LASER INTERSTITIAL THERMAL THERAPY

Policy Number: SURGERY 108.1 T2

Effective Date: October 1, 2017

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

APPLICABLE LINES OF BUSINESS/PRODUCTS

This policy applies to Oxford Commercial plan membership.

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits (“EHBs”). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.
NON-COVERAGE RATIONALE

Laser interstitial thermal therapy is considered unproven and not medically necessary for treating ANY condition or diagnosis, including but not limited to:

- Brain tumors
- Breast tumors (i.e., benign or malignant)
- Epilepsy (e.g., drug-resistant epilepsy, focal cortical dysplasias, mesial temporal lobe epilepsy)
- Lung tumors (i.e., benign or malignant)
- Prostate cancer
- Radiation necrosis

There is insufficient published evidence in the clinical literature supporting the safety and efficacy of this minimally invasive surgical procedure. Further studies are needed to determine whether such treatment is beneficial for health outcomes.

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies may apply.

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DESCRIPTION OF SERVICES

Laser interstitial thermal therapy/thermotherapy (LITT) is an emerging treatment modality. The LITT treatment produces focal thermal ablation leading to lesion cytoreduction through tissue coagulation, necrosis, and cellular apoptosis. Historically, laser ablation techniques have been limited by an inability to assess ablation progress and parenchymal temperature during the course of treatment. Advances in MRI capabilities have overcome these limitations, leading to the use of this technology for select conditions.

CLINICAL EVIDENCE

Epilepsy

A systematic review and analysis by Lagman et al. examined 2 commercially available magnetic resonance-guided laser interstitial thermal therapy (MRgLITT) systems used in neurosurgery: the Visualase® thermal therapy and NeuroBlate® Systems. Data extraction was performed in a blinded fashion. Twenty-two articles reflecting 223 patients were included analysis. The majority of patients received treatment with Visualase (n=154, 69%) with epilepsy being the most common indication (n=8 studies, 47%). Brain mass was the most common indication for NeuroBlate (n=3 studies, 60%). There were no significant differences, except in age, wherein the NeuroBlate group was nearly twice as old as the Visualase group (p<0.001). Frame, total complications, and length-of-stay were non-significant when adjusted for age and number of patients. Several limitations were cited in this analysis, including but not limited to inherent bias in selection and reporting and recognized issues of retrospective studies. The authors concluded that MRgLITT procedures have demonstrated effectiveness in the treatment of a variety of epilepsy etiologies and tumor pathologies. While laser neurosurgery has evolved over recent decades and clinical indications are currently being defined, long-term outcomes have yet to be fully elucidated (2017).

In a retrospective review, Waseem et al. evaluated a number of outcome measures, including seizure freedom, neuropsychological performance, complications, and other considerations on a total of 38 patients presenting exclusively with mesial temporal lobe epilepsy (MTLE) and no other lesions (including neoplasia), who underwent MRgLITT. Eighteen (53%) had an Engel class I outcome, 10 patients had repeat procedures/operations, and 12 post-procedural complications occurred. Follow-up time ranged from 6 to 38.5 months. There was a decreased length of procedure time, hospitalization time, and analgesic requirement when compared to open surgery. In cases of well-localized MTLE, MRgLITT may offer similar (albeit slightly lower) rates of seizure freedom versus traditional surgery. The authors concluded that MRgLITT may be an alternative treatment option for high risk surgical patients and, more
importantly, could increase referrals for surgery in patients with medically refractory MTLE. However, data is limited and long-term outcomes have not been evaluated. Further investigation is required to understand the potential of this minimally invasive technique for MTLE (2016).

