A novel use of the NeuroBlate SideFire probe for minimally invasive disconnection of a hypothalamic hamartoma in a child with gelastic seizures

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The authors describe the case of a 22-month-old boy who presented with gelastic seizures and developmental delay. Magnetic resonance imaging and video-electroencephalography monitoring revealed a primarily intraventricular hypothalamic hamartoma and gelastic seizures occurring 20–30 times daily. The patient was treated with various regimens of antiepileptic medications for 16 months, but the seizures remained medically intractable. At 3 years of age, he underwent stereotactic laser ablation with an aim of disconnection of the lesion. The procedure was performed with the NeuroBlate SideFire probe. To the authors’ knowledge, this is the first reported use of this technology for this procedure and serves as proof of concept. There were no perioperative complications, and 2 years postprocedure, the patient remains seizure free with marked behavioral and cognitive improvements.

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HYPOTHALAMIC hamartomas (HHs) are rare, nonneoplastic lesions composed of disorganized neurons and glial cells centered around the tuber cinereum in the inferior hypothalamus. The estimated incidence of this rare condition is about 1/200,000, and the lesions are commonly associated with precocious puberty, behavioral impairment, and gelastic seizures (GSs), defined as bouts of uncontrollable laughter and altered mental status.22 GSs are notoriously refractory to pharmaceutical treatment, and many patients develop secondary epileptogenesis and encephalopathy that are associated with behavioral impairment and cognitive decline.22

Open and endoscopic surgical approaches in the treatment of HHs have been described, with a reduction in seizure frequency and cessation of behavioral and cognitive decline.7 However, most studies report seizure freedom in only 49%–54% of the patients.28 Furthermore, open surgery is associated with significant morbidity and mortality rates. Minimally invasive alternatives include stereotactic radiosurgery (SRS) and stereotactic radiofrequency thermocoagulation (SRT). More recently, laser-induced thermal therapy (LITT) has been used to minimize the risks posed by conventional surgical treatments and reduce seizure recurrence rates.21 LITT uses thermal energy to induce intracellular damage and destroy tissues, and the incorporation of MRI thermography software with LITT enables near–real–time thermal mapping and feedback to the surgeon that enables informed clinical decision making.

Currently, 2 LITT platforms have been approved for commercial use: Visualase thermal ablation (Medtronic Inc.) and the NeuroBlate System (Monteris Medical). Visualase has been used in the successful treatment of cerebral lesions, including the total ablation and disconnection of HHs resulting in freedom from seizures9,10,23,35,39 and NeuroBlate has also demonstrated efficacy in the treatment of cerebral masses17,37 and has recently received investigational device exemption (IDE) approval from the FDA for evaluation of efficacy in medically refractory epilepsy. This report describes a novel treatment technique utilizing the NeuroBlate SideFire directional laser probe in the dis-
connection of a pediatric HH. This patient presented with GSs and has since maintained total seizure freedom in 2 years of follow-up.

Case Report
Clinical Presentation
A 22-month-old boy with a history of global developmental delay and autism spectrum disorder presented with daily episodes of uncontrollable laughter, which first manifested at 3 days of age. MRI demonstrated a $10 \times 11 \times 15$-mm, well-defined globular mass involving the hypothalamus and tuber cinereum, with mild splaying of the interpeduncular cistern and an arachnoid cyst in the posterior fossa (Fig. 1). Electroencephalography (EEG) monitoring showed that the patient experienced 20–30 episodes of GSs per day, each lasting up to 30 seconds. Oxcarbazepine therapy was initiated and eventually titrated to 30 mg/kg/day. The patient’s seizure frequency decreased to 3–4 times per day, but he then developed intractable head jerking and full-body shaking while receiving the maximum dosage of medication. At 38 months of age, the patient developed generalized atonic seizures, and his GS frequency increased to 6–7 times per day. Valproic acid was then added to his daily regimen but resulted in no improvement in his symptoms; following this he was then referred for surgical evaluation. The risks of open surgery were considered to be unjustified, so our team collectively decided to undertake disconnection of the HH using a LITT device, the NeuroBlate SideFire laser.

