Epilepsy Surgery

Number: 0394

Policy
*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

I. Epilepsy Surgery

Aetna considers cerebral hemispherectomy, corpus callosotomy, and temporal lobectomy (including selective amygdalohippocampectomy) medically necessary when all of the following selection criteria are met:

A. Non-epileptic attacks such as cardiogenic syncope and psychogenic seizures have been ruled out; and

B. The diagnosis of epilepsy has been documented, and the epileptic seizure type and syndrome has been clearly defined. In general, appropriate candidates for epilepsy surgery are members who are incapacitated by their frequent seizures as well as the toxicity of anti-epileptic drugs. The general characteristics of individuals for each type of surgical procedure for epilepsy are as follows:

1. Cerebral hemispherectomy: Members with unilateral multi-focal epilepsy associated with
infantile hemiplegia (especially in hemimegalencephaly and Sturge-Weber disease);

2. Corpus callosotomy: Members with focal to bilateral seizures (formerly known as secondarily generalized seizures);

3. Temporal lobectomy: Members with focal impaired awareness seizures (formerly known as complex partial seizures) of temporal or extratemporal origin; and

C. Members' quality of life may significantly improve with surgery; and

D. Seizures occur at a frequency that interferes with members' daily living and threatens their well being; and

E. There must have been an adequate period of therapy of two or more antiepileptic drugs, namely, the correct drugs used in the correct dosage, carefully monitored for treatment effects and members' compliance.

Aetna considers cerebral hemispherectomy, corpus callosotomy, and temporal lobectomy (including selective amygdalohippocampectomy) experimental and investigational when selection criteria are not met.

II. Deep Brain Stimulation

Aetna considers deep brain stimulation medically necessary for members with intractable seizures. (See CPB 0208 - Deep Brain Stimulation (.//200_299/0208.html)

III. Localized Neocortical Resections
Aetna considers localized neocortical resections experimental and investigational for uncontrolled focal impaired awareness seizures (formerly complex partial seizures) because its effectiveness has not been established.

IV. Hippocampal Electrical Stimulation

Aetna considers hippocampal electrical stimulation for the treatment of mesial temporal lobe epilepsy experimental and investigational because its effectiveness has not been established.

V. Responsive Cortical Stimulation

Aetna considers responsive cortical stimulation/responsive neurostimulation (e.g., the NeuroPace RNS System) medically necessary for adults with intractable focal aware seizures (formerly partial seizures (motor or sensory)) or focal impaired awareness seizures (formerly complex partial seizures) (with motor manifestations)) with or without focal to bilateral seizures (formerly known as secondarily generalized seizures) when the following criteria are met:

A. Non-epileptic attacks such as cardiogenic syncope and psychogenic seizures have been ruled out; and

B. The diagnosis of epilepsy has been documented, and the epileptic seizure type and syndrome has been clearly defined. In general, appropriate candidates for responsive cortical stimulation are members who are incapacitated by their frequent seizures as well as the toxicity of anti-epileptic drugs; and

C. The member has been diagnosed with no more than two epileptogenic regions; and

D. Member has one of the following indications for responsive cortical stimulation:

1. Independent onset of left and right temporal lobe onset seizures in persons who are not candidates
for resection due to the loss of memory and
language that bilateral temporal resection is
known to cause; or
2. Left temporal lobe onset seizures where there is
concern of language or memory impairment with
a resection based upon WADA testing and the
rest of the diagnostic work up; or
3. More than one zone of ictal onset, either
temporal lobe, neocortical, or both, clearly
localized by intracranial recordings, MEG, or other
suitable presurgical evaluation making surgical
resection unlikely to be successful; or
4. A well-defined neocortical focus for seizures, with
or without anatomic abnormality on
neuroimaging, either with or without overlap of
eloquent cortex; and.

E. Member has seizures that are severe enough to
cause injuries or significantly impair functional ability
in domains including employment, psychosocial,
education and mobility; and
F. Members' quality of life may significantly improve
with responsive cortical stimulation; and
G. There must have been an adequate period
of therapy of two or more antiepileptic drugs,
namely, the correct drugs used in the correct dosage,
carefully monitored for treatment effects and
members' compliance; and
H. Member does not have an electronic medical device
that delivers electrical energy to the head; and
I. Member's seizure onset zones are not located below
the level of the subthalamic nucleus (lead placement
would present too high a risk).

Proprietary
Aetna considers responsive cortical stimulation experimental and investigational for primary generalized seizures and for all other indications.

VI. Stereotactic Radiosurgery

Aetna considers the use of stereotactic radiosurgery including radiofrequency amygdalohippocampectomy for medial temporal lobe epilepsy and epilepsy arising in other functional cortical regions experimental and investigational because its effectiveness for these indications has not been established (see CPB 0083 - Stereotactic Radiosurgery (../1_99/0083.html))

VII. Stem Cell Therapy and Gene Therapy

Aetna considers stem cell therapy as well as gene therapy for the treatment of refractory epilepsy experimental and investigational because their effectiveness has not been established.

VIII. Trigeminal Nerve Stimulation

Aetna considers trigeminal nerve stimulation experimental and investigational for members with intractable seizures because its effectiveness has not been established.

IX. Subpial Transection Surgery

Aetna considers subpial transection surgery for refractory epilepsy experimental and investigational because its effectiveness has not been established.

X. High-frequency Oscillations

Aetna considers the use of high-frequency oscillations in epilepsy surgery planning experimental and investigational because its effectiveness has not been established.
XI. Magnetic Resonance-guided Laser Interstitial Thermal Therapy

Aetna considers magnetic resonance-guided laser interstitial thermal therapy (MRgLITT) (e.g. the NeuroBlate and the Visualase Thermal Therapy System) medically necessary as an alternative to standard surgery where criteria in section I on epilepsy surgery are met.

**Note:** The Wada test (intra-carotid amobarbital procedure), part of the pre-surgical evaluation of members who may undergo temporal lobectomy, is considered a medically necessary service.

**Note:** Examination of genetic variations in members with refractory epilepsy to guide the selection of surgical candidates is considered experimental and investigational because the effectiveness of this approach has not been established.

See also:

- CPB 0191 - Vagus Nerve Stimulation
  - [../100_199/0191.html](../100_199/0191.html)

- CPB 0208 - Deep Brain Stimulation
  - [../200_299/0208.html](../200_299/0208.html)

- CPB 0221 - Quantitative EEG (Brain Mapping)
  - [../200_299/0221.html](../200_299/0221.html)

- CPB 0322 - Electroencephalographic (EEG) Video Monitoring (0322.html)

- CPB 0425 - Ambulatory Electroencephalography
  - [../400_499/0425.html](../400_499/0425.html)
Background

For patients who have intractable seizures despite adequate treatment with appropriate antiepileptic drugs, surgery is their last hope. The goal of epilepsy surgery is not only to decrease the frequency of seizures, but also to improve quality of life.

Temporal lobectomy has been found to be safe and effective for treating patients with complex partial seizures of temporal or extratemporal origin. Patients who have a single identifiable focus in a restricted cortical area that can be safely excised without producing additional disability can be considered as candidates for temporal lobectomy.

Corpus callosotomy has been found to be safe and effective for treating patients with partial and secondarily generalized seizures.

There is only limited evidence that cerebral hemispherectomy is effective in managing unilateral multi-focal epilepsy associated with infantile hemiplegia (especially in hemimegalencephaly and Sturge-Weber disease). However, it is the last hope for these patients to eliminate/alleviate their disabling epileptic seizures, and to avoid adverse irreversible psychosocial consequences that may lead to lifelong disability.

Since the advent of deep brain stimulation (DBS) for the treatment of a variety of movement disorders, studies have been performed to ascertain whether this method can reduce
seizure frequency. Evidence from experimental animal studies suggests the existence of a nigral control of the epilepsy system. The results of animal studies are promising, but work on humans is preliminary.

In a pilot study, Boon et al (2007) assessed the effectiveness of long-term DBS in medial temporal lobe (MTL) structures in patients with MTL epilepsy. A total of 12 consecutive patients with refractory MTL epilepsy were included in this study. The protocol included invasive video-EEG monitoring for ictal-onset localization and evaluation for subsequent stimulation of the ictal-onset zone. Side effects and changes in seizure frequency were carefully monitored. Ten of 12 patients underwent long-term MTL DBS; 2 of 12 patients underwent selective amygdalo-hippocampectomy. After mean follow-up of 31 months (range of 12 to 52 months), 1 of 10 stimulated patients was seizure-free (more than 1 year), 1 of 10 patients had a greater than 90% reduction in seizure frequency; 5 of 10 patients had a seizure-frequency reduction of greater than equal to 50%; 2 of 10 patients had a seizure-frequency reduction of 30 to 49%; and 1 of 10 patients was a non-responder. None of the patients reported side effects. In 1 patient, magnetic resonance imaging (MRI) showed asymptomatic intra-cranial hemorrhages along the trajectory of the DBS electrodes. None of the patients showed changes in clinical neurological testing. Patients who underwent selective amygdalo-hippocampectomy are seizure-free (more than 1 year), anti-epileptic drugs are unchanged, and no side effects have occurred. The authors concluded that this open pilot study demonstrated the potential efficacy of long-term DBS in MTL structures that should now be further confirmed by multi-center randomized controlled trials (RCTs).

