INTRO

MRI-guided neurosurgical ablation (cytoreductive surgery).

monitors ablation contours in 3-Dimensions and provides real time MRI thermographic analysis to support surgeon's decisions.

+diode laser energy delivered via cooled* fiber-optic minimally invasive probe which allows to selectively ablate lesions in brain that may have been previously deemed inoperable.

*to control thermal spread within tissue and protect device tip.

MINIMALLY-INVASIVE

Craniotomy approach:

Laser approach:

BIOPHYSICS

- based on Arrhenius equation:

Temperature ≤ 45º - tissue damage never occurs, no matter how long exposed.

Temperature > 60º - instantaneous tissue damage (protein denaturation).
LASER ABLATION TECHNIQUES

**INDICATIONS**

1. **Epilepsy**
   a. Mesial temporal epilepsy (incl. mesial temporal sclerosis, temporal encephalocele) – see p. E15 >>
   b. Insular epilepsy
   c. Periventricular nodular heterotopias – see p. Dev7 >>
   d. Focal cortical dysplasias – see p. Dev7 >>
   e. Tubers – see p. Pha5
   f. Hypothalamic hamartomas – see p. Dev7 >>
   g. Corpus callosumy – see p. E21 >>
   h. Poststroke epilepsy

2. **Tumors - metastases, gliomas**
   a. recurrent superficial tumors (do not warrant morbidity of craniotomy)
   b. deep-seated brain tumors (not amenable to traditional resection, e.g. insular – see p. Onc12 >)
   N.B. there is evidence of tumor stem cell resistance to thermal damage across the entire temperature range they were exposed (mechanisms of thermoresistance might involve the overexpression of members of the heat shock protein family)

3. **Cavernomas** – see p. Vas30 >>

4. **Symptomatic radiation necrosis**

- **LITT** can be done anywhere intra-axially (incl. brainstem); if near eloquent areas; o it can be done awake (monitor for delayed deficits within 3 weeks and give steroids PRN).
- **LITT is not good for**:
  1) extra-axial tumors; exception – separation surgery for spinal epidural tumors (give margin for SRS to spare cord) but respirations are problematic for MRI monitoring.
  2) calcified lesions
  - target size:
    o creates 25-35 mm diameter lesion.
    o no volume limits for LITT (up to 50 mL).
  - FDA cleared for: - to ablate, necrose or coagulate intracranial soft tissue through interstitial irradiation or thermal therapy in discipline of neurosurgery.

**LITT candidate selection**

1. Lesions that are favorable for LITT are (1) deep seated, (2) spherical or oblong such that the laser probe can be passed through the long axis of the lesion, (3) well circumscribed, and (4) positioned such that a safe trajectory avoiding critical structures/tracts can be designed.
2. Transgression of vascular planes (Sylvian fissure, sulci) and ventricles is avoided.
3. Lesions unfavorable for LITT include: a) hypervascular lesions b) cystic lesions – difficult to ablate, laser does not control cyst mass effect; H: aspirate cyst and then ablate.
   c) diffuse lesions involving bilateral or multiple lobes, and very large lesions in which treatment would be subtotal.
4. Lesions in eloquent or constricted locations (basal ganglia, posterior fossa) are more difficult to target, although it is not a contraindication to treatment.
5. Patient positioning, the profile of the laser apparatus, and patient body habitus, which together must fit into the MRI bore.

**Callosal lesions**
FDA
- First reported for treatment of epilepsy in 2012.

### SYSTEMS

#### COMPARISON

<table>
<thead>
<tr>
<th></th>
<th>Visualase</th>
<th>Monteris</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wave length</td>
<td>984 nm</td>
<td>1064 nm*</td>
</tr>
<tr>
<td>Power</td>
<td>15 W</td>
<td>14 W, pulsed sequences</td>
</tr>
<tr>
<td>Directionality</td>
<td>Diffuse</td>
<td>Diffuse (FullFire®), Directional (SideFire®)</td>
</tr>
<tr>
<td>Outer diameter</td>
<td>1.65 mm (5F)</td>
<td>2.2 mm (diffuse), 1.3 mm (diffuse, directional)**</td>
</tr>
<tr>
<td>Diffuser window length</td>
<td>3 and 10 mm</td>
<td>6 mm (diffuse), 1 mm (directional)</td>
</tr>
<tr>
<td>Cooling</td>
<td>Saline</td>
<td>CO₂*</td>
</tr>
<tr>
<td>Laser fiber advancement during procedure</td>
<td>Manual</td>
<td>Robotic (hands-off)****</td>
</tr>
<tr>
<td>Multiple trajectories with one laser probe</td>
<td>N/A</td>
<td>Yes</td>
</tr>
<tr>
<td>MRI thermography refresh rate</td>
<td>5 sec (monitors 1 plane)</td>
<td>7.8 sec (monitors simultaneously 3 planes)</td>
</tr>
</tbody>
</table>