Kang et al (2016) prospectively tracked seizure outcome from a single center study which included 20 patients with drug-resistant mTLE who underwent MRgLITT from December 2011 to December 2014. Surgical outcome was assessed at 6 months, 1 year, 2 years, and at the most recent visit. Volume-based analysis of ablated mesial temporal structures was conducted in 17 patients with mesial temporal sclerosis (MTS) and results were compared between the seizure-free and not seizure-free groups. Following LITT, proportions of patients who were free of seizures impairing consciousness (including those with auras only) are as follows: 8 of 15 patients after 6 months (53%), 4 of 11 patients after 1 year (36.4%), and 3 of 5 patients a 2-year follow up (60%). Median follow-up was 13.4 months post-LITT. Seizure outcome after LITT suggests an all or none response. Four patients had anterior temporal lobectomy (ATL) after LITT; 3 are seizure-free. There were no differences in total ablated volume of the amygdalohippocampus complex or individual volumes of hippocampus, amygdala, entorhinal cortex, parahippocampal gyrus, and fusiform gyrus between seizure-free and non-seizure-free patients. Contextual verbal memory performance was preserved after LITT, although decline in noncontextual memory task scores were noted. The authors concluded that MRI-guided stereotactic LITT is a safe alternative to ATL in patients with medically intractable mTLE. Individualized assessment is warranted to determine whether the reduced odds of seizure freedom are worth the reduction in risk, discomfort, and recovery time. Larger prospective studies are needed to confirm preliminary findings, and to define optimal ablation volume and ideal structures for ablation. Limitations to this review include a prospective review in a single center, as well as small sample size.

A 2016 systematic review of LITT analyzed 2 studies on epilepsy and 4 on intracranial lesions (2 of which assessed the same patient population.) Three studies were case series, and 2 were non-randomized controlled studies. There was substantial heterogeneity among the included studies, in terms of LITT device used, type of LITT, comparator, patient population, and outcomes measured. Among the 2 studies on epilepsy, 1 found that the LITT group experienced significantly less decline in famous face recognition and common names compared to stereotactic laser ablation hippocampectomy (SLAH). The other study found no statistically significant difference between seizure rates for those who had MRgLITT compared to anterior mesial temporal resection. Findings showed that length of stay was significantly shorter as was surgical time for those in the MRgLITT group, and the need for pain control was significantly less. Despite not finding a statistically significant improvement in seizure rates for those in the LITT group, this result suggests that LITT is equally effective at reducing seizures, while resulting in less pain, and shorter length of stay for patients. The authors did note that LITT is not included in any clinical practice guidelines or incorporated into clinical care pathways for brain tumors or epilepsy (Leggett et al.).

To report the feasibility, safety, and clinical outcomes of an exploratory study of MRgLITT as a minimally invasive surgical procedure for the ablation of epileptogenic foci in children with drug-resistant, lesional epilepsy, Lewis et al. (2015) performed a retrospective chart review of all MRgLITT procedures at a single tertiary care center. All procedures were performed using a U.S. Food and Drug Administration (FDA)-cleared surgical laser ablation system (Visualase Thermal Therapy System). Predefined clinical and surgical variables were extracted from archived medical records. From May 2011 to January 2014, 17 patients underwent 19 MRgLITT procedures. Mean age at seizure onset was 7.1 years, and mean age at surgery was 15.3 years. Surgical substrates were mixed but mainly composed of focal cortical dysplasia (n = 11). Complications occurred in 4 patients. Average length of hospitalization postsurgery was 1.56 days. Mean follow-up was 16.1 months (n = 16; range 3.5-35.9 months). Engel class I outcome was achieved in 7 patients (7/17; 41%), Engel class II in 1 patient (1/17; 6%), Engel class III in 3 patients (3/17; 18%), and Engel class IV in 6 patients (6/17; 35%). Three patients (3/8; 38%) with class I and II outcomes and 5 patients (5/9; 56%) with class III and IV outcomes had at least 1 prior resection. Fisher’s test was not statistically significant for the association between Engel class outcome and previous resection. The authors concluded that the study provided descriptive results regarding the use of MRgLITT in a mixed population of pediatric, lesional, drug-resistant epilepsy cases. Further multicenter, prospective studies are required to delineate optimal candidates for MRgLITT, and larger cohorts are needed to more accurately define outcome and complication rates.

**Professional Societies**

**American Association of Neurological Surgeons (AANS)**

The AANS has not taken a position on LITT for treating patients with refractory epilepsy.

**American Academy of Neurology (AAN)**

The AAN does not address LITT for treating patients with epilepsy.