The Wada test (intra-carotid amytal procedure) is commonly used as a predictor of memory dysfunction following temporal lobectomy for intractable epilepsy. Asymmetry in memory scores can provide focus lateralizing information.
The Agency for Healthcare Research and Quality's technology assessment on the management of treatment-resistant epilepsy stated that the data are inconsistent across studies and do not allow for firm evidence-based conclusions as to the exact proportion of patients who will become seizure-free or who will not benefit from multiple subpial transection. In addition, too few studies were available to allow for an evidence-based evaluation of parietal or occipital lobe surgery (Chapell et al, 2003). The American Academy of Neurology (AAN)'s practice parameter on temporal lobe and localized neocortical resections for epilepsy stated that there remains no Class I or II evidence regarding the safety and efficacy of localized neocortical resections. Further studies are needed to determine if neocortical seizures benefit from surgery (Engel et al, 2003).

Candidates for epilepsy surgery and their family, if applicable, should receive detailed information regarding the specific surgical procedures and their possible benefits and side effects. Candidates for epilepsy surgery should not have co-existent progressive neurological disease or major psychological or medical disorder. Persons with progressive neurological diseases or major medical or psychological disorders are generally unsuitable candidates for epilepsy surgery because of the possibility that surgery could worsen the course of these other conditions.

In a pilot study (n = 5), Velasco and colleagues (2005) examined the safety and effectiveness of cerebellar stimulation (CS) on patients with medically refractory motor seizures, and especially generalized tonic-clonic seizures. Bilateral modified 4-contact plate electrodes were placed on the cerebellar superomedial surface through 2 sub-occipital burr holes. The implanted programmable, battery-operated stimulator was adjusted to 2.0 microC/cm²/phase with the stimulator case as the anode; at this level, no patient experienced the stimulation. Patients served as their own controls, comparing their seizure frequency in pre-implant
basal phase (BL) of 3 months with the post-implant phases from 10 months to 4 years (average, 8 epochs of 3 months each). During the month after implantation, the stimulators were not activated. The patient and the evaluator were blinded as to the next 3-month epoch, as to whether stimulation was used. The patients were randomized into 2 groups: (i) 3 with the stimulator ON, and (ii) 2 with the stimulator OFF. After a 4-month post-implantation period, all patients had their stimulator ON until the end of the study and beyond. Medication was maintained unchanged throughout the study. EEG paroxysmal discharges also were measured.

Generalized tonic-clonic seizures: in the initial 3-month double-blind phase, 2 patients were monitored with the stimulation OFF; no change was found in the mean seizure rate (patient 1, 100%, and patient 5, 85%; mean, 93%), whereas the 3 patients with the stimulation initially ON had a reduction of seizures to 33% (patient 2, 21%; patient 3, 46%; patient 4, 32%) with a statistically significant difference between OFF and ON phase of \( p = 0.023 \). All 5 patients then were stimulated and monitored. At the end of the next 6 months of stimulation, the 5 patients had a mean seizure rate of 41% (14 to 75%) of the BL. The second patient developed an infection in the implanted system, which had to be removed after 11 months of stimulation; the seizures were being reduced with stimulation to a mean of 1 per month from a mean of 4.7 per month (BL level) before stimulation. At the end of 24 months, 3 patients were monitored with stimulation, resulting in a further reduction of seizures to 24% (11 to 38%).

Tonic seizures: 4 patients had these seizures, which at 24 months were reduced to 43% (10 to 76%). Follow-up surgery was necessary in 4 patients because of infection in 1 patient and lead/electrode displacement needing repositioning in 3 patients. The statistical analysis showed a significant reduction in tonic-clonic seizures \( (p < 0.001) \) and tonic seizures \( (p < 0.05) \). These investigators concluded that the superomedial cerebellar cortex appears to be a safe and effective target for electrical stimulation for decreasing motor
seizures over the long-term. The effect shows generalized
tonic-clonic seizure reduction after 1 to 2 months and
continues to decrease over the first 6 months and then
maintains this effectiveness over the study period of 2 years
and beyond. The results of this pilot study needed to be
validated by additional trials with larger patient populations.

Fountas et al (2010) reviewed the pertinent literature to outline
the role of CS in the management of medically refractory
epilepsy. The pertinent articles were categorized into 2 large
groups: (i) animal experimental and (ii) human clinical
studies. Particular emphasis on the following aspects was
given when reviewing the human clinical studies: their
methodological characteristics, the number of participants,
their seizure types, the implantation technique and its
associated complications, the exact stimulation target, the
stimulation technique, the seizure outcome, and the patients'
psychological and social post-stimulation status. Three clinical
double-blind studies were found, with similar implantation
surgical technique, stimulation target, and stimulation
parameters, but quite contradictory results. Two of these
studies failed to demonstrate any significant seizure reduction,
whereas the third one showed a significant post-stimulation
decrease in seizure frequency. All possible factors
responsible for these differences in the findings were analyzed
in the present study. The authors concluded that CS seems to
remain a stimulation target worth exploring for defining its
potential in the treatment of medically intractable epilepsy,
although the data from the double-blind clinical studies that
were performed failed to establish a clear benefit in regard to
seizure frequency. They noted that a large-scale, double-blind
clinical study is needed for accurately defining the efficacy of
CS in epilepsy treatment.

Electrical stimulation of the hippocampus has been proposed
as a possible treatment for mesial temporal lobe epilepsy
(MTLE). Tellez-Zenteno et al (2006) reported their findings of
4 patients with refractory MTLE (whose risk to memory contraindicated temporal lobe resection) who underwent implantation of a chronic stimulating depth electrode along the axis of the left hippocampus. These investigators used continuous, sub-threshold electrical stimulation (90 microsec, 190 Hz) and a double-blind, multiple cross-over, randomized controlled design, consisting of 3 treatment pairs, each containing two 1-month treatment periods. During each treatment pair, the stimulator was randomly turned ON 1 month and OFF 1 month. Outcomes were assessed at monthly intervals in a double-blind manner, using standardized instruments and accounting for a washout period. These researchers compared outcomes between ON, OFF, and baseline periods. Hippocampal stimulation produced a median reduction in seizures of 15%. All but 1 patient's seizures improved; however, the results did not reach significance. Effects seemed to carry over into the OFF period, and an implantation effect cannot be ruled out. These researchers found no significant differences in other outcomes. There were no adverse effects. One patient has been treated for 4 years and continued to experience substantial long-term seizure improvement. The authors demonstrated important beneficial trends, some long-term benefits, and absence of adverse effects of hippocampal electrical stimulation in MTLE. However, the effect sizes observed were smaller than those reported in non-randomized, unblinded studies. They stated that large scale, double-blind RCTs are needed to ascertain the effectiveness of hippocampal electrical stimulation in patients with MTLE.

Velasco and colleagues (2007) evaluated the safety and effectiveness of electrical stimulation of the hippocampus in a long-term follow-up study, as well as its impact on memory performance in the treatment of patients with refractory MTLE. A total of 9 patients were included. All had refractory partial complex seizures, some with secondary generalizations. All patients had a 3-month-baseline-seizure count, after which they underwent bilateral hippocampal diagnostic electrode
implantation to establish focus laterality and location -- 3 patients had bilateral; 6 had unilateral foci. Diagnostic electrodes were explanted and definitive Medtronic electrodes were implanted directed into the hippocampal foci. Position was confirmed with MRI and afterwards, the DBS system internalized. Patients attended a medical appointment every 3 months for seizure diary collection, DBS system checkup, and neuropsychological testing. Follow-up ranged from 18 months to 7 years. Patients were divided in 2 groups: (i) 5 had normal MRIs and seizure reduction of greater than 95 %, and (ii) 4 had hippocampal sclerosis and seizure reduction of 50 to 70 %. No patient had neuropsychological deterioration, nor did any patient show side effects. Three patients were explanted after 2 years due to skin erosion in the trajectory of the system. The authors concluded that electrical stimulation of the hippocampus provides a non-lesional method that improves seizure outcome without memory deterioration in patients with hippocampal epileptic foci. This is a small study; its findings need to be validated by studies with larger patient populations.

Sun and associates (2008) stated that with the success of DBS for treatment of movement disorders, brain stimulation has received renewed attention as a potential treatment option for epilepsy. Responsive stimulation aims to suppress epileptiform activity by delivering stimulation directly in response to electrographic activity. Animal and human data support the concept that responsive stimulation can abort epileptiform activity, and this modality may be a safe and effective treatment option for epilepsy. Responsive stimulation has the advantage of specificity. In contrast to the typically systemic administration of pharmacotherapy, with the concomitant possibility of side effects, electrical stimulation can be targeted to the specific brain regions involved in the seizure. In addition, responsive stimulation provides temporal specificity. Treatment is provided as needed, potentially reducing the likelihood of functional disruption or habituation.
due to continuous treatment. The authors reviewed current animal and human research in responsive brain stimulation for epilepsy and discussed the NeuroPace RNS System, an investigational implantable responsive neurostimulator system that is being evaluated in a multi-center, randomized, double-blinded trial to assess the safety and efficacy of responsive stimulation for the treatment of medically refractory epilepsy.