*1064 nm wavelength has a lower water absorption and theoretically higher tissue penetration, although longer treatment times may be required to ablate a similar region of tissue.
**Thicker probe gives more rigidity for deep targets but no bigger ablations
***Pressurized Carbon Dioxide is continuously adjusted by NeuroBlate Fusion Software™ to maintain probe tip temperature.
****Monteris robot travel distance (for moving laser along axis) is 4 cm and rotation 340º

### VISUALASE THERMAL THERAPY SYSTEM (Medtronic, Inc.)

**Materials >>**
LASER ABLATION TECHNIQUES

FDA-approved

15 W, 980 nm (near infrared) diode laser coupled to an optical fiber with a light-diffusing tip within a light-transmitting saline-irrigated cooling sheath.

outer 1.6-mm-diameter clear (light-transmitting) polycarbonate cooling catheter; comes with radiopaque stylet (can be seen on O-arm).

N.B. once stylet is removed (and before laser fiber is placed) catheter is very fragile – can bend and fracture just from its own weight – need to support it!

inner 0.73-mm-diameter flexible laser optical fiber terminating in a 3 mm or 10-mm-long diffuser tip.

catheter ends to pointed tip 2.9 mm in length; thus, the center of 10-mm laser diffuser is 8 mm proximal from catheter tip – advance stereotactic target 8 mm deeper than ablation target.

N.B. always insert laser catheter deeper as laser fiber can be easily moved up and down inside catheter during procedure!

near real-time thermal monitoring (approximately 4-6 second delay).

if user-defined undesirable conditions are detected (such as heat spread to the safety margin), the workstation may be set to automatically deactivate the laser as a safety mechanism.

NEUROBLATE® SYSTEM (Monteris Medical)
(formerly known as AutoLITT® System, LITT - laser interstitial thermal therapy)
http://www.monteris.com/technology

Instructions for use: https://www.monteris.com/healthcare-professionals/instructions-for-use-ifus/

FDA LABEL:

The Monteris Medical NeuroBlate™ System is indicated for use to ablate, necrotize, or coagulate intracranial soft tissue, including brain structures, through interstitial irradiation or thermal therapy in medicine and surgery in the discipline of neurosurgery with 1064 nm lasers.

The Monteris Medical NeuroBlate™ System is intended for planning and monitoring thermal therapies under MRI visualization. It provides MRI based trajectory planning assistance for the stereotaxic placement of MRI compatible (conditional) NeuroBlate™ Laser Delivery Probes. It also provides near-real time thermographic analysis of selected MRI images.

When interpreted by a trained physician, this System provides information that may be useful in the determination or assessment of thermal therapy. Patient management decisions should not be made solely on the basis of the NeuroBlate™ System analysis.

No age limit! (but watch for skull thickness in pediatric patients – recommend at least 3 mm)

REGULATORY ACTIONS
3/23/2018 - Class I recall by FDA (Z-0194-2018): the most serious type of recall - device may cause serious injuries or death – due to the risk of unintended probe tip heating.

caused by an interaction between the metallic thermocouple in the probe, and the MRI environment independent of laser energy delivery, and have been associated with damage to the tip of the probe implanted within the brain (e.g., charring, release of carbon dioxide).

Update – metallic thermocouple was replaced by nonmetal fiber optic temperature sensor (FOTS) to avoid unintended current induction and heating – Monteris system is back on market.

