Magnetic Resonance guided Laser Interstitial Thermal Therapy for medically intractable epilepsy

Alexander G. Weil, MD, FRCSC, FAANS, FACS

1Division of Pediatric Neurosurgery, Department of Surgery, Sainte Justine Hospital, University of Montreal, Montreal, QC, Canada
2Neurosurgery Service, Department of Surgery, Notre Dame Hospital, CHUM, Montreal, QC, Canada

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  • **Other:** None

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  • Participated on the Medtronic advisory Board Meeting
  • I have not received any compensation
Introduction

• 40% of epilepsy patients are medically refractory

• Epilepsy surgery: Seizure freedom can comes at the cost of neurological and surgical morbidity
  • Expected vs. unexpected
  • Up to 6% major and 17% minor neurological morbidity
  • Surgical morbidity (infection, wound complication, CSF leak)
  • <1% death

• Any new technology that can be as effective as open surgery with less risk is a welcomed addition

Weil AG, Bhatia S. The surgical treatment of Extratemporal Epilepsy, Pediatric Neurosurgery: Tricks of the Trade, 2015
All epilepsy surgeries are not created equal

Left temporal periventricular heterotopia

Left operculo-insular (prior surgery+GKS)

Hypothalamic hamartoma
MRgLITT is rapidly gaining in popularity as a new alternative to craniotomy for tumors and DRE

Visualace (approved by FDA in 2010) as of August 1st 2014

Data provided by Visualace
MRgLITT is rapidly gaining in popularity as a new alternative to craniotomy for tumors and DRE.
What are lasers?

- light amplification by stimulated emission of radiation

Laser = Coherent emission of light
Temperatures in Laser Ablation

• > 100°C – Rupture of membranes and vaporization of intra/extra cellular water

• 60-100°C – Instant denaturation of proteins and cellular components. Tissue coagulation

• 44-59°C – Time dependent thermal damage. Thermal denaturation of critical enzymes; cell death

• ~43°C – Below this thermal damage does not occur
What is MRgLITT?

- Stereotactic placement of laser probe to thermally ablate a CNS lesion (epileptic foci) under MRI-guidance (thermal maps)

**Accurate**

**Real-time feedback**

Real-time thermal mapping

Real-time ablation damage estimate

T1 proton spin-echo MRI

**NOTE:** It is for the physician to determine which product to use for which patient condition. This text is provided as a general guide for convenience of product appropriateness.
A MINIMALLY INVASIVE ALTERNATIVE

Craniotomy

MRgLITT
<table>
<thead>
<tr>
<th></th>
<th>Monteris® (NeuroBlate)</th>
<th>Medtronic® (Visualace)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Probe width</strong></td>
<td>2.2 or 3.3 mm</td>
<td>1.6 mm</td>
</tr>
<tr>
<td><strong>Wavelength</strong></td>
<td>1064 nm</td>
<td>980 nm</td>
</tr>
<tr>
<td><strong>W</strong></td>
<td>12-W pulse mode</td>
<td>15-W</td>
</tr>
<tr>
<td><strong>Cooling mechanism</strong></td>
<td>CO2</td>
<td>cold saline</td>
</tr>
<tr>
<td><strong>Laser beam emission</strong></td>
<td>side-fire or ellipsoid</td>
<td>ellipsoid only</td>
</tr>
<tr>
<td><strong>Probe advancement</strong></td>
<td>Robotic</td>
<td>Manual</td>
</tr>
</tbody>
</table>
Rationale for MRgLITT in drug-resistant epilepsy

- May be particularly suitable for
  - Deep location
  - Eloquent
  - Reoperation

Ramantani et al., Neurosurgery, 2013
Rationale for MRgLITT in drug-resistant epilepsy

- Minimally invasive
- Small Incision, less pain
- No ICU stay
- 1-2 day surgery
- Real-time feedback
- Reduce infection rate
- Reduce neuro morbidity
MR-guided laser interstitial thermal therapy for pediatric drug-resistant lesional epilepsy

*¹Evan Cole Lewis, †²Alexander G. Weil, *Michael Duchowny, †Sanjiv Bhatia, †John Ragheb, and *Ian Miller


doi: 10.1111/epi.13106
The CHU Sainte-Justine performs first-ever laser surgery in a patient with epilepsy

A Canadian First!
Clinical case 1

- 11 year-old boy
- Initial presentation in infancy (2006) in first year of life:
  - gelastic seizures and developmental delay

2007: undergoes open partial resection of HH through transcallosal approach
Immediately postoperative MRI