NeuroBlate Procedure
The Monteris Atoma frame and split head fixation ring were used for cranial fixation with standard adult pins. Given the patient’s age, care was taken to avoid overtightening the fixation system. The Brainlab optical neuronavigation system with Z-touch and Softouch was used for stereotactic registration with the patient’s preoperative MR images. The AxiiiS Stereotactic Miniframe (Monteris Medical) was placed, and the orientation was optimized based on a preoperative plan made on the Brainlab platform. After infiltrating the incision site, a small incision was made with a no. 11 blade, and hemostasis achieved with Bovie cautery. A 3.6-mm drill was used to create a burr hole, and the Bovie stick was again used for hemostasis and to penetrate the dura mater.

The patient was then transferred to the intraoperative MRI suite where the side-firing NeuroBlate probe was placed about 10 mm short of the calculated target. A volumetric MRI scan was then acquired using gradient, T1, and T2 paradigms. The borders of the neoplasm, optic chiasm, and optic nerves were identified and outlined. The probe was then advanced to the intended final depth, targeting the medial and posterior aspect of the neoplasm in an attempt at ablative disconnection (Fig. 2). The SideFire probe was chosen for its selective contouring abilities.

After double-checking the location of the probe, we treated with 17 minutes and 49 seconds of “laser-on time,” which treated approximately 70%–80% of the lesion volume to the yellow thermal damage threshold line and 50% to the blue threshold line, indicating a lesion temperature of 43°C for 2 minutes and 10 minutes, respectively. Only a single probe position was used. The probe was then removed without difficulty. Postprocedural MRI revealed no intraoperative hemorrhage or damage to surrounding structures. The patient returned to the operating room for standard closure. The total operative room time was 4 hours 57 minutes. Operative data are listed in Table 1.

Postoperative Course
The patient was then transferred to the pediatric ICU for a period of 24 hours for close neuromonitoring. Dexamethasone was given intraoperatively and continued in the postoperative period at a dose of 2 mg twice daily for a total of 4 days, when it was discontinued. An MRI study obtained on postoperative day 1 showed expected therapeutic changes consistent with ablation (Fig. 3). The patient was ultimately transferred to the regular pediatric nursing floor and discharged without incident on postoperative day 5.

At the 2-week follow-up, the patient’s caregivers reported that he had experienced only a single seizure postoperatively. Since then, the patient has remained seizure free for 2 years following surgical disconnection of the HH. He has made significant improvements in his eating and sleeping habits, is making eye contact, and has expanded his vocabulary. His caregivers report episodes of nonstop head banging that began with initiation of clobazam, which is currently being weaned. His seizures are now successfully

FIG. 1. A: Sagittal T2-weighted MR image obtained at time of diagnosis. B: Axial FLAIR MR image obtained at time of diagnosis. C: Coronal T1-weighted MR image obtained at time of diagnosis. Figure is available in color online only.
managed with valproic acid, oxcarbazepine, and risperidone. He continues to receive physical, occupational, and speech therapy for autistic spectrum disorder.

**Discussion**

Hypothalamic hamartomas are considered intrinsically epileptogenic, and microsurgical resection can result in reduced seizure frequency or complete seizure freedom, which can halt behavioral impairment and cognitive decline. However, patients can develop postoperative memory dysfunction, visual impairment, endocrine disorders, and hemiparesis. Furthermore, it has been suggested that postoperative seizure outcome is actually independent of the degree of HH resection. As such, surgical disconnection of the HH from the surrounding hypothalamus has emerged as a safe and elegant alternative to resective surgery. The mammillothalamic tract may be considered a conduit for GS propagation, as the projection to the anterior thalamic nucleus and subsequently to the anterior cingulate gyrus potentially has a role in the production of normal laughter. Thus, it has been suggested that disconnection of the lesion from this region should be the primary goal of surgery.

A variety of minimally invasive approaches have been developed to minimize the risks posed by conventional surgical treatments while maintaining reduced seizure recurrence rates. Despite initial promising results with Gamma Knife SRS, long-term studies have reported overall seizure remission rates of only 27%. Furthermore, the use of radiation therapy in the pediatric population poses concerns for the potential development of brain maturation, cognitive impairment, and malignancy. SRT is a minimally invasive approach that does not use radiation but is associated with postoperative complications in the majority of patients. LITT is another minimally invasive procedure that uses thermal energy to destroy tissues, and it requires the stereotactic placement of a small-diameter laser into the lesion, from which light passes into the tissues and is converted to thermal energy that induces cell death and coagulative tissue necrosis. Unlike SRT, MRI thermography software incorporated into LITT enables the surgeon to modulate treatment in near real time, allowing precise control of the volume, shape, and location of lesions not possible with SRT. This enables the surgeon to treat through a portion of the target HH but to stop treatment when the damage zone begins to impinge on surrounding normal tissues. The Visualase system was the first MRI-guided LITT technology approved for commercial use and has been used successfully in the treatment of benign and malignant brain tumors, as well as the ablation of epileptogenic foci in pediatric patients. It has since been used in the complete ablation and disconnection of HHs in both adult and pediatric populations, including cases in which the lesions were refractory to other types of initial surgical therapy. Studies have reported seizure freedom in up to 86% of LITT-treated patients, who have shown improve-
ments in behavior and precocious puberty without significant side effects.\textsuperscript{9,10,35,39} Table 2 provides a summary of reports of laser ablation for HH.\textsuperscript{19–12,30,35,39,41}