COMPONENTS
Laser Ablation Techniques

See below >>

BOLT
LASER PROBE
- wave length: 1064 nm
- available laser outside diameters:
  a) 2.2 mm – less stiff so it is strongly recommended to create a path in brain parenchyma using metal stylet, s. alignment mandrel, biopsy needle, or stylet (at least 80% of trajectory length).
  b) 3.3 mm – born larger diameter tissue but may have trouble inserting through dura (use dura dilator in OR).
- available laser lengths: 133, 154, 175, 196, 217, 238, 259 mm
- laser probe configurations:
  - Directional (SideFire®), approx. 78º angle – 3.3 mm outer diameter, 1 mm laser window
  - Diffuse (FullFire®) – 2.2 mm and 3.3 mm outer diameters, 6 mm laser window
- all Monteris Probes incorporate an internal temperature sensor which measures the probe tip's internal temperature.
  N.B. sensor is not utilized for determining the patient’s brain tissue temperature!

**PROCEDURE PLANNING**

- make sure, if patient has various stimulators, those will be MRI-compatible and will not give MRI-artefacts.

**ENTRY**

- it is OK to go through the suture – it has lots of strong cortical bone (make sure trajectory is symmetric, i.e. dead center in the suture, rather than skiving it).
- do not exceed 40° away from perpendicular to the skull:
  - when using two Monteris bolts, the minimum spacing between bolts is 11 mm center to center (inadequate spacing may interfere with the Robotic Probe Driver attachment).
  - if skull is too thin to use bolt, may use skull-mounted AXiiiS mini-frame (Monteris, Plymouth, Minnesota).

**TARGET**

- always aim to place the laser along the longest axis of the lesion!
- Monteris FullFire emits laser energy in all directions (including forward from its tip) equally in both radial and longitudinal directions centered at the midpoint of the FullFire fiber (which is approximately 6 mm proximal from the distal tip of the FullFire).

If an ablation area of 7.5 mm in the radial direction is created the user can expect a 7.5 mm ablation margin in the longitudinal direction as well - this would result in an ablation margin extending 2-3 mm beyond the FullFire tip - set laser probe deepest point (PDP)* inside of the intended ablation area to prevent thermal damage from extending beyond the intended ablation area.
**LASER ABLATION TECHNIQUES**

*stereotactic surgical target can be deeper (always can pull laser back)

**WARNING:** creating a greater than 7.5 mm radial ablation area may exceed the NeuroBlate System’s ability to monitor thermal dose in the longitudinal direction.

**OR**

Always biopsy oncologic targets before you ablate! (make sure not to introduce air bubbles – interfere with thermography)

- general endotracheal anesthesia on bed.
- transfer supine to MRI-compatible AtamA board on OR table, bump under ipsilateral shoulder, head on towels and gel donut (will remove later for transportation to MRI) and rotated to opposite side.
- ensure patient has ear plugs in both ears in preparation for MRI scanning.

- secure patient tightly with Velcro wraps.
- place lower body Bair hugger and turn this on (cannot have bairhugger in MRI, so need to start warming patient as soon as possible in the OR).
- SCDs very important for longer procedures (reports if DVT with PE during LITT).

**SECURING THE HEAD**

- depends on stereotactic platform being used

**ROSA robot** – may use:

a) Mayfield frame
b) 4-post stereotactic frame base (screwdriver sockets at the end of each pin may be used for ROSA registration – likely need O-arm 2.0 with 40 cm FOV to encompass all four pin tips) – more secure platform compared to Mayfield.

**Optional** – apply stereotactic AtamA ring with rigid pin fixation (alternative – make sure that patient does not move in MRI by using constant IV infusion of paralytics – might be challenging for patients with history of multiple AED use, so establish IV rate while in OR): *becomes especially useful when using > 1 trajectory

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**Intended Ablation Area**

**WARNING:** creating a greater than 7.5 mm radial ablation area may exceed the NeuroBlate System’s ability to monitor thermal dose in the longitudinal direction.
- plan head position so that guidance bolt sits along MRI bore long axis (as close as possible) – least chance for collision with MRI bore.
- Atama ring can be full ring or split ring (has two parts that assemble to make a full ring).
- Atama ring rigidly attaches to MRI-compatible board; board has aluminium starburst attachment that can dock ROSA robot to make a rigid connection.
post for AtamA ring come in 3 sizes: long (fits most patients), medium, short.