- Initially 90% improvement in seizures
  - Over last year
    - Seizures increasing, particularly at night, Behavioral and cognitive issues, Anxiety, Memory impairment
  - Medications: Lupron, Tegretol, Frisium
MRI at follow-up (2016)
What are the traditional treatment options?
Options for Hypothalamic Hamartoma

<table>
<thead>
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<td>70%</td>
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<td>Morbidity</td>
<td>77% transient 0% permanent</td>
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<td>25% transient 6% permanent</td>
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<tr>
<td>Mortality</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0-10%</td>
</tr>
<tr>
<td>Limitations</td>
<td>Precision, size, experience</td>
<td>HH Size &lt;1.5 cm and location, delayed action, RT-injury (optic)</td>
<td>Surgical difficulty, HH size &lt;1 cm and location</td>
<td>Morbidity</td>
</tr>
</tbody>
</table>
2-Stage bilateral laser ablation

November 22\textsuperscript{nd} 2016
• LOH 1 day
• Seizures improved, improved cognitively (more alert, improved attention), behavior unchanged
Second phase

- 8 month postop:
- LOH 2 days (No ICU stay)
- Overall Seizure improvement
- Cognition: returned to baseline before first procedure
- Behavior: not changed

Lesson: learning curve
Case 2: 4 year-old girl, refractory gelastic seizures, behavioral issues

Mainly Left-sided attached HH
Preop MRI coronal T1

Because of the orientation of attachment, we decided to approach this from a contralateral approach to optimize disconnection.

Main side of attachment

Fiber orientation
Contralateral approach (Left-side disconnection through a right-side approach)

Immediate post-ablation irreversible damage estimate
Immediate postoperative MRI (T2)
6 months postop:
- LOH 24 hours (No ICU)
- No complications
- Seizure-free for first 2 weeks
- After decadron weaned, seizure recurrence
- Currently, seizures have returned to daily, we are planning re-imaging and assessment for phase 2 treatment

Lesson: challenging cases remain challenging
Case 3: 19 year old girl, medically refractory CPS, lesional with congruent non-invasive data

What are the options?
1 month postop:
- LOH 1 day (no ICU)
- Seizure free
- Mild language (word finding) difficulties which are improving

Lesson: not risk-free
Case 4 – 17 yr old, left temporal lesional DRE, congruent non-invasive data
Clinical course: LOH 1.5 days, seizure free, No deficit

Lesson: open still safe and effective
Is it the end of craniotomy/resective surgery in epilepsy lesionectomy?
Goals of the study

• **Primary question:**
  • What is the *efficacy* and *safety* of MRgLITT for DRE?

• **Secondary question:**
  • What are the *characteristics* of the reported patient population undergoing MRgLITT
  • What are the *independent predictors* of success following MRgLITT?
Methods

• **Systematic review and meta-analysis from IPD**
  
  • 13 Terms (MRI-guided laser ablation, etc) and 11 databases

• **Eligibility criteria**

  • **Inclusion criteria** for the studies were the following:
    • [1] Case-control, cohort, or randomized controlled trial methodology
    • [2] Consecutive participants (minimum of 2)
    • [3] At least 90% of patients undergoing MRgLITT have epilepsy
    • [4] Outcome reported for individual participants

  • **Exclusion criteria** for the studies were the following:
    • [1] Single case reports
    • [2] Reviews
    • [3] Participants reported due to anomalous features
    • [4] Participants that had undergone MRgLITT for conditions other than DRE
    • [5] Individual patient data (IPD) not available after contacting the authors
    • [6] Published prior to 2010
PRISMA 2009 Flow Diagram

Total (n=5915)
- Africa-Wide Information (n=8)
- AMED (n=1)
- BIOSIS (n=226)
- CINAHL (n=15)
- Cochrane (n=14)
- Embase (n=3930)
- Global Health (n=50)
- LILACS (n=1)
- Medline (n=1538)
- PubMed (n=26)
- Web of Science (n=445)

Additional records identified through other sources; hand searching of reference lists, conference abstracts, and recent (n=2)

Records excluded (n=184); Editorials, Meetings, Notes, Surveys, Letters, Comments, Correspondence, News, and interviews

Records after duplicates removed and search limited to 2010-current (n=1959)

Records excluded after title and abstract screening (n=1859)

Full-text articles excluded, with reasons (n=4):
- Case report (n=2)
- Review article (n=1)
- No IPD available (n=2)

Records screened (n=1875)

Full-text articles assessed for eligibility (n=16)

Studies included in qualitative synthesis (n=12)

Studies included in qualitative synthesis (meta-analysis) (n=12)