**Brain Tumors**

Tovar-Spinoza and Choi published the preliminary results of the first series of pediatric brain tumors treated with MRgLITT at a single pediatric center. Outcomes were evaluated retrospectively for 11 patients with 12 tumors of 6 different types, all treated with the Visualase thermal laser system (Medtronic) between February 2012 and August
2014. Medical records, radiological findings, surgical data, complications, and results of tumor volumetric analyses were reviewed. A single laser and multiple overlapping ablations were used for all procedures. The mean hospital stay was 3.25 days, and the mean follow-up time was 24.5 months. Tumor volume in all patients decreased in the first 3 months after surgery and continued to decrease by the 4- to 6-month followup. Two patients experienced transient post-ablation complications. The authors concluded that MRgLITT is an effective first- or second-line treatment for select pediatric brain tumors. Larger multi-institutional clinical trials are necessary to evaluate its use for different types of lesions to further standardize practices (2016).

Hayes conducted a review of published literature on LITT for treatment of glioblastoma. Eighteen abstracts were retrieved, including 6 prospective studies (collective number of study participants = 64); 5 retrospective studies (n=127, collectively); 1 cost-benefit analysis (n = unspecified); 3 systematic reviews; and 3 review articles. A few abstracts for pediatric studies of LITT for glioblastoma were noted but were not retrieved as this report was focused on adult glioblastoma. Researchers concluded that there is sufficient published evidence to evaluate LITT for treatment of glioblastoma, however the study abstracts present conflicting findings regarding this technology. Full text review is required to confirm abstract content and, therefore, conclusions about the safety and efficacy of this technology cannot be made until a full assessment has been completed (2017).

Lee et al. (2016) conducted a review of the peer reviewed literature evaluating the role of LITT in the treatment of recurrent high-grade gliomas (HGGs) for which current treatments have limited efficacy, and to discuss the possible role of LITT in the disruption of the blood-brain barrier to increase delivery of chemotherapy locoregionally. Six of 17 articles were thought to be most appropriate for this review. Sixty-four lesions in 63 patients with recurrent HGGs were treated with LITT. Frontal (n = 34), temporal (n = 14), and parietal (n = 16) were the most common locations. Permanent neurological deficits were seen in 7 patients (12%), vascular injuries occurred in 2 patients (3%), and wound infection was observed in 1 patient (2%). Ablation coverage of the lesions ranged from 78% to 100%. The authors concluded that although experience using LITT for recurrent HGGs is growing, current evidence is insufficient to offer a recommendation about its role in the treatment paradigm for recurrent HGGs.

Barnett et al. conducted a systematic review and meta-analysis of the peer-reviewed literature to identify studies which examined extent of resection (EOR) or extent of ablation (EOA) and major complications (defined as neurocognitive or functional complications which last >3 months duration after surgery) associated with either brain LITT or open craniotomy in HGGs in or near areas of eloquence. Eight studies on brain LITT (n = 79) and 12 craniotomy studies (n = 1,036) were identified which examined either/both EOR/EOA and complications. Meta-analysis demonstrated an EOA/EOR of 85.4 ± 10.6% with brain LITT versus 77.0 ± 40% with craniotomy (mean difference 8%) and major complications of 5.7% and 13.8% for LITT and craniotomy, respectively. The authors concluded that in patients presenting with HGGs in or near areas of eloquence, early results demonstrate that brain LITT may be a viable surgical alternative (2016).

Evidence-based clinical practice guidelines endorsed by the Agency for Healthcare Research and Quality (AHRQ) do not address LITT in the management of patients with diffuse low grade glioma (Ryken, et al. 2015) or progressive glioblastoma (Olson et al., 2014).

Professional Societies
American Society for Radiation Oncology (ASTRO)
ASTRO does not address LITT in an executive summary of its evidence-based clinical practice guidelines on treatment for glioblastoma (Cabrera, 2016).

Breast Tumors
Kerbage et al. (2017) performed a systematic review to evaluate the scientific publications investigating the LITT approach in malignant and benign breast disease. Three preclinical studies and eight clinical studies (2 studies including fibroadenomas and 6 studies including breast cancers) were reviewed. Although the feasibility and safety of LITT have been confirmed in a phase I trial, heterogeneous inclusion criteria and methods seem to be the main reason for LITT not being yet an extensively used treatment option. The authors concluded that further development is necessary before this technique can be used in daily practice.