Morrell et al (2011) evaluated the safety and effectiveness of responsive cortical stimulation as an adjunctive therapy for partial onset seizures in adults with medically refractory epilepsy. A total of 191 adults with medically intractable partial epilepsy were implanted with a responsive neurostimulator connected to depth or subdural leads placed at 1 or 2 pre-determined seizure foci. The neurostimulator was programmed to detect abnormal electrocorticographic activity. One month after implantation, subjects were randomized 1:1 to receive stimulation in response to detections (treatment) or to receive no stimulation (sham). Safety and effectiveness were assessed over a 12-week blinded period and a subsequent 84-week open-label period during which all subjects received responsive stimulation. Seizures were significantly reduced in the treatment (-37.9 %, n = 97) compared to the sham group (-17.3 %, n = 94; p = 0.012) during the blinded period and there was no difference between the treatment and sham groups in adverse events. During the open-label period, the seizure reduction was sustained in the treatment group and seizures were significantly reduced in the sham group when stimulation began. There were significant improvements in overall quality of life (p < 0.02) and no deterioration in mood or neuropsychological function. The authors concluded that responsive cortical stimulation reduces the frequency of disabling partial seizures, is associated with improvements in quality of life, and is well-tolerated with no mood or cognitive effects. They noted that responsive stimulation may provide another adjunctive treatment option for adults with medically intractable partial seizures. However, with its more invasive surgical component, this approach
(responsive cortical stimulation) carries greater risks and requires careful patient selection; identification of factors predicting good outcome prior to electrode implantation would be of great value. Furthermore, responsive cortical stimulation has yet to be approved for use in the U.S.

Gamma knife (GK) radiosurgery has been proposed as an alternative to classic microsurgery in MTLE. Bartolomei and colleagues (2008) reported the efficacy and tolerance of GK radiosurgery in MTLE after a follow-up of more than 5 years. A total of 15 patients were included in this study; 8 were treated on the left side, and 7 were treated on the right. The mean follow-up was 8 years (range of 6 to 10 years). At the last follow-up, 9 of 16 patients (60%) were considered seizure-free (Engel Class I) (4/16 in Class IA, 5/16 in Class IB).

Seizure cessation occurred with a mean delay of 12 months (+/- 3) after GK radiosurgery, often preceded by a period of increasing aura or seizure occurrence (6/15 patients). The mean delay of appearance of the first neuroradiological changes was 12 months (+/- 4). Nine patients (60%) experienced mild headache and were placed on corticosteroid treatment for a short period. All patients who were initially seizure-free experienced a relapse of isolated aura (10/15, 66%) or complex partial seizures (10/15, 66%) during anti-epileptic drug tapering. Restoration of treatment resulted in good control of seizures.

In an editorial that accompanied the afore-mentioned paper, Spencer (2008) stated that "gamma knife treatment in mesial temporal lobe epilepsy, then, is still searching for a place. Right now, its disadvantages (slightly lower seizure response rate, delayed response, absolute requirement for continued medications, higher mortality) compared to anterior medial temporal resection seem to outweigh its noninvasive status, which so far does not appear to carry any clear benefits in terms of neurologic or cognitive function, or seizure response. Whether gamma knife treatment should be considered for intractable epilepsy arising in other functional cortical regions
that can not be treated with resection remains unexplored. Its efficacy, as well as morbidity, in those situations has not been examined, and the volume and definition of the tissues to be targeted are considerably less well-defined than for mesial lobe epilepsy.

In a pilot study, Barbaro et al (2009) reported the 3-year outcomes of a multi-center, study of GK radiosurgery for MTLE. Radiosurgery was randomized to 20 or 24 Gy targeting the amygdala, hippocampus, and parahippocampal gyrus. Seizure diaries evaluated the final seizure remission between months 24 and 36. Verbal memory was evaluated at baseline and 24 months with the Wechsler Memory Scale-Revised (WMS-R) and California Verbal Learning Test (CVLT). Patients were classified as having "significant improvement," "no change," and "significant impairment" based on relative change indices. Thirteen high-dose and 17 low-dose patients were treated. Both groups showed significant reductions in seizures by 1 year after treatment. At the 36-month follow-up evaluation, 67% of patients were seizure-free for the prior 12 months (high-dose: 10/13, 76.9%; low-dose: 10/17, 58.8%). Use of steroids, headaches, and visual field defects did not differ by dose or seizure remission. The prevalence of verbal memory impairment was 15% (4/26 patients); none declined on more than 1 measure. The prevalence of significant verbal memory improvements was 12% (3/26). The authors concluded that GK radiosurgery for unilateral MTLE offers seizure remission rates comparable with those reported previously for open surgery. There were no major safety concerns with high-dose radiosurgery compared with low-dose radiosurgery. They stated that additional research is needed to determine if GK radiosurgery may be a treatment option for some patients with MTLE.

Vojtech et al (2009) examined the effectiveness of GK radiosurgery in the treatment of MTLE due to mesial temporal sclerosis. A total of 14 patients underwent radiosurgical entorhino-amygdalo-hippocampectomy with a marginal dose
of 18-, 20-, or 25-Gy to the 50% isodose following a standard pre-operative epilepsy evaluation. One patient was classified as Engel Class Ib, 3 were Engel Class Iic, 1 was Engel Class IIIa, and 2 were Engel Class IVb in a subgroup of 7 patients who were unoperated 2 years prior to the last visit and at least 8 years after irradiation (average of 116 months). The insufficient effect of irradiation led these investigators to perform epilepsy surgery on another 7 patients an average of 63.5 months after radiosurgery. The average follow-up period was 43.5 months after the operation. Four patients are seizure-free; 1 is Engel Class IIb and 1 is Engel Class IId. One patient can not be classified due to the short period of follow-up. The frequency of seizures tended to rise after irradiation in some patients. Collateral edema was observed in 9 patients, which started earlier and was more frequent in those irradiated with higher doses. It had a marked expansive character in 3 cases and clinical signs of intra-cranial hypertension were present in 3 cases. Partial upper lateral quadrant anopia as a permanent side effect was observed in 2 patients. Repeated psychotic episodes (2 patients) and status epilepticus (2 patients) were also seen after treatment. No significant memory changes occurred in the group as a whole. The authors concluded that radiosurgery with 25-, 20-, or 18-Gy marginal dose levels did not lead to seizure control in this patient series, although subsequent epilepsy surgery could stop seizures. Higher doses were associated with the risk of brain edema, intra-cranial hypertension, and a temporary increase in seizure frequency.

Malikova et al (2009) described MRI changes following stereotactic radiofrequency amygdalohippocampectomy (AHE) and correlated the hippocampal and amygdalar volumes reduction with the clinical seizure outcome. A total of 18 patients were included. Volumetry was calculated from pre-operative MRI and from MRI obtained 1 year after the operation. The clinical outcome was examined 1 and 2 years after the treatment. Hippocampal volume decreased by 54 +/- 19 %, and amygdalar volume decreased by 49 +/- 18 %. One
year after the procedure, 13 (72 %) patients were classified as Engel's Class I (9 as Class IA), 4 (22 %) patients as Class II and 1 (6 %) patient as Class III. Two years after the operation, 14 patients (82 %) were classified as Class I (7 as Class IA) and 3 patients (18 %) as Class II. There were 3 surgical complications after the procedure: 1 small subdural hematoma, and twice a small electrode tip left in operation field (these patients were excluded from the study). In 3 patients, temporary meningeal syndrome developed. The authors concluded that results of stereotactic radiofrequency AHE are promising.

Naegele et al (2010) stated that the potential applications of stem cell therapies for treating neurological disorders are enormous. Many laboratories are focusing on stem cell treatments for diseases of the central nervous system, including amyotrophic lateral sclerosis, epilepsy, Huntington's disease, multiple sclerosis, Parkinson's disease, spinal cord injury, stroke, and traumatic brain injury. Among the many stem cell types under testing for neurological treatments, the most common are fetal and adult brain stem cells, embryonic stem cells, induced pluripotent stem cells, and mesenchymal stem cells. An expanding toolbox of molecular probes is now available to allow analyses of neural stem cell fates prior to and after transplantation. Concomitantly, protocols are being developed to direct the fates of stem cell-derived neural progenitors, and also to screen stem cells for tumorigenicity and aneuploidy. The rapid progress in the field suggested that novel stem cell therapy as well as gene therapy for neurological disorders are in the pipeline.

Tellez-Zenteno and Wiebe (2011) stated that hippocampal stimulation should be regarded as an experimental therapy for epilepsy, and patients considered for this intervention should do so in the context of a well-designed RCT. The authors concluded that only well-conducted, blinded, randomized trials,
followed by long-term systematic observation will yield a clear picture of the effect of this promising therapy, and will help guide its future use.