Methods

12 articles, 90 patients

For more information, visit www.prisma-statement.org.
### Patient population

**Mean age 21 (range 1-76)**

**41 pediatric cases (<21 years)**

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>42 (46.6)</td>
</tr>
<tr>
<td>Female</td>
<td>43 (47.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>5 (5.4)</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td></td>
</tr>
<tr>
<td>MTA/S</td>
<td>44 (48.9)</td>
</tr>
<tr>
<td>HH</td>
<td>15 (16.7)</td>
</tr>
<tr>
<td>FCD</td>
<td>8 (8.9)</td>
</tr>
<tr>
<td>Other etiology (TSC, cavernoma, heterotopia, gliosis, GNT)</td>
<td>23 (25.6)</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td></td>
</tr>
<tr>
<td>Medial temporal lobe</td>
<td>50 (55.6)</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>15 (16.7)</td>
</tr>
<tr>
<td>Neocortical</td>
<td>25 (27.8)</td>
</tr>
<tr>
<td><strong>Lesions on MRI</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>85 (94.4)</td>
</tr>
<tr>
<td>No</td>
<td>5 (5.6)</td>
</tr>
</tbody>
</table>
## Patient population

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive monitoring</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7 (7.8)</td>
</tr>
<tr>
<td>No</td>
<td>85 (92.2)</td>
</tr>
<tr>
<td>Prior surgeries</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 (13.3)</td>
</tr>
<tr>
<td>No</td>
<td>78 (86.7)</td>
</tr>
</tbody>
</table>
Results
Safety

• 19 complications /14 patients (15.5%)
  • 4 probe-related
    • 3 misplaced probes (SAH, visual deficit, aborted procedure)
    • 1 cooling mechanism failure
  
  • 5 new-onset neurological deficits
  
  • 3 oedema-related
    • HH (n=1), transient ophthalmic-paresis (n=1), steroid gastritis (n=1)
  
  • 2 asx hemorrhages (aHSD, HSA)
Case Report

Disabling amnestic syndrome following stereotactic laser ablation of a hypothalamic hamartoma in a patient with a prior temporal lobectomy

Sarah Zubkov\textsuperscript{a}, Victor A. Del Bene \textsuperscript{b}, William S. MacAllister \textsuperscript{a}, Timothy M. Shepherd \textsuperscript{a}, Orrin Devinsky \textsuperscript{a,*}

\textsuperscript{a} NYU Langone Medical Center, New York, NY 10016, USA
\textsuperscript{b} Ferkauf Graduate School of Psychology, Yeshiva University, 1165 Morris Park Avenue, Bronx, NY 10461, USA
Results: *Length of stay*

Mean: 1.9 days (range 1-14)
Results: *Efficacy*

- Median follow-up: 12 months (range 1-38.5)
- 57.6 % had Engel class 1 at last FUP
- Twelve (13.3%) patients required repeat MRgLITT
- Time-to-event (seizure recurrence) analysis

![Kaplan-Meier Survival Function following MRgLITT](image)

70.8% (4.9) at 6 months
53.2% (6.1) at 12 months

Mean duration of seizure freedom: 19.4 months (95% CI, 15.0-23.8)
### Univariate Cox regression analysis of assessed covariates

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Hazard ratio</th>
<th>95% confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&lt; 21 years)</td>
<td>1.028</td>
<td>0.55-1.93</td>
<td>.930</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTA/S</td>
<td>0.886</td>
<td>0.42-1.88</td>
<td>.752</td>
</tr>
<tr>
<td>HH</td>
<td>0.639</td>
<td>0.20-2.01</td>
<td>.444</td>
</tr>
<tr>
<td>FCD</td>
<td>1.284</td>
<td>0.47-3.47</td>
<td>.623</td>
</tr>
<tr>
<td>Other (reference)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mTLE</td>
<td>0.802</td>
<td>0.41-1.58</td>
<td>.525</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>0.572</td>
<td>0.19-1.75</td>
<td>.327</td>
</tr>
<tr>
<td>Neocortical (reference)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No previous surgery</td>
<td>0.994</td>
<td>0.44-2.26</td>
<td>.988</td>
</tr>
</tbody>
</table>
Age

Kaplan-Meier Survival Function following MRgLITT (by age)

Univariate cox regression analysis, P=0.90
Prior surgery

Univariate cox regression analysis, P=0.988
Location

Hypothalamus

Medial TL

Neocortical

Kaplan-Meier Survival Function following MRgLITT (by location)

