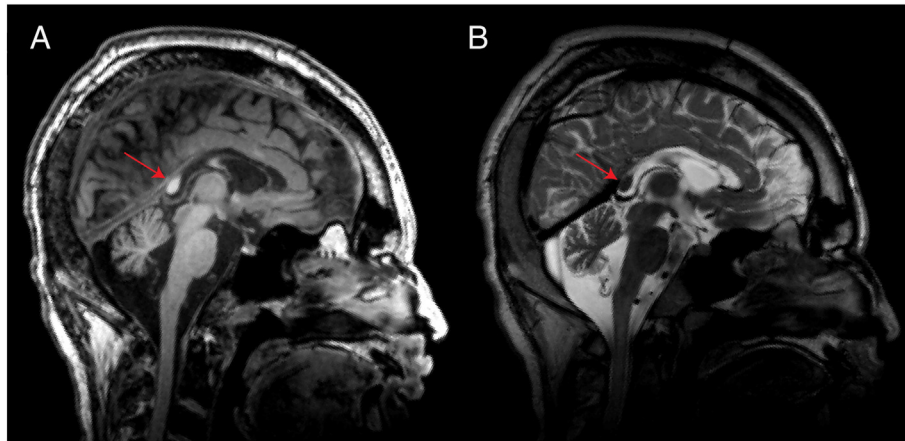


Fig. 1. Splenial remnant. Sagittal T1W (A) and T2W (B) MRI images of the patient's remaining splenium remnant status-postpartial corpus callosotomy. This remaining anatomic remnant of the corpus callosum was the anatomic target of our MRI-guided stereotactic laser interstitial thermal ablation of the splenium.

seizures each day, and weekly atonic seizures. An Athena screen for commonly identified seizure genes was negative. Additional therapies included felbamate, phenobarbital, rufinamide, and levetiracetam, in combination with a ketogenic diet and combinations of previously used medications. In May of 2013, a 24-hour continuous EEG captured at least 3 different types of seizures: focal left hemisphere seizures, myoclonic–atonic seizures, and tonic–clonic seizures. Both the myoclonic–atonic and tonic–clonic seizures appeared to have bisynchronous onset, suggesting a possible justification for completing the callosotomy. Epileptiform spikes and polyspikes also showed bilateral synchrony (Fig. 2).

Preoperatively, the patient was having 15–25 seizures per day, including 1–2 drop attacks per day. Functional status and wakefulness were compromised by the frequent seizures and the side effects of medications. In April of 2015, a stereotactic laser interstitial thermal ablation of the splenium was performed to complete his corpus callosotomy.

2.2. Operative details

The operation utilized standard technique for laser-induced thermal therapy [8], which is a minimally invasive approach for frameless stereotactic placement of a laser fiber at an intracranial target, in this case, the splenium (Fig. 1), utilizing the Medtronic Visualase® system. A unilateral trajectory was first mapped from the right parietal region down to the splenium on preoperative MRI scans (Fig. 3a) that were merged with a preoperative CT scan and then coregistered to an intraoperative CT with skull fiducials, a Medtronic O-arm®, and the StealthStation® Navigation System. The patient was placed in Mayfield pin fixation and turned prone. Five skull fiducials were used for registration with an error of less than 0.2 mm, and the target was acquired with an alignment error of less than 0.4 mm. The periosteum was exposed, a twist-drill burr hole was made, and the trajectory was rechecked prior to passing the guide cannula and advancing the laser fiber down the