- posts for AtamA ring are not disposable and made of PEEK; posts have a seat for MRI-conditional disposable titanium DORO pin.
- drape patient, may not need Ioban.

## StereoTaxis

- can use any platform to implant laser probe:
  a) ROSA robot
  b) Nexframe (disposable)
  c) ClearPoint (disposable)
  d) STarFix (custom made, disposable) – open old scalp stab incisions and expose bone anchor fiducials → attach plastic standoffs → mount STarFix platform
  e) Axiiis stereotactic miniframe:

## Frameless

- make scalp incision with No. 10 blade targeted over entry point (make skin mark with pen where stylet touches it) → cricket retractor
- twist hole is made in skull: (Midas Rex with M8 to create divot for start to avoid skull migration if using ROSA* → handheld Stryker TPS electrical drill (non-skive drill bit with stop depth set - measure skull bone thickness on CT)
- dura is opened with pointed Monteris probe (may touch with Bovie to facilitate dura opening and hemostasis – make sure probe does not touch skin or bone and sits only on dura)
- Monteris metal laser probe guide skull bolt has outer diameter 4.5 mm and is tightly screwed into the twist hole (16 half turns or less if feels as good purchase):

### Notes:
- if bolt is fully threaded into skull, the top of bolt is 3 cm
- N.B. 3.3 mm bolt has 2 mm with no threads at the tip (may need to advance bolt deeper, especially in the thinner bone)

### Create track in brain parenchyma (mandatory for thinner laser probes, optional for 3.3 mm probe, esp. if target is firm tissue):
- steel blunt-tip dilator (has diameter of laser probe) with marked depth is placed through skull bolt all way (or at least 80%) through trajectory → O-arm and image fusion (e.g. on FrameLink or ROSA software) – to verify accurate instrument guiding bolt trajectory (optional) and to open pathway for flexible laser probe → stylet is removed:

### Table:

<table>
<thead>
<tr>
<th>Number of Turns</th>
<th>Depth Into Skull</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>3.2mm</td>
</tr>
<tr>
<td>5</td>
<td>4.0mm</td>
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<td>6</td>
<td>4.8mm</td>
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<td>7</td>
<td>5.6mm</td>
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<tr>
<td>8</td>
<td>6.4mm</td>
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<td>10</td>
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<tr>
<td>11</td>
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<tr>
<td>12</td>
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<tr>
<td>13</td>
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<tr>
<td>14</td>
<td>11.2mm</td>
</tr>
<tr>
<td>15</td>
<td>12.0mm</td>
</tr>
</tbody>
</table>
optional - stereotactic needle biopsy (for permanent pathology).

optional - STarFix platform and bone anchors are removed → (incisions closed with 4-0 Vicryl interrupted stitches for the galea followed by) 4-0 Monocryl / staples for skin.

incision around the bolt is closed with inverted interrupted 3-0 Vicryl stitches to the galea and then with staples to the skin. → “figure of 8” 2-0 nylon stitch is placed around the bolt and is left not tied (attach to scalp with SteriStrip)

optional - bacitracin ointment applied around incisions (bacitracin makes nylon slippery – difficult to tie at the end).

insert laser in:
  a) OR – avoids all sorts of unexpected problems (incl. CSF loss – brain shift) but have to transport patient while guarding the laser (may cover with sterile specimen cup).
  b) MRI – risk of technical problems of laser insertion (may need to remove patient from MRI or use MRI-compatible instruments, e.g. plastic or titanium probe to open dura wider) – use 2.2 or 3.3 mm Monteris stylet to make sure it goes through the dura in OR → cap the bolt (to maintain sterility and prevent CSF leak):

  a) older version - peg:
  b) newer – silicone cap.

wrap bolt with Xeroform gauze with Betadine ± put sterile glove over.

FINAL

● optional - sterile transfer bag advanced around sterile field and head and cinched on neck side of stereotactic ring for transport; alternative – leave guide-bolt exposed with sterile cap on.