Haraldsdóttir et al (2015) reviewed the effect of immunological changes induced by interstitial laser thermotherapy (ILT) on long-term outcome of patients with breast cancer. Twenty-four patients with invasive breast cancer were treated with ILT followed by standard surgical excision. Immunohistological reactions on immunocompetent cells were performed on specimens obtained before and after ILT. Follow-up time ranged from 91-136 months. The authors concluded that ILT did not have any long-term adverse effects. The clinical impact should be examined in a larger patient population.
Prostate Tumors

A systematic review & meta-analysis by Valerio et al. (2017) summarized the evidence regarding sources of energy employed in focal therapy for treatment of prostate cancer. Thirty-seven articles reporting on 3,230 patients undergoing focal therapy were selected, with one of the focal therapies being LITT. Four prospective Stage 1 to 2a studies evaluating LITT in 50 patients have been reported in literature. One study included only men with low-risk disease, whereas the other studies included also Gleason ≤4+3, although risk stratification was not clearly reported. The median age was 63.5 yrs; median PSA was 5.4 ng/ml; median follow-up was 4.5 months with all series including mandatory sampling after treatment. In the Stage 1 study, all men underwent radical prostatectomy, whereas in the other three studies men underwent TRUS standard and/or targeted biopsy. Overall, the presence of significant and insignificant cancer was 4.8% and 22.2%, respectively. The probability of transition to secondary local treatment was 0%; overall and disease-specific survival, pad-free continence and potency preservation were 100% and 100%, respectively. No adverse events were reported in any study. The authors concluded that focal therapy seems safe and appears to offer good preservation of genito-urinary function. Cancer control in studies with intention to treat is encouraging, although this needs to be verified against standard of care in high quality comparative effectiveness trials.

Hayes conducted a review of published literature on MRI-guided focal laser ablation for the treatment of prostate cancer. Eight abstracts were retrieved which included prospective studies, a longitudinal outcomes study, a case series, 2 case reports, and a consensus paper. The 7 clinical studies retrieved evaluated very small numbers of patients (total n=64) using poor-quality study designs, without standardization of prostate-specific antigen (PSA), clinical stage, Gleason score, or life expectancy. Oncological follow-up was either not performed or was short-term (3-12 months). Researchers concluded that there was insufficient published evidence to assess the safety and/or impact on health outcomes or patient management with MRI-guided focused laser ablation for the treatment of prostate cancer (2016).

Radiation Necrosis

Medvid et al. discussed radiation necrosis (RN) in an overview of applications of MRgLITT when treating brain pathology. Studies during the past 20 years report the use of LITT to treat a variety of brain lesions. The most studied lesions include glioma and metastases. Epilepsy and RN represent a much smaller subset of treated lesions reported in the literature, but RN is one of the 4 most common indications for the procedure. LITT induces resolution of RN, but long-term data are limited due to low numbers and lack of sufficient long-term follow-up. The authors concluded that LITT may provide a safe curative option in cases of RN. While studies offer a plethora of evidence on the safety profile of the procedure, evidence is limited because to date, all studies consist of noncontrolled, nonrandomized retrospective reports, case series, or case reports, thus predisposing to selection bias. Also, many of the studies mix multiple disease entities to increase the number of enrolled subjects; this mixture makes the evaluation of survival benefits for a given disease entity difficult (2015).

The National Comprehensive Cancer Network (NCCN) Practice Guidelines do not address laser thermal therapy or laser ablation as treatment in cancers of the prostate, central nervous system, or lung, or as treatment for radiation necrosis.

There are multiple clinical trials studying LITT for various conditions which are in varying stages of activity. Additional information is available at www.clinicaltrials.gov.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

LITT is a procedure and, therefore, not subject to FDA regulation.

The NeuroBlate® System (Monteris Medical, MN) enables MRI-guided neurosurgical ablation, monitoring 3-D and providing real time imaging to support a surgeon’s clinical decision matrix. The device was FDA approved on October 26, 2016. Additional information is available at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K162762. (Accessed April 12, 2017)

The Visualase® Thermal Therapy System (Medtronic, MN) provides advanced MRI-guided laser ablation technology for thermal ablation markets, including neurosurgery. Delivery of laser energy results in rising temperatures in the target area, destroying the unwanted tissue. The device was FDA approved on September 10, 2008. Additional information is available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K081656. (Accessed April 12, 2017)

REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealthcare Medical Technology Assessment Committee. [2017T05844A]


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