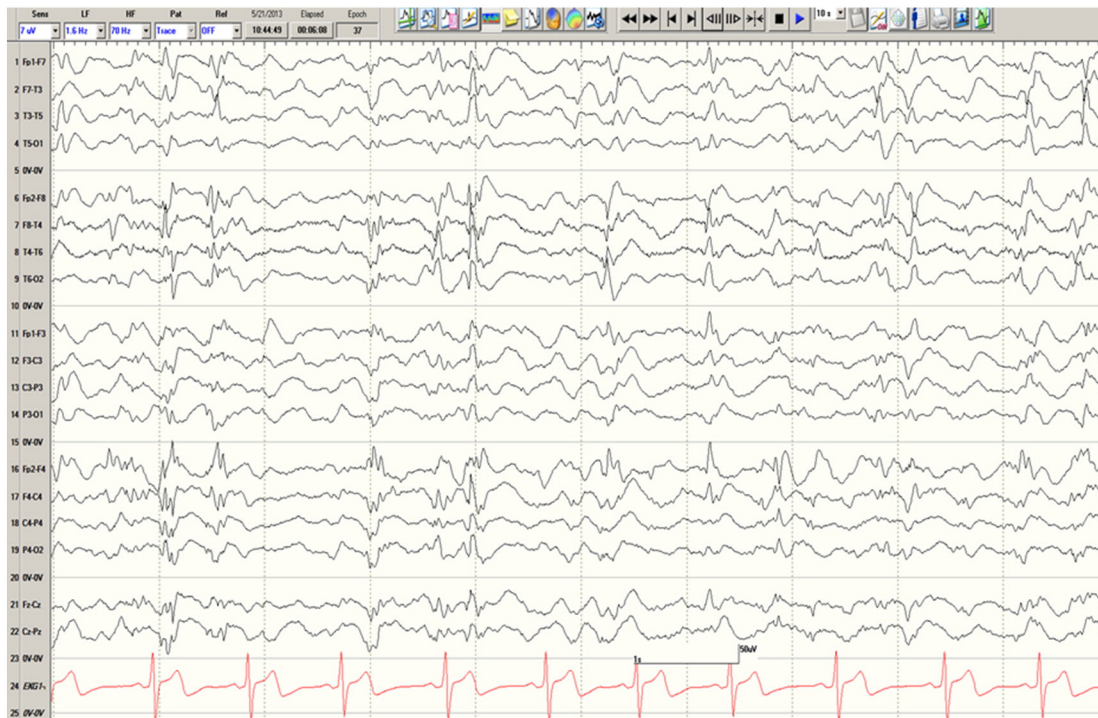


Fig. 2. EEG. Ten seconds of interictal EEG showing bilateral, sometimes synchronous spikes.