In a pilot feasibility study, Degiorgio et al (2006) evaluated the safety and preliminary effectiveness of trigeminal nerve stimulation (TNS) of the infra-orbital and supra-orbital branches of the trigeminal nerve for the treatment of epilepsy. Trigeminal nerve stimulation was well-tolerated. Four (57%) of 7 subjects who completed greater than or equal to 3 months experienced a greater than or equal to 50% reduction in seizure frequency. The authors concluded that the results of this pilot study supported further investigation into the safety and effectiveness of TNS for epilepsy.

In a double-blind, randomized controlled trial, Degiorgio et al (2013) examined the safety and effectiveness of external TNS (eTNS) in patients with drug-resistant epilepsy (DRE), and tested the suitability of treatment and control parameters in preparation for a phase III multi-center clinical trial. A total of 50 subjects with 2 or more partial onset seizures per month (complex partial or tonic-clonic) entered a 6-week baseline period, and then were evaluated at 6, 12, and 18 weeks during the acute treatment period. Subjects were randomized to treatment (eTNS 120 Hz) or control (eTNS 2 Hz) parameters. As entry, subjects were highly drug-resistant, averaging 8.7 seizures per month (treatment group) and 4.8 seizures per month (active controls). On average, subjects failed 3.35 anti-epileptic drugs prior to enrollment, with an average duration of epilepsy of 21.5 years (treatment group) and 23.7 years (active control group), respectively. External TNS was well-tolerated. Side effects included anxiety (4%), headache (4%), and skin irritation (14%). The responder rate, defined as greater than 50% reduction in seizure frequency, was 30.2% for the treatment group versus 21.1% for the active control group for the 18-week treatment period (not significant, p = 0.31, generalized estimating equation [GEE] model). The treatment group experienced a significant within-group
Improvement in responder rate over the 18-week treatment period (from 17.8% at 6 weeks to 40.5% at 18 weeks, p = 0.01, GEE). Subjects in the treatment group were more likely to respond than patients randomized to control (odds ratio 1.73, confidence interval [CI]: 0.59 to 0.51). External TNS was associated with reductions in seizure frequency as measured by the response ratio (p = 0.04, analysis of variance [ANOVA]), and improvements in mood on the Beck Depression Inventory (p = 0.02, ANOVA). The authors concluded that the findings of this study provided preliminary evidence that eTNS is safe and may be effective in subjects with DRE. Side effects were primarily limited to anxiety, headache, and skin irritation. They stated that these results will serve as a basis to inform and power a larger multi-center phase III clinical trial.

In an editorial that accompanied the afore-mentioned study by Degiorgio et al, Faught and Tatum (2013) stated that "The beneficial effect demonstrated by Degiorgio et al was modest, but is sufficient to encourage design of a more definitive study".

Liu and associates (2013) stated that with an annual incidence of 50/100,000 people, nearly 1% of the population suffers from epilepsy. Treatment with anti-epileptic medication fails to achieve seizure remission in 20 to 30% of patients. One treatment option for refractory epilepsy patients who would not otherwise be surgical candidates is electrical stimulation of the brain, which is a rapidly evolving and reversible adjunctive therapy. Therapeutic stimulation can involve direct stimulation of the brain nuclei or indirect stimulation of peripheral nerves. There are 3 stimulation modalities that have class I evidence supporting their uses: (i) vagus nerve stimulation (VNS), (ii) stimulation of the anterior nuclei of the thalamus (ANT), and, (iii) the most recently developed, responsive neurostimulation (RNS). While the other treatment modalities outlined deliver stimulation regardless of neuronal
activity, the RNS administers stimulation only if triggered by seizure activity. The lower doses of stimulation provided by such responsive devices can not only reduce power consumption, but also prevent adverse reactions caused by continuous stimulation, which include the possibility of habituation to long-term stimulation. Responsive neurostimulation, as an investigational treatment for medically refractory epilepsy, is currently under review by the Food and Drug Administration.

Ge and colleagues (2013) reviewed the targets of the deep brain and RNS to identify the best optimal stimulation parameters and the best mode of stimulation, whether cyclical, continuous, or smarter. This review was based on data obtained from published articles from 1950 to 2013. To perform the PubMed literature search, the following keywords were input: deep brain stimulation (DBS), RNS, and refractory epilepsy. Articles containing information related to brain stimulation or RNS for the treatment of refractory epilepsy were selected. The currently available treatment options for those patients who resist multiple anti-epileptic medications and surgical procedures include electric stimulation, both direct and indirect, of brain nuclei thought to be involved in epileptogenesis. The number of potential targets has increased over the years to include the ANT, the centromedian nucleus of the thalamus, the hippocampus, the subthalamic nucleus, the caudate nucleus, and the cerebellum, among others. The results of a RCT and the RNS trial were published to reveal the effectiveness. The authors concluded that although statistically significant reductions in seizures had been observed using several different stimulation techniques, including VNS, DBS, and RNS, these effects are currently only palliative and do not approach the effectiveness comparable with that seen in resection in appropriately selected patients. They stated that more research is needed to determine optimal stimulation targets and techniques as well as to determine which epilepsy patients will benefit most from this technology.
Krishnaiah and co-workers (2013) stated that nearly 30% of patients with epilepsy continue to have seizures in spite of several anti-epileptic drug (AED) regimens. In such cases they are regarded as having refractory, or uncontrolled epilepsy. There is no universally accepted definition for uncontrolled or medically refractory epilepsy, but for the purpose of this review, these investigators considered seizures to be drug resistant if they failed to respond to a minimum of 2 AEDs. It is believed that early surgical intervention may prevent seizures at a younger age and improve the intellectual and social status of children. There are many types of surgery for refractory epilepsy with subpial transection being one. In a Cochrane review, these researchers determined the benefits and adverse effects of subpial transection for partial-onset seizures and generalized tonic-clonic seizures in children and adults. They searched the Cochrane Epilepsy Group Specialised Register (August 8, 2013), the Cochrane Central Register of Controlled Trials (CENTRAL Issue 7 of 12, The Cochrane Library July 2013), and MEDLINE (1946 to August 8, 2013). They did not impose any language restrictions. These investigators considered all randomized and quasi-randomized parallel group studies either blinded or non-blinded. Two review authors independently screened the trials identified by the search. The same 2 authors planned to independently assess the methodological quality of studies. If studies had been identified for inclusion, 1 author would have extracted the data and the other would have verified it. No relevant studies were found. The authors concluded that there is no evidence to support or refute the use of subpial transection surgery for medically refractory cases of epilepsy. Moreover, they stated that well-designed RCTs are needed to guide clinical practice.

Gloss and colleagues (2014) stated that approximately 2/3 of seizures can be controlled with anti-epileptic medications. For some of the others, surgery can completely eliminate or significantly reduce the occurrence of disabling seizures. Localization of epileptogenic areas for resective surgery is far
from perfect, and new tools are being investigated to more accurately localize the epileptogenic zone and improve the likelihood of freedom from post-surgical seizures. Recordings of pathological high-frequency oscillations (HFOs) may be one such tool. In a Cochrane review, these investigators evaluated the ability of HFOs to improve the outcomes of epilepsy surgery by helping to identify more accurately the epileptogenic areas of the brain. They searched the Cochrane Epilepsy Group Specialized Register (April 15, 2013), the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library (2013, Issue 3), MEDLINE (Ovid) (1946 to April 15, 2013), CINAHL (EBSCOhost) (April 15, 2013), Web of Knowledge (Thomson Reuters) (April 15, 2013), www.clinicaltrials.gov (April 15, 2013), and the World Health Organization International Clinical Trials Registry Platform (April 15, 2013). These researchers included studies that provided information on the outcomes of epilepsy surgery at 6 months or more and which used HFOs in making decisions about epilepsy surgery. The primary outcome of the review was the Engel Class Outcome System. Secondary outcomes were responder rate, International League Against Epilepsy (ILAE) epilepsy surgery outcome, frequency of adverse events from any source and quality of life outcomes. They intended to analyze outcomes via an aggregated data fixed-effect model meta-analysis. Two studies met the inclusion criteria. Both studies were small non-randomized trials, with no control group and no blinding. The quality of evidence for all outcomes was very low. The combination of these 2 studies resulted in 11 participants who prospectively used ictal HFOs for epilepsy surgery decision making. Results of the post-surgical seizure freedom Engel class I to IV outcome were determined over a period of 12 to 38 months (average of 23.4 months) and indicated that 6 participants had an Engel class I outcome (seizure freedom), 2 had class II (rare disabling seizures), 3 had class III (worthwhile improvement). No adverse effects were reported. Neither study compared surgical results guided by HFOs versus surgical results guided
without HFOs. The authors concluded that no reliable conclusions can be drawn regarding the effectiveness of using HFOs in epilepsy surgery decision making at present.