The efficacy of NeuroBlate is well established in the ablation of intracranial lesions and has proven to be a safe and viable option in the treatment of gliomas and brain metastases.\textsuperscript{17,37} However, there are limited data regarding its use in epilepsy.\textsuperscript{6,18} Efforts are currently underway to evaluate the efficacy of NeuroBlate in an open-label study on patients with drug-refractory medial temporal lobe epilepsy (https://clinicaltrials.gov/ct2/show/NCT02820740).

NeuroBlate technology provides 2 different options for ablation: the standard diffusing tip for concentric volumetric ablation (FullFire; similar to the standard Visualase probe), and the directional SideFire laser probe. The SideFire probe enables contoured ablation at an approximate 90° angle to the catheter over a 15° arc, giving the surgeon enhanced control over the ablation zone and purportedly preserving healthy tissue, particularly for small lesions at low thermal intensities. In addition, this technology potentially allows for probe placement in a slightly “off-target” position, either based on preoperative planning to avoid eloquent structures or to correct for minor variability between preoperative planning and imaging confirmation of probe placement. There have yet to be any reports comparing the lesional potential between these 2 probe types, but subjective experience suggests that the FullFire probe produces a larger concentric ablation zone, whereas the SideFire probe produces a smaller asymmetrical ablation zone due to its directionality.

This report describes, to our knowledge, the first reported use of NeuroBlate technology, and specifically the SideFire directional laser probe, to successfully treat a pediatric patient with an HH. We used a disconnection approach, which treats GSs by disrupting the epileptic network of neurons created by the HH, without having Table 2. Summary of reports on laser ablation for HH in the literature