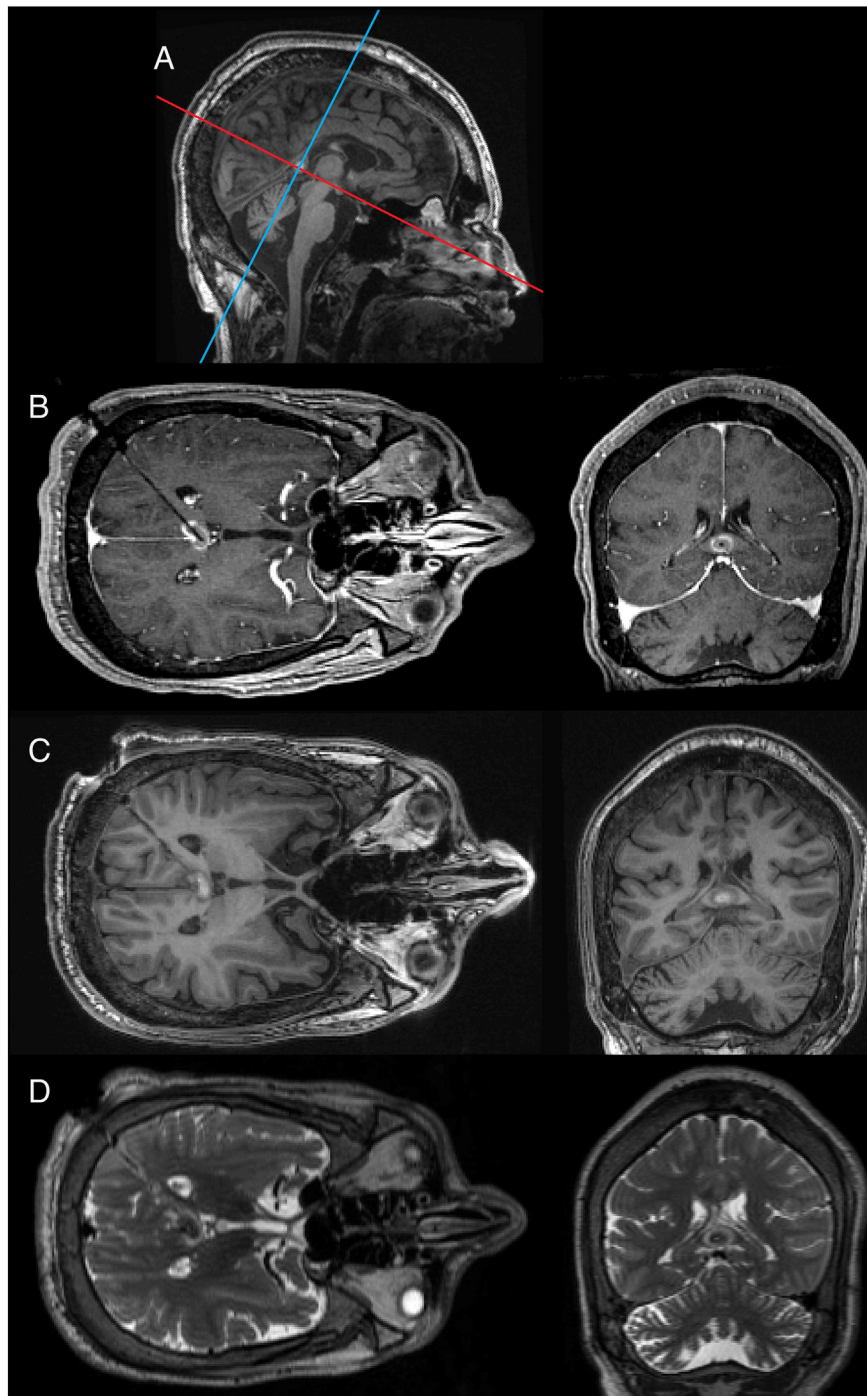


Fig. 3. Splenic ablation trajectory and postoperative MRI. (A) Preoperative sagittal T1W MRI demonstrating the planned anatomic trajectory (red) of the laser thermal ablation of the splenium. The blue line indicates the plane of the coronal cuts in the subsequent postoperative MRI slices. (B) Postablation contrast enhanced T1W MRI with axial slice in place with the laser trajectory (red) and perpendicular coronal slice (blue) demonstrating the extent of splenic ablation achieved. (C) Postablation T1W MRI with axial slice in place with the laser trajectory (red) and perpendicular coronal slice (blue) demonstrating the extent of splenic ablation achieved. (D) Postablation T2W MRI with axial slice in place with the laser trajectory (red) and perpendicular coronal slice (blue) demonstrating the extent of splenic ablation achieved with minimal surrounding edema.

planned trajectory. After removing the stylet, the laser was secured with a bolt system, and the O-arm imaging (coregistered to preoperative CT and MRI) was utilized to verify placement of the laser, which was found to be within 1 mm of the planned target. After removal of skull fiducials and Mayfield pin fixation, the patient was transferred to the MRI suite for target acquisition and performance of the laser ablation procedure. Trajectory and target acquisition were shown to be excellent, and

a test dose was administered. This was followed by a 3-minute, 70-°C thermal ablation of the splenium. Subsequent MRI confirmed adequate splenic ablation and the absence of any significant hemorrhage. Only one ablation was sufficient to cover the entire area of the splenium (Fig. 3b–d). After removal of all surgical equipment and closure of the wound site, the patient was transferred to the recovery room and discharged the next day.

2.3. Outcome

The laser-induced thermal ablation of the splenium was well-tolerated without any associated neurological impairment. At 4 months after surgery, seizure frequency has declined more than 50%, and atonic seizures have disappeared. Most seizures now occur during sleep, and patient's functional status has improved. The sedating medicines, phenobarbital and clonazepam, have been reduced. Because of the severe developmental disability and nonverbal status of the patient, it is not possible to evaluate for the presence of a disconnection syndrome [9].

3. Discussion

Corpus callosotomy has been utilized since at least the 1940s as an effective treatment for medically refractory epilepsy, particularly for patients who are not good candidates for a focal resection [4, 10]. By severing the primary connection between hemispheres, the spread of epileptic activity from one hemisphere to another can be prevented. While this does not eliminate seizures, it has been shown to achieve significant reduction in symptom severity and frequency, especially for tonic and atonic seizures that cause drop attacks [11].

Partial callosotomies are thought to offer some advantages over complete callosotomies by preserving perceptual connections between hemispheres and limiting so called disconnection syndromes sometimes associated with total callosotomy, while still achieving meaningful reductions in symptoms [3]. Nevertheless, there is good evidence that completion of corpus callosotomy can reduce symptoms when a partial resection has been unsuccessful [4]. Ours is the first report on stereotactic laser interstitial thermal ablation of the splenium following anterior callosotomy.

Traditionally, callosotomy is performed as an open surgery with all the associated risks. Another approach to lesioning callosum is stereotactic radiosurgery [12–16]. Radiosurgery has been employed specifically to ablate the posterior callosum [17]. However, stereotactic radiosurgery entails a delay of benefit and long-term risks of radiation. This current laser-ablation based, minimally invasive technique marks a novel iteration of this procedure that offers numerous advantages over open surgery while producing the same surgical goal of complete division of the corpus callosum. Magnetic resonance imaging-guided laser interstitial thermal ablation may be particularly effective for callosotomy because laser interstitial thermal therapy is dependent on the absorbance properties of the target tissue, and is best suited for relatively homogenous tissues, such as the corpus callosum, that will ablate uniformly with rapid heat drop-off to adjacent structures [18]. This technique may even offer advantages over other minimally invasive techniques, such as stereotactic radiosurgery, because the extremely well-demarcated region of ablation (with transition zone depth of less than 1 mm) can be confirmed immediately with T1-weighted or FLAIR MR images [18]. The current study applies to a small posterior callosal ablation. Modification of the approach and trajectory would be required for an anterior two-thirds or complete callosotomy.

4. Conclusions

Because of its numerous advantages over traditional surgery, MTLA is likely to be an important treatment of medically refractory epilepsy in the years to come. While its initial application has largely been in the treatment of focal seizures due to temporal lobe epilepsy, reports of its use in hypothalamic hamartomas, periventricular heterotopia, and the current splenial ablation demonstrate that the technique can be effective in a variety of scenarios. More experience will be needed to provide a comparison of the completeness of anatomical or physiological resection of laser versus open posterior callosotomy, to evaluate the technique for full callosotomies, and to measure the long-term efficacy.

Conflict of interest

None of the authors have any conflicts of interest to disclose with respect to this manuscript.

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