The NeuroPace RNS System is a responsive cortical stimulator for the treatment of medically intractable partial epilepsy. The RNS System includes a cranially implanted programmable neurostimulator that is connected to one or two depth and/or subdural cortical strip leads that are surgically placed in or on the brain at the seizure focus. The neurostimulator continuously senses brain electrical activity through the leads. When abnormal brain electrical activity typical of the activity that precedes that patient's seizures is detected, the neurostimulator delivers pulses of stimulation through those same electrodes before an individual experiences seizures.

Heck et al (2014) sought to evaluate the safety and effectiveness of responsive stimulation at the seizure focus as an adjunctive therapy to reduce the frequency of seizures in adults with medically intractable partial onset seizures arising from 1 or 2 seizure foci. The investigators conducted a randomized multi-center double-blinded controlled trial of responsive focal cortical stimulation (RNS System). Subjects with medically intractable partial onset seizures from 1 or 2 foci were implanted, and 1 month post-implant were randomized 1:1 to active or sham stimulation. After the 5th post-implant month, all subjects received responsive stimulation in an open label period (OLP) to complete 2 years of post-implant follow-up. All 191 subjects were randomized. The percent change in seizures at the end of the blinded period was -37.9 % in the active and -17.3 % in the sham stimulation group (p = 0.012, Generalized Estimating Equations). The median percent reduction in seizures in the OLP was 44 % at 1 year and 53 % at 2 years, which represents a progressive and significant improvement with time (p < 0.0001). The investigators reported that serious adverse event rate was not different between subjects receiving active and sham stimulation.
Adverse events were consistent with the known risks of an implanted medical device, seizures, and of other epilepsy treatments. There were no adverse effects on neuropsychological function or mood.

Bergey et al (2014) assessed the long-term efficacy and safety of responsive direct cortical stimulation in adults with medically refractory partial onset seizures. Adults with medically refractory partial onset seizures were treated with a cranially implanted responsive neurostimulator that delivers stimulation to 1 or 2 seizure foci via chronically implanted electrodes when specific electrocorticographic patterns are detected (RNS® System). Subjects had completed a 2-year primarily open label safety study (n = 65) or a 2-year randomized blinded controlled safety and efficacy study (n = 191); 230 subjects transitioned into an ongoing 7-year long-term study to assess safety and efficacy. The average subject was 34 years old (18 to 66) with epilepsy for 19.6 years (2 to 57). The median pre-implant frequency of disabling partial or generalized tonic clonic seizures was 10.2 seizures a month. Prior treatments included the vagus nerve stimulator (32 %) and epilepsy surgery (34 %). Mean post-implant follow-up was 4.7 years (5 weeks to 8.6 years) with an accumulated experience of 1,199 patient implant years and 1,107 patient stimulation years. The median percent seizure reduction in the randomized blinded controlled trial at 1 year was 44 % and at 2 years was 53 % (p < 0.0001 GEE) and ranged from 55 % to 60 % over post-implant years 3 through 6 for patients followed in the long-term study. Significant improvements in quality of life (QOL) were maintained (p < 0.05). The most common serious adverse events related to the device in all studies combined were implant site infection (8.2 %) and neurostimulator explantation (3.9 %).

Patients with RNS Stimulators cannot undergo magnetic resonance imaging (MRI) procedures, nor can they undergo diathermy procedures, electro-convulsive therapy (ECT) or transcranial magnetic stimulation (TMS). The energy created
from these procedures can be sent through the neurostimulator and cause permanent brain damage, even if the device is turned off. The most frequent adverse events reported in clinical trials of the Neuropace were implant site infection and premature battery depletion.

The AAN’s practice parameter on “Temporal lobe and localized neocortical resections for epilepsy” (Engel et al, 2003) supported surgery (including amygdalohippocampectomy) for refractory TLE.

Maguire et al (2011) stated that “There is consensus that amygdalohippocampectomy is likely to be beneficial for people with drug-resistant temporal lobe epilepsy”.

Kuang et al (2014) noted that TLE is a recurrent chronic nervous system disease. The conventional treatment is medicine. So far, anterior temporal lobectomy (ATL) and selective amygdalohippocampectomy (SAH; removal of the amygdala and hippocampus only) are becoming the 2 main approaches. These investigators compared the therapeutic effects between SAH and ATL in the treatment of TLE. They conducted a meta-analysis of published RCTs. The review applied the search strategy developed by the Cochrane Epilepsy Group and the Rev. Man 5.0 software to analyze. These researchers also drew the forest plots with Risk Ratio (RR) as effect size. A total of 6 studies were eligible, with a total of 626 patients (337 patients with SAH and 289 patients with ATL). There was no statistical significance of post-operative seizure control rate after 1 year, as well as the increase rate and decrease rate of verbal memory function between SAH and ATL. There is no statistical difference of therapeutic effects between SAH and ATL in the treatment of TLE. The authors concluded that it is advised that clinically, physicians should choose the appropriate approach according to operation indications to improve the results of post-operative recovery.
Kovanda et al (2014) stated that a number of different surgical techniques are effective for treatment of drug-resistant MTLE. Of these, trans-sylvian SAH, which was originally developed to maximize temporal lobe preservation, is arguably the most technically demanding to perform. Recent studies have suggested that SAH may result in better neuropsychological outcomes with similar post-operative seizure control as standard ATL, which involves removal of the lateral temporal neocortex. These investigators described technical nuances to improve the safety of SAH. Wide sylvian fissure opening and use of neuro-navigation allows an adequate exposure of the amygdala and hippocampus through a corticotomy within the inferior insular sulcus. Avoidance of rigid retractors and careful manipulation and mobilization of middle cerebral vessels will minimize ischemic complications. Identification of important landmarks during amygdalohippocampectomy, such as the medial edge of the tentorium and the third nerve within the intact arachnoid membranes covering the brainstem, further avoids operator disorientation. The authors concluded that SAH is a safe technique for resection of medial temporal lobe epileptogenic foci leading to drug-resistant MTLE.

Malikova et al (2014) compared 2 different surgical approaches, standard microsurgical ATL and stereotactic radiofrequency SAHE for MTLE, with respect to the extent of resection or destruction, clinical outcomes, and complications. A total of 75 MTLE patients were included: 41 treated by SAH (11 right-sided, 30 left-sided) and 34 treated by ATL (21 right-sided, 13 left-sided). SAH and ATL seizure control were comparable (Engel I in 75.6 and 76.5 % 2 years after surgery and 79.3 and 76.5 % 5 years after procedures, respectively). The neuropsychological results of SAH patients were better than in ATL. In SAH patients, no memory deficit was found. Hippocampal (60.6 ± 18.7 %) and amygdalar (50.3 ± 21.9 %) volume reduction by SAH was significantly lower than by ATL (86.0 ± 12.7 % and 80.2 ± 20.9 %, respectively). The overall rate of surgical non-silent complications without permanent neurological deficit after ATL was 11.8 %, and another 8.8 %
silent infarctions were found on MRI. The rate of clinically manifest complications after SAH was 4.9%. The rate of visual field defects after SAH was expectably less frequent than after ATL. The authors concluded that seizure control by SAH was comparable to ATL. However, SAH was safer with better neuropsychological results.

Jobst and Cascino (2015) reviewed resective surgery outcomes for focal epilepsy to identify which patients benefit the most. These investigators noted that similar procedures such as selective amygdalohippocampectomy and temporal lobectomy for TLE were associated with subtle differences in seizure and neuropsychological outcome.

Laser Amygdalohippocampectomy

Willie and colleagues (2014) described technical and clinical outcomes of stereotactic laser amygdalohippocampectomy with real-time MR thermal imaging guidance. With patients under general anesthesia and using standard stereotactic methods, a total of 13 adult patients with intractable MTLE (with and without mesial temporal sclerosis [MTS]) prospectively underwent insertion of a saline-cooled fiber-optic laser applicator in amygdalohippocampal structures from an occipital trajectory. Computer-controlled laser ablation was performed during continuous MR thermal imaging followed by confirmatory contrast-enhanced anatomic imaging and volumetric reconstruction. Clinical outcomes were determined from seizure diaries. A mean 60% volume of the amygdalohippocampal complex was ablated in 13 patients (9 with MTS) undergoing 15 procedures. Median hospitalization was 1 day. With follow-up ranging from 5 to 26 months (median of 14 months), 77% (10/13) of patients achieved meaningful seizure reduction, of whom 54% (7/13) were free of disabling seizures. Of patients with pre-operative MTS, 67% (6/9) achieved seizure freedom. All recurrences were observed before 6 months. Variances in ablation volume and length did not account for individual clinical outcomes.
Although no complications of laser therapy itself were observed, 1 significant complication, a visual field defect, resulted from deviated insertion of a stereotactic aligning rod, which was corrected before ablation. The authors concluded that real-time MR-guided stereotactic laser amygdalohippocampotomy is a technically novel, safe, and effective alternative to open surgery. They stated that further evaluation with larger cohorts over time is needed.