● transport from operating room to MRI suite:
Laser Ablation Techniques

- Turn VNS magnet output to 1 mA.
- Set of images is obtained according to Monteris / Visualase workflow starting with volumetric FLAIR*, then MPRAGE - confirm that laser probe is in excellent position for delivering therapy to planned target.
- System first starts with testing make sure saline / CO₂ cooling works - see on screen brain cooling pixels.
- Laser thermotherapy is delivered sequentially in multiple sequences: draw area on MRI image that needs to be treated → transfer data to MRI tech → adjust probe depth and angle → turn laser on → MRI monitors tissue temperatures in real time in treated slice - keep laser on until achieving good coverage (isotemperature area covers contrast enhancing area):
  1) Yellow 45°C isotemperature area - temperatures necessary to induce apoptosis - considered only partially effective
  2) Blue 52°C isotemperature area - temperatures necessary to induce necrosis
  3) White isotemperature area

Safety Points
Low safety points, usually set at 43-50°C, above which the laser turns off, are placed to protect adjacent tissue.
High safety points are usually set at 90°C and placed near the diffuser tip to prevent vaporization and gas expansion, charring, or melting of the catheter.

Ablation Strategy
"Top-down" - starting at the superior-most tumor location and ending at the inferior-most location.
"Bottom up" - conventional way.

Visualase

- >77°C, red; >67°C, yellow; >57°C, green; >47°C, light blue; >37°C, dark blue

MonteRIS

- Attach to AtamaA:
  - Newer (2019) RPD: no longer use separate locking sleeve for bolt:
  - Legacy RPD:

N.B. may not tighten locking thumbscrews – in case of cardiopulmonary catastrophe in MRI, patient needs to be extracted immediately (will not have time to move head out to undo screws).

Setup
- Remove bolt protection (gauze and plug/cap)
- Attach Robotic Probe Driver (RPD) to bolt:
  - Newer (2019) RPD: no longer uses separate locking sleeve for bolt:
  - Legacy RPD:
If using SideFire, need to attach MRI marker on the bottom of RPD prior to securing RPD on the bolt.

**Step 2**
- Adjust laser length (RPD adds 27 mm from bolt top):
  - Test with visible pilot laser:
  - Laser probe is inserted through motorized steering guidance adapter system (RPD) attached to metal probe guide:
LASER ABLATION TECHNIQUES

Apply head coil:
Use only whole body transmitting coils and compatible local receiving coil!
Laser probe MRI artifact can extend as much as 13 mm for 1.5 T (18 mm for 3.0 T) away from distal end of the Mini-Bolt (inner table of the skull) into brain tissue.

- If thermal imaging at depths less than this is required, user should proceed with extreme caution - thermal data pixel dropout at shallow depths should be evaluated prior to laser energy delivery - acquire the thermal gradient echo sequence and assess for MRI artifact prior to ablating!

Fast 3D spoiled GRE (or Fast Spin Echo) sequences such as FSPGR or MPRAGE can be used for laser delivery probe artifact identification.

Parallel (top row) and perpendicular (bottom row) MPRAGE 1.5 T MR images near the distal end of the probe; representation of the probe overlaid on the right-most images.

Same at 3.0 T:
Laser energy is delivered in a pulsed manner – allows laser tip cooling.

- User can select 3 energy settings.
- The rate of tissue heating with NeuroBlate is between 0.125 - 0.25 degrees Celsius per second (1-2 degrees Celsius rise per MRI scan every 8 seconds) at the area next to the probe tip.
- Ablation volume plateaus at 200 sec (3.5 mins) – so turn power up bigger and faster ablation, but MRI more inaccurate.
- More power doesn’t always work.

Thermography:
- Gradient Recalled Echo (GRE) pulse sequence (s. NeuroBlate Thermal Sequence) is used.
- Accurate within 1.5 ± 0.7 mm of displayed thermal dose threshold (TDT) lines.
- Accuracy is ± 3.0°C.

Screenshot of Monteris workstation:
Three top windows show probe’s eye view at, distal, and proximal to laser window (each 5 mm apart) – temperature monitored volume is 15 mm thick and 60 mm diameter. Two bottom windows show perpendicular planes along trajectory (there is option to show treatment in orthogonal anatomic planes).