P=NS
## Etiology

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Seizure freedom at 6 months % (SD)</th>
<th>Seizure freedom at 12 months % (SD)</th>
<th>Overall seizure freedom % (SD)</th>
<th>Engel 1 at last FUP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTA/S</td>
<td>68.4 (7.0)</td>
<td>56.5 (8.5)</td>
<td>60.9</td>
<td>68.0</td>
</tr>
<tr>
<td>HH</td>
<td>68.8 (13.1)</td>
<td>68.8 (12.6)</td>
<td>73.3</td>
<td>75.0</td>
</tr>
<tr>
<td>FCD</td>
<td>85.7 (13.2)</td>
<td>42.9 (18.7)</td>
<td>25.0</td>
<td>37.5</td>
</tr>
<tr>
<td>Other</td>
<td>71.1 (10.0)</td>
<td>47.9 (11.8)</td>
<td>47.6</td>
<td>60.8</td>
</tr>
</tbody>
</table>

**HH > MTA-S > other > FCD**
Etiology
Kaplan-Meier Survival Function following MRgLITT for mesial temporal sclerosis by age

Above 21 years

Below 21 years

P=0.879
## Discussion: Hypothalamic Hamartoma

<table>
<thead>
<tr>
<th></th>
<th>Radiofreq. ablation</th>
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<td>Surgical difficulty, HH size &lt;1 cm and location</td>
<td>morbidity</td>
<td>Learning curve, lesion size</td>
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## Discussion: SAH for mesial TLE

<table>
<thead>
<tr>
<th></th>
<th>Open SAH</th>
<th>MRgLITT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy (Sz-free rate)</strong></td>
<td>50-70%</td>
<td>60%</td>
</tr>
<tr>
<td><strong>VFD rate</strong></td>
<td>50-100%</td>
<td>6%</td>
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Better Object Recognition and Naming Outcome With MRI-Guided Stereotactic Laser Amygdalohippocampotomy for Temporal Lobe Epilepsy

Daniel L. Drane, Ph.D.¹,²,³, David W. Loring, Ph.D.¹,², Natalie L. Voets, Ph.D.⁴, Michele Price, MSW¹, Jeffrey G. Ojemann, MD⁵, Jon T. Willie, MD, Ph.D.¹,⁶, Amit M. Saindane, MD⁷, Vaishali Phatak, Ph.D.⁸, Mirjana Ivanisevic, BS¹, Scott Millis, Ph.D.⁹, Sandra L. Helmers, MD, MPH¹,², John W. Miller, MD, Ph.D.¹,³,⁵, Kimford J. Meador, MD¹,², and Robert E. Gross, MD, Ph.D.¹,⁶

**SIGNIFICANCE**—Preliminary results suggest 1) naming and recognition functions can be spared in TLE patients undergoing SLAH, and 2) the hippocampus does not appear to be an essential component of neural networks underlying name retrieval or recognition of common objects or famous faces.
Conclusions

• MRgLITT: Associated with reduced post-operative LOH and a moderate morbidity profile

• Variably effective procedure dependent on etiology of DRE
  • HH: Should be considered first line treatment

  • mTLE requiring SAH: appealing minimally invasive alternative, preliminary evidence suggests a lower rate of VFD and possibly less neurocognitive impairment

  • Extra-temporal FCD: Role is less clear and may be best suited for deep lesions (e.g. depth of sulci), reoperations in select cases and focal disruption of epileptogenic networks.

• Applications: reoperations, deep-seated lesions (e.g. heterotopias)

• Large long-term prospective multicenter observational studies are required
Limitations of MRgLITT

• Acquisition and ongoing cost of the laser program
• Learning curve
• Lesion size (4 cm)
• Histopathological diagnosis
• Functional and epileptogenic zone mapping
Acknowledgments

Collaborators

Anthony C. Wang, MD
Bethany Myers
Aria Fallah, MD, MSc, FRCSC,

Evan C Lewis, MD

Lionel Carmant, MD
Anne Lortie, MD
Philippe Major, MD
Elsa Rossignol, MD
Claude Mercier, MD, FRCSC

Alain Bouthillier, MD, FRCSC
Dang K Nguyen, MD, PhD

Sami Obaid, MD
Harrison Westwick, Md, MSc

Adil Harroud, MD
Elena Guadagno, MLIS
Technique: Stereotaxy

Vs. frameless neuronavigation (more superficial lesions)
Frame localisation

Frame-based CT and Preop MRI-CT coregistration

Frame-based MRI
-MRI-compatible Frame)
Probe trajectory planning
4-mm incision
Dural opening
Bolt placement
Patient taken to MRI

Accessing the Tumor
Laser fiber placement
The Monteris Mini-Bolt delivery platform's robust titanium design allows complete versatility with your stereotactic approach.
Laser Ablation
Real Precision, Real Control

The Robotic Probe Driver allows uninterrupted, remote surgeon control of the laser probe.