Mathon and associates (2015) reviewed the published literature related to the outcome of the surgical treatment of MTLE associated with hippocampal sclerosis (HS) and described the future prospects in this field. Surgery of MTLE associated with HS achieves long-term seizure freedom in about 70 % (62 to 83 %) of cases. Seizure outcome is similar in the pediatric population. Mortality following temporal resection is very rare (less than 1%) and the rate of definitive neurological complication is low (1%). Gamma knife stereotactic radiosurgery used as a treatment for MTLE would have a slightly worse outcome to that of surgical resection, but would provide neuropsychological advantage. However, the average latency before reducing or stopping seizures is at least 9 months with radiosurgery. Regarding palliative surgery, amygdalohippocampal stimulation has been demonstrated to improve the control of epilepsy in carefully selected patients with intractable MTLE who are not candidates for resective surgery. Recent progress in the field of imaging and image-guidance should allow to elaborate tailored surgical strategies for each patient in order to achieve seizure freedom. Concerning therapeutics, closed-loop stimulation strategies allow early seizure detection and responsive stimulation. It may be less toxic and more effective than intermittent and continuous neuro-stimulation. Moreover, stereotactic radiofrequency amygdalohippocampectomy is a recent approach leading to hopeful results. Closed-loop stimulation and stereotactic radiofrequency amygdalohippocampectomy may provide a new treatment option for patients with drug-resistant MTLE. The authors
concluded that mesial temporal lobe surgery has been widely evaluated and has become the standard treatment for MTLE associated with HS. Alternative surgical procedures like gamma knife stereotactic radiosurgery and amygdalohippocampal stimulation are currently under assessment, with promising results.

Chang et al (2015) noted that surgery can be a highly effective treatment for medically refractory TLE. The emergence of minimally invasive resective and non-resective therapeutic options has led to interest in epilepsy surgery among patients and providers. Nevertheless, not all procedures are appropriate for all patients, and it is critical to consider seizure outcomes with each of these approaches, as seizure freedom is the greatest predictor of patient quality of life. Standard ATL remains the gold standard in the treatment of TLE, with seizure freedom resulting in 60 to 80% of patients. It is currently the only resective epilepsy surgery supported by RCTs and offers the best protection against lateral temporal seizure onset. Selective amygdalohippocampectomy techniques preserve the lateral cortex and temporal stem to varying degrees and can result in favorable rates of seizure freedom but the risk of recurrent seizures appears slightly greater than with ATL, and it is unclear if neuropsychological outcomes are improved with selective approaches. Stereotactic radiosurgery presents an opportunity to avoid surgery altogether, with seizure outcomes now under investigation. Stereotactic laser thermo-ablation allows destruction of the mesial temporal structures with low complication rates and minimal recovery time, and outcomes are also under study. Finally, while neuromodulatory devices such as responsive neuro-stimulation, vagal nerve stimulation, and deep brain stimulation have a role in the treatment of certain patients, these remain palliative procedures for those who are not candidates for resection or ablation, as complete seizure freedom rates are low. The authors concluded that further development and investigation of both established and novel strategies for the surgical treatment of TLE will be critical moving forward, given the significant burden of this disease.
Magnetic Resonance-Guided Laser Interstitial Thermal Therapies

Lewis and colleagues (2015) reported the feasibility, safety, and clinical outcomes of an exploratory study of magnetic resonance-guided laser interstitial thermal therapy (MRgLITT) as a minimally invasive surgical procedure for the ablation of epileptogenic foci in children with drug-resistant, lesional epilepsy. These investigators performed a retrospective chart review of all MRgLITT procedures at a single tertiary care center. All procedures were performed using a Food and Drug Administration (FDA)-cleared surgical laser ablation system (Visualase Thermal Therapy System). Pre-defined clinical and surgical variables were extracted from archived medical records. A total of 17 patients underwent 19 MRgLITT procedures from May 2011 to January 2014. Mean age at seizure onset was 7.1 years (range of 0.1 to 14.8). Mean age at surgery was 15.3 years (range of 5.9 to 20.6). Surgical substrates were mixed but mainly composed of focal cortical dysplasia (n = 11); complications occurred in 4 patients. Average length of hospitalization post-surgery was 1.56 days. Mean follow-up was 16.1 months (n = 16; range of 3.5 to 35.9). Engel class I outcome was achieved in 7 patients (7/17; 41 %), Engel class II in 1 (1/17; 6 %), Engel class III in 3 (3/17; 18 %), and Engel class IV in 6 (6/17; 35 %); 3 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 exact test was not statistically significant for the association between Engel class outcome and previous resection (p = 0.64). The authors concluded that this study provided descriptive results regarding the use of MRgLITT in a mixed population of pediatric, lesional, drug-resistant epilepsy cases. The ability to classify case-specific outcomes and reduce technical complications is anticipated as experience develops. They stated that further multi-center, prospective studies are needed to delineate optimal candidates for MRgLITT, and larger cohorts are needed to more accurately define outcome and complication rates.
Kang et al (2016) described mesial temporal lobe ablated volumes, verbal memory, and surgical outcomes in patients with medically intractable MTLE treated with MRI-guided stereotactic laser interstitial thermal therapy (LiTT). These researchers prospectively tracked seizure outcome in 20 patients with drug-resistant MTLE who underwent MRI-guided LiTT 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 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 (53 %, 95 % CI: 30.1 to 75.2 %) after 6 months, 4 of 11 patients (36.4 %, 95 % CI: 14.9 to 64.8 %) after 1 year, 3 of 5 patients (60 %, 95 % CI: 22.9 to 88.4 %) at 2-year follow-up. Median follow-up was 13.4 months after LiTT (range of 1.3 months to 3.2 years). Seizure outcome after LiTT suggested an all or none response; 4 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, para-hippocampal gyrus, and fusiform gyrus between seizure-free and non-seizure-free patients. Contextual verbal memory performance was preserved after LiTT, although decline in non-contextual 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 needed to examine if the reduced odds of seizure freedom are worth the reduction in risk, discomfort, and recovery time. Moreover, they stated that larger prospective studies are needed to confirm these preliminary findings, and to define optimal ablation volume and ideal structures for ablation.
McCracken and colleagues (2016) noted that surgery is indicated for cerebral cavernous malformations (CCM) that cause medically refractory epilepsy. Real-time magnetic resonance thermography (MRT)-guided stereotactic laser ablation (SLA) is a minimally invasive approach to treating focal brain lesions; SLA of CCM has not previously been described. These researchers described MRT-guided SLA, a novel approach to treating CCM-related epilepsy, with respect to feasibility, safety, imaging, and seizure control in 5 consecutive patients. Patients with medically refractory epilepsy undergoing standard pre-surgical evaluation were found to have corresponding lesions fulfilling imaging characteristics of CCM and were prospectively enrolled. Each underwent stereotactic placement of a saline-cooled cannula containing an optical fiber to deliver 980-nm diode laser energy via twist drill craniostomy; MR anatomic imaging was used to evaluate targeting prior to ablation. Magnetic resonance imaging provided evaluation of targeting and near real-time feedback regarding extent of tissue thermocoagulation. Patients maintained seizure diaries, and remote imaging (6 to 21 months post-ablation) was obtained in all patients. Imaging revealed no evidence of acute hemorrhage following fiber placement within presumed CCM; MRT during treatment and immediate post-procedure imaging confirmed desired extent of ablation. These investigators identified no adverse events or neurological deficits; 4 of 5 (80%) patients achieved freedom from disabling seizures after SLA alone (Engel class 1 outcome), with follow-up ranging 12 to 28 months. Re-imaging of all subjects (6 to 21 months) indicated lesion diminution with surrounding liquefactive necrosis, consistent with the surgical goal of extended lesionotomy. The authors concluded that minimally invasive MRT-guided SLA of epileptogenic CCM is a potentially safe and effective alternative to open resection; additional experience and longer follow-up are needed.
LaRiviere and Gross (2016) stated that epilepsy is a common, disabling illness that is refractory to medical treatment in approximately 1/3 of patients, particularly among those with MTL epilepsy. While standard open mesial temporal resection is effective, achieving seizure freedom in most patients, efforts to develop safer, minimally invasive techniques have been underway for over 50 years.