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>Sex &amp; Age</th>
<th>Equipment &amp; Approach</th>
<th>Outcome in Sz Frequency</th>
<th>Complications</th>
<th>LOS (days)</th>
<th>FU (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akai et al., 2002</td>
<td>1</td>
<td>F; age 5</td>
<td>NS; partial endoscopic resection w/ laser coagulation</td>
<td>Remarkable reduction (prior SRS)</td>
<td>Lt hemiparesis &amp; decreased level of consciousness for 1 wk following 2nd op</td>
<td>NS</td>
<td>16</td>
</tr>
<tr>
<td>Curry et al., 2012</td>
<td>2</td>
<td>2 M; ages 9 &amp; 15</td>
<td>Visualase; complete ablation</td>
<td>Both Sz free</td>
<td>Transient, nondisabling memory impairment in 1 patient</td>
<td>5, 8</td>
<td>2, 5</td>
</tr>
<tr>
<td>Wilfong &amp; Curry, 2013</td>
<td>14</td>
<td>3 F, 11 M; age range 0.9–20 (mean 7.8)</td>
<td>Visualase; disconnection</td>
<td>Sz free: 7/14 (3 w/ prior TCR, RT or GKS, 1 undergoing 2 ops); 50% reduction: 2/14; Engel class I: 4/14</td>
<td>Self-limiting, asymptomatic subarachnoid hemorrhage in 1 patient</td>
<td>Range 1–8 (mean 2)</td>
<td>Range 1–24 (mean 9.3)</td>
</tr>
<tr>
<td>Calisto et al., 2014</td>
<td>7</td>
<td>5 F, 2 M; age range 0.8–37 (mean 11.7)</td>
<td>RevoLix; disconnection followed by destruction of inner mass w/ coagulator</td>
<td>Engel class I: 1/7; Engel class II: 2/7 (1 w/ prior GKS ×2); Engel class II: 3/7 (1 w/ prior resection ×2, 1 w/ prior AH); Engel class III: 1/7 (1 w/ prior GKS &amp; resection ×2)</td>
<td>Postop drowsiness &amp; thalamic hypodensity on CT in 1 patient; postop memory deficit in 1 patient; postop fever in 1 patient</td>
<td>NS</td>
<td>12</td>
</tr>
<tr>
<td>Zubkov et al., 2015</td>
<td>1</td>
<td>M; age 19</td>
<td>NS</td>
<td>Disabling frequency</td>
<td>Damage to bilateral mammillary bodies &amp; disabling amnestic syndrome</td>
<td>NS</td>
<td>8</td>
</tr>
<tr>
<td>Rolston &amp; Chang, 2016</td>
<td>2</td>
<td>2 M; ages 20 &amp; 28</td>
<td>Visualase; disconnection</td>
<td>Sz free: 2/2 (1 w/ prior GKS, 1 w/ prior GKS ×2)</td>
<td>Transient hyperphagia &amp; amnesia w/ resolution by FU in 1 patient; nondisabling auras continued in 1 patient</td>
<td>NS</td>
<td>5, 7</td>
</tr>
<tr>
<td>Burrows et al., 2016</td>
<td>3</td>
<td>1 M, 2 NS; ages 25, 28, &amp; 48</td>
<td>Visualase; complete ablation</td>
<td>Engel class I &amp; ILAE class I: 1/3 (1 w/ prior SRS); Engel class III &amp; ILAE class IV: 1/3 (1 w/ prior SRS); NS: 1/3</td>
<td>Increased craving for sweets leading to significant weight gain; hypothalamic symptoms postdischarge, including hyponatremia due to SIADH in 1 patient; small tract hematoma in 1 patient</td>
<td>Range 2–5 (avg 3)</td>
<td>28 &amp; 32 (1 none)</td>
</tr>
<tr>
<td>Brandmeir et al., 2016</td>
<td>1</td>
<td>M; age 63</td>
<td>Visualase; complete ablation</td>
<td>Sz free (prior GKS ×2)</td>
<td>20 kg weight loss, transient r-handed hemiparesis, leg DVT</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Pruitt et al., 2017</td>
<td>6</td>
<td>1 M, 5 NS; age 24</td>
<td>Visualase; NS</td>
<td>NS</td>
<td>Epidural hematoma due to inadequate dural puncture</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

AH = amygdalohippocampectomy; avg = average; DVT = deep vein thrombosis; FU = follow-up; GKS = Gamma Knife surgery; ILAE = International League Against Epilepsy; LOS = length of hospital stay; NS = not specified; RT = radiation therapy; SIADH = syndrome of inappropriate antidiuretic hormone secretion; Sz = seizure; TCR = transcallosal resection.
to completely remove the lesion. This approach has been documented to be safer than, and as effective as, conventional treatments.\textsuperscript{23–25} The novelty of this case is demonstrated by achieving treatment from within the ventricle by choosing a trajectory that placed the probe on the surface of the lesion (Fig. 2). It is unlikely that a standard diffusion probe would have resulted in the same disconnection and clinical efficacy, as concentric ablation within the third ventricle would likely disperse heat due to CSF shunting.\textsuperscript{12} Probe placement centrally within the lesion would have allowed for concentric ablation, although with potential greater morbidity due to the probe’s proximity to eloquent structures. Thus, the directionality of the probe allows for customizing trajectories that would otherwise not likely be possible with the standard diffusion probes. Contoured lesion anatomy generated with Surgical Theater software is demonstrated in Fig. 4. This case serves as proof of principle for a new method of treating intraventricular lesions adjacent to vital structures, with our having demonstrated that careful trajectory selection and probe placement, along with use of a directional laser, can be successful without significant heat sink effect from CSF or damage to surrounding structures.

Preoperatively, our patient suffered from 20–30 epileptic episodes per day. Following disconnection and ablation of the HH, the patient suffered only a single GS within the first 2 postoperative weeks and has since remained seizure free for 2 years. This result should be interpreted with caution due to our experience with only a single patient; however, this is a promising result that merits further study into the safety and long-term efficacy of HH disconnection using NeuroBlate SideFire technology.

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**Disclosures**

Dr. Sloan has served as a paid consultant to Monteris Medical.

**Author Contributions**

Conception and design: all authors. Acquisition of data: Wright, Staudt, Alonso. Analysis and interpretation of data: Wright, Staudt. Drafting the article: Wright, Staudt, Alonso. Critically revising the article: Sloan, Wright, Staudt, Miller. Reviewed submitted version of manuscript: all authors. Study supervision: Sloan, Miller.

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