Green area (opacity is adjustable) shows the area where temperature is being monitored.
Orange circles – reference points (for phase drift* compensation) - ensure the points are picked only within actual brain tissue** (grey or white matter) avoiding sulci, blood vessels, ventricles and bone.
*Proton resonance phase drift is inherent with all MRI scanners and can account for a several degree variance over short time intervals
**> 15 mm away from laser and > 3 mm away from treatment area

Blue line – treatment area (equivalent of 43°C for 10 minutes duration); there is ± 1.5 mm variance – depicted by dotted blue line:

Yellow line – time-dependent thermal damage area – equivalent of 43°C for 2 minutes duration (predicts very well where blue line is going to spread); keep 1-3 mm away from eloquent brain!

- Tissue between the blue and yellow lines may experience thermal damage; but cell death is not guaranteed.

White line – equivalent of 43°C for 60 minutes – all tissue experiences cell death within ≤ 48 hours.
There are 13 slice plane locations available for thermal imaging along the set trajectory which are numbered Distal 2 (D2), Distal 1 (D1), 1 through 9, Proximal 1 (P1), Proximal 2 (P2):

- the center of each slice plane is described by the parallel white dotted lines above.
- the position of the slice planes are determined when the user sets the Probe Deepest Penetration (PDP) during trajectory planning.
- the PDP point is identified by the center of the orange circle at the tip of the LDP when the probe position is at 0 mm.

SideFire (SF) - the default position for the middle (second) slice of the three active monitoring planes is centered directly over the laser exit position which is ~3 mm superior to the distal tip of the SFP:

- FullFire LDP requires a slightly different positional setup – laser window is 6 mm so move monitoring planes proximally 3 mm.

- planes can be adjusted if needed:
  
  Center: Aligns slice planes centered on laser exit position.
  
  Deep: Aligns slice planes distal to laser exit position.
  
  Shallow: Aligns slice planes proximal to laser exit.

- laser tip has temperature probe - actual baseline body temperature is used as an input, rather than assuming 37° C - this assures that the ablation temperature is accurate for cell death.
DWI, FLAIR, and especially T1-IV gadolinium (MPRAGE) or GRE shows predictable treatment effects:

- (1) new ring of enhancement at treatment zone edge (rim of enhancement must be at the margin of the treated volume as expected).
- (2) hemorrhagic necrosis within lesion.
- (3) new ring of diffusion restriction within treatment zone and treatment zone edge (4) peritumoral edema.
- this ablation distribution and volume, decreases and stabilizes after 24 h. laser probe removed → metal probe guide removed (using sterile hex wrench) → previously placed 2-0 nylon / Monocryl stitch is tied.
- some would do GRE to look for hemorrhages.

POSTOP

- patient is brought out of the scanner and escorted to PACU → floor (ideally, EMU) → home next day.
- home next day with steroids (esp. if ablation volume > 20 mL).
  - b) max 4q6 for 7 days then rapid taper.
- some experts (esp. for risky targets) start steroids 1 week prior to LITT.

CAVEATS

- MR image acquisition time (e.g., up to 8 seconds) may contribute to inaccurate MR thermometry readings and potential errors in the ablation assessment.
- MRgLITT devices may not account for the continued thermal spread of energy to the surrounding tissue (as the target ablation area returns to its baseline temperature), which may result in an underestimation of thermal damage.

Solutions

- heating the target tissue slowly - to reduce the potential for inaccurate MR thermometry readings (e.g. heating tissue at a rate of 4 degrees Celsius per second, and an MR acquisition time of 8 seconds, may result in uncertainties of up to 8 degrees Celsius during MR thermometry readings vs. heating tissue at a rate of 1 degrees Celsius per second, and an MR acquisition time of 8 seconds, may result in uncertainties of up to 8 degrees Celsius).
- set the low temperature targets on nearby critical structures to ≤ 43 degrees Celsius (vs. 48).
- follow the outer perimeter or isothermal contour line at the Cumulative Equivalent Minutes of 43 degree Celsius (CEM43) ≤ 2 minutes so that no critical structures are within the contour line.

FOLLOW UP

- MRI 3-6 mo following ablation ± annually thereafter.

TRIALS

Laser Ablation of Abnormal Neurological Tissue Using Robotic NeuroBlate® System (LAANTERN)

- prospective, multi-center registry that will include data collection to evaluate procedural success, local control failure rate, and Quality of Life (QoL).
- 1,000 patients and up to 50 sites (9/24/2019 enrolled 500th patient).