Stereotactic ablative techniques, in particular, radiofrequency (RF) ablation, were first developed in the 1960s, with refinements in the 1990s with the advent of modern computed tomography and magnetic resonance-based imaging. In the past 5 years, the most recent techniques have used MRI-guided laser interstitial thermotherapy (LITT), the development of which began in the 1980s, saw refinements in MRI thermal imaging through the 1990s, and was initially used primarily for the treatment of intra-cranial and extra-cranial tumors. The authors described the original stereotactic ablation trials, followed by modern imaging-guided RF ablation series for MTL epilepsy, and reviewed the 2 currently available MRI-guided LITT systems for their role in the treatment of MTL and other medically refractory epilepsies. These investigators noted that the use of laser ablation for mesial temporal sclerosis is only in its infancy, but its superior targeting and intra-operative feedback control makes it an exciting candidate for further investigation. A prospective trial comparing MRI-guided stereotactic laser ablation with open mesial temporal lobectomy would be instrumental in demonstrating the safety and effectiveness of this promising new technique for the treatment of epilepsy. Other clinical trial approaches will be necessary to demonstrate relative safety and effectiveness with respect to standard open resection techniques. However, it must be considered that the comparison of minimally invasive techniques is not solely to standard open techniques but also to continued medical therapy, as there is a significant number of patients as well as referring physicians who consider the risk, discomfort, or inconvenience of conventional resective surgery prohibitive.
Waseem and co-workers (2017) stated that there is a new focus on minimally invasive treatments for medically refractory MTLE; and MRgLITT is one such minimally invasive procedure that utilizes MRI guidance and real-time feedback to ablate an epileptogenic focus. A total of 38 patients presenting exclusively with MTLE and no other lesions (including neoplasia), who underwent MRgLITT were reviewed. These investigators evaluated a number of outcome measures, including seizure freedom, neuropsychological performance, complications, and other considerations; 18 (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. The authors stated that in cases of well-localized MTLE this procedure may offer similar (albeit slightly lower) rates of seizure freedom versus traditional surgery. They 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 are limited and long-term outcomes have not been evaluated. They stated that further investigation is needed to understand the potential of this minimally invasive technique for MTLE.

Lagman and associates (2017) stated that MRgLITT is a novel minimally invasive modality that uses heat from laser probes to destroy tissue. Advances in probe design, cooling mechanisms, and real-time MRT have increased laser utilization in neurosurgery. The authors performed a systematic analysis of 2 commercially available MRgLITT systems used in neurosurgery: (i) the Visualase thermal therapy and (ii) the NeuroBlate Systems. Data extraction was performed in a blinded fashion. A total of 22 articles were included in the quantitative synthesis. A total of 223 patients were identified with the majority having undergone treatment
with Visualase (n = 154, 69%). Epilepsy was the most common indication for Visualase therapy (8 studies, 47%). Brain mass was the most common indication for NeuroBlate therapy (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 (LOS) were non-significant when adjusted for age and number of patients. The authors concluded that laser neurosurgery has evolved over recent decades; clinical indications are currently being defined and will continue to emerge as laser technologies become more sophisticated.

Hoppe and co-workers (2017) noted that in common with other stereotactic procedures, stereotactic laser thermocoagulation (SLT) promises gentle destruction of pathological tissue, which might become especially relevant for epilepsy surgery in the future. Compared to standard resection, no large craniotomy is necessary, cortical damage during access to deep-seated lesions can be avoided and interventions close to eloquent brain areas become possible. These researchers described the history and rationale of laser neurosurgery as well as the 2 available SLT systems (Visualase and NeuroBlate). Both systems are coupled with MRI and MR thermometry, thereby increasing patient safety. These investigators reported the published clinical experiences with SLT in epilepsy surgery (altogether approximately 200 cases) with respect to complications, brain structural alterations, seizure outcome, neuropsychological findings and treatment costs. They stated that the rate of seizure-free patients appeared to be slightly lower than for resection surgery; however, due to the inadequate quality of studies, the neuropsychological superiority of SLT has not yet been unambiguously demonstrated.

Shukla and colleagues (2017) noted that medically intractable epilepsy is associated with increased morbidity and mortality. For those with focal epilepsy and correlated
electrophysiological or radiographic features, open surgical resection can achieve high rates of seizure control, but can be associated with neurologic deficits and cognitive effects. Recent innovations have allowed for more minimally invasive methods of surgical seizure control such as MRgLITT, which achieves the goal of ablating seizure foci while preserving neuropsychological function and offering real-time feedback and monitoring of tissue ablation. These investigators summarized the utilization of MRgLITT for mesial temporal lobe epilepsy and other seizure disorders. Based on studies of laser ablation for primary glial neoplasms in adults, MRgLITT for focal epilepsy stemming from low-grade glioneuronal tumors in children is under study. The full range of applications of MRgLITT in the context of medically refractory epilepsy is still being explored. The authors concluded that MRgLITT is a safe and effective therapeutic option for the management of medically intractable epilepsy in the adult and pediatric populations. Of particular significance is the minimally invasive nature of MRgLITT, which enables the surgical management of patients who are not good candidates for, or are otherwise averse to, open resection.

Compared to other minimally invasive procedures, MRgLITT is associated with improved outcomes and better side effect profile. While open surgical procedures have demonstrated slightly higher rates of seizure freedom, MRgLITT is associated with reduced hospitalization time, decreased post-operative pain, and improved neuropsychological function. Moreover, these researchers stated that it is important to note that the studies reviewed were limited by small samples sizes and the relative novelty of the procedure. Other limitations of the currently available data include the lack of availability of long-term outcomes data and a scarcity of RCTs. They stated that future studies may seek to address these gaps while also looking at questions regarding the use of the procedure for multi-focal epilepsy and the relationship between time from diagnosis and MRgLITT efficacy.
Kang and Sperling (2018) noted that a procedure called laser interstitial thermal ablation has been utilized to treat drug resistant epilepsy. With this technique, a probe is stereotactically inserted into a target structure responsible for seizures, such as mesial temporal lobe, hypothalamic hamartoma, or a small malformation of cortical development, and the tip is then heated by application of laser energy to ablate structures adjacent to the probe tip. This procedure has the advantage of selectively targeting small lesions responsible for seizures, and is far less invasive than open surgery with shorter hospitalization, less pain, and rapid return to normal activities. Initial results in mesial temporal lobe epilepsy are promising, with perhaps 50% of patients becoming seizure-free after the procedure.

Neuropsychological deficits appear to be reduced because of the smaller volume of ablated cortex in contrast to large resections. The authors concluded that more research must be done to establish optimal targeting of structures for ablation and selection of candidates for surgery, and more patients must be studied to better establish efficacy and adverse effect rates.

Cerebellar and Deep Brain Stimulation

In a Cochrane review, Sprengers and associates (2017) evaluated the safety, efficacy, and tolerability of DBS and cortical stimulation for refractory epilepsy based on RCTs. These investigators searched the Cochrane Epilepsy Group Specialized Register on September 29, 2015, but it was not necessary to update this search, because records in the Specialized Register are included in CENTRAL. They searched the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library 2016, Issue 11, November 5, 2016), PubMed (November 5, 2016), ClinicalTrials.gov (November 5, 2016), the World Health Organization (WHO) International Clinical Trials Registry Platform ICTRP (November 5, 2016) and reference lists of retrieved articles. They also contacted device manufacturers and other
researchers in the field. No language restrictions were imposed; RCTs comparing DBS or cortical stimulation versus sham stimulation, resective surgery, further treatment with anti-epileptic drugs or other neurostimulation treatments (including vagus nerve stimulation). Four review authors independently selected trials for inclusion; 2 review authors independently extracted the relevant data and assessed trial quality and overall quality of evidence. The outcomes investigated were seizure freedom, responder rate, percentage seizure frequency reduction, adverse events (AEs), neuropsychological outcome and QOL. If additional data were needed, the study investigators were contacted.

Results were analyzed and reported separately for different intra-cranial targets for reasons of clinical heterogeneity. A total of 12 RCTs were identified, 11 of these compared 1 to 3 months of intra-cranial neurostimulation with sham stimulation.

One trial was on anterior thalamic DBS \((n = 109; \, 109 \text{ treatment periods})\); 2 trials on centromedian thalamic DBS \((n = 20; \, 40 \text{ treatment periods})\), but only 1 of the trials \((n = 7; \, 14 \text{ treatment periods})\) reported sufficient information for inclusion in the quantitative meta-analysis; 3 trials on cerebellar stimulation \((n = 22; \, 39 \text{ treatment periods})\); 3 trials on hippocampal DBS \((n = 15; \, 21 \text{ treatment periods})\); 1 trial on nucleus accumbens DBS \((n = 4; \, 8 \text{ treatment periods})\); and 1 trial on responsive ictal onset zone stimulation \((n = 191; \, 191 \text{ treatment periods})\). In addition, 1 small RCT \((n = 6)\) compared 6 months of hippocampal DBS versus sham stimulation.

Evidence of selective reporting was present in 4 trials and the possibility of a carry-over effect complicating interpretation of the results could not be excluded in 5 cross-over trials without any or a sufficient wash-out period. Moderate-quality evidence could not demonstrate statistically or clinically significant changes in the proportion of patients who were seizure-free or experienced a 50% or greater reduction in seizure frequency (primary outcome measures) after 1 to 3 months of anterior thalamic DBS in (multi)focal epilepsy, responsive ictal onset zone stimulation in (multi)focal epilepsy patients and hippocampal DBS in (medial) temporal lobe epilepsy.
However, a statistically significant reduction in seizure frequency was found for anterior thalamic DBS (mean difference (MD), -17.4 % compared to sham stimulation; 95 % CI: -31.2 to -1.0; high-quality evidence), responsive ictal onset zone stimulation (MD -24.9 %; 95 % CI: -40.1 to -6.0; high-quality evidence) and hippocampal DBS (MD -28.1 %; 95 % CI: -34.1 to -22.2; moderate-quality evidence). Both anterior thalamic DBS and responsive ictal onset zone stimulation did not have a clinically meaningful impact on QOL after 3 months of stimulation (high-quality evidence). Electrode implantation resulted in post-operative asymptomatic intra-cranial hemorrhage in 1.6 % to 3.7 % of the patients included in the 2 largest trials and 2.0 % to 4.5 % had post-operative soft tissue infections (9.4 % to 12.7 % after 5 years); no patient reported permanent symptomatic sequelae. Anterior thalamic DBS was associated with fewer epilepsy-associated injuries (7.4 versus 25.5 %; p = 0.01) but higher rates of self-reported depression (14.8 versus 1.8 %; p = 0.02) and subjective memory impairment (13.8 versus 1.8 %; p = 0.03); there were no significant differences in formal neuropsychological testing results between the groups. Responsive ictal-onset zone stimulation appeared to be well-tolerated with few side effects. The limited number of patients precluded firm statements on safety and tolerability of hippocampal DBS. With regards to centromedian thalamic DBS, nucleus accumbens DBS and cerebellar stimulation, no statistically significant effects could be demonstrated but evidence is of only low to very low quality. The authors concluded that except for 1 very small RCT, only short-term RCTs on intra-cranial neurostimulation for epilepsy are available. Compared to sham stimulation, 1 to 3 months of anterior thalamic DBS ((multi)focal epilepsy), responsive ictal onset zone stimulation ((multi)focal epilepsy) and hippocampal DBS (temporal lobe epilepsy) moderately reduced seizure frequency in refractory epilepsy patients. Anterior thalamic DBS was associated with higher rates of self-reported depression and subjective memory impairment. Thee investigators stated that there is insufficient evidence to make firm conclusive statements on the safety and efficacy of
hippocampal DBS, centromedian thalamic DBS, nucleus accumbens DBS and cerebellar stimulation. They stated that there is a need for more, large and well-designed RCTs to validate and optimize the safety and efficacy of invasive intracranial neurostimulation treatments.

High-Frequency Oscillations in Epilepsy Surgery Planning

Gloss and colleagues (2017) noted that epilepsy is a serious brain disorder characterized by recurrent unprovoked seizures. Approximately 2/3 of seizures can be controlled with antiepileptic medications. For some of the others, surgery can completely eliminate or significantly reduce the occurrence of disabling seizures. Localization of epileptogenic areas for resective surgery is far from perfect, and new tools are being examined to more accurately localize the epileptogenic zone and improve the likelihood of freedom from post-surgical seizures. Recordings of pathological high-frequency oscillations (HFOs) may be one such tool. In a Cochrane review, these researchers evaluated the ability of HFOs to improve the outcomes of epilepsy surgery by helping to identify more accurately the epileptogenic areas of the brain. For the latest update, these investigators searched the Cochrane Epilepsy Group Specialized Register (July 25, 2016), the Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies Online (CRSO, July 25, 2016), Medline (Ovid, 1946 to July 25, 2016), CINAHL Plus (EBSCOhost, July 25, 2016), Web of Science (Thomson Reuters, July 25, 2016), ClinicalTrials.gov (July 25, 2016), and the WHO International Clinical Trials Registry Platform ICTRP (July 25, 2016). They included studies that provided information on the outcomes of epilepsy surgery for at least 6 months and which used HFOs in making decisions regarding epilepsy surgery. The primary outcome of the review was the Engel Class Outcome System (class I = no disabling seizures, II = rare disabling seizures, III = worthwhile improvement, IV = no worthwhile improvement). Secondary outcomes were responder rate, ILAE epilepsy surgery
outcome, frequency of AEs from any source and QOL outcomes. These researchers intended to analyze outcomes via an aggregated data fixed-effect model meta-analysis. A total of 2 studies representing 11 participants met the inclusion criteria. Both studies were small non-randomized trials, with no control group and no blinding. The quality of evidence for all outcomes was very low. The combination of these 2 studies resulted in 11 participants who prospectively used ictal HFOs for epilepsy surgery decision-making. Results of the postsurgical seizure freedom Engel class I to IV outcome were determined over a period of 12 to 38 months (average of 23.4 months) and indicated that 6 participants had an Engel class I outcome (seizure freedom), 2 had class II (rare disabling seizures), 3 had class III (worthwhile improvement); no AEs were reported. Neither study compared surgical results guided by HFOs versus surgical results guided without HFOs. The authors concluded that no reliable conclusions can be drawn regarding the efficacy of using HFOs in epilepsy surgery decision-making at present.

Feyissa and associates (2018) examined the relationship between HFOs and the presence of pre-operative seizures, WHO tumor grade, and isocitrate dehydrogenase 1 (IDH1) mutational status in gliomas. These investigators retrospectively studied intra-operative ECoG recorded in 16 patients with brain tumor (12 presenting with seizures) who underwent awake craniotomy and surgical resection between September 2016 and June 2017. The number and distribution of HFOs were determined and quantified visually and with an automated HFO detector. A total of 5 patients had low-grade (1 with grade I and 4 with grade II) and 11 had high-grade (6 with grade III and 5 with grade IV) brain tumors. An IDH1 mutation was found in 6 patients. Patients with a history of pre-operative seizures were more likely to have HFOs than those without pre-operative seizures (9 of 12 versus 0 of 4, p = 0.02). The rate of HFOs was higher in patients with IDH1 mutant (mean of 7.2 per minute) than IDH wild-type (mean of 2.3 per minute) genotype (p = 0.03). The authors concluded
that HFOs were common in brain tumor-related epilepsy, and HFO rate may be a useful measure of epileptogenicity in gliomas.

The authors stated that the retrospective, single-center design of this study had inherent limitations. The small sample size (n = 16) limited definitive conclusions to be drawn regarding the association between HFOs and seizures in brain tumor-related epilepsy (BTRE). In this cohort, HFOs were not detected independently of spikes or sharp waves, although in 1 patient these researchers observed periodic sharp wave discharges without accompanying HFOs. This raised the question of whether HFO analysis added any degree of sensitivity over standard “Berger band” analysis of ECoG in this population. These observation should, however, be interpreted cautiously, particularly given the low sampling rate, which might have resulted in higher-frequency HFOs (fast ripples) being missed. Oscillations in the gamma frequency range, as seen in the majority of this cohort, have been implicated in generating ictal-like discharges in an in-vitro model of epilepsy. Moreover, locally generated gamma oscillations preceding inter-ictal discharges have been found to occur more frequently in the seizure-onset zone in non-tumoral epilepsies. Conversely, some studies suggested that fast ripples were more reliable biomarkers for the epileptogenic zone than slower-frequency oscillations. Although the distinction between the type of HFO and epileptogenicity is not absolute, it is of interest to examine if these observations endure in BTRE. Although these investigators observed that in their cohort HFO-generating tissue was completely resected (on the basis of post-operative MRI findings along with intra-operative photos of grid and/or strip placement), they did not examine the completeness of resection of HFO-generating tissue because of the lack of post-resection ECoG in the majority. However, the favorable seizure freedom outcome of the cohort (9 of 12 become seizure-free), albeit with a short follow-up period, could reflect the extent of surgery, with a majority (9 of 12) undergoing gross-total resection. Indeed, peri-tumoral tissue could be
associated with subtle pathologies such as mild forms of cortical dysplasia that could be highly epileptogenic and may result in seizure recurrence if left unresected. The authors stated that future prospective studies assessing the completeness of resection of HFO-generating tissue vis-à-vis seizure freedom outcome in BTRE are needed. Moreover, they noted that given the short-term post-operative follow-up, the seizure freedom outcome of this cohort should be interpreted cautiously. Taken together, given that HFOs were seen only in those presenting with seizures, the lack of surgical tailoring using HFOs as a surrogate, and the non-controlled surgical outcome data, these findings should be interpreted cautiously; and prospective studies addressing these issues are needed to reproduce these findings and to further highlight the clinical utility of HFOs in BTRE.

Examination of Genetic Variations in Refractory Epilepsy to Guide the Selection of Surgical Candidates

Stevelink and colleagues (2018) stated that in recent years, many different DNA mutations underlying the development of refractory epilepsy have been discovered. However, genetic diagnostics are still not routinely performed during pre-surgical evaluation and reports on epilepsy surgery outcome for patients with genetic refractory epilepsy are limited. These researchers provided an overview of the literature on seizure outcome following epilepsy surgery in patients with different genetic causes of refractory epilepsy. They systematically searched PubMed and Embase prior to January 2017 and included studies describing treatment outcome following epilepsy surgery in patients with genetic causes of epilepsy. They excluded studies in which patients were described with epilepsy due to tuberous sclerosis complex or Sturge-Weber syndrome (since this extensive body of research has recently been described elsewhere) and articles in which surgery was aimed to be palliative. These researchers identified 24 eligible articles, comprising a total of 82 patients who had undergone surgery for (mainly childhood-onset) refractory epilepsy due to
15 different underlying genetic causes. The success rate of surgery varied widely across these different genetic causes. Surgery was almost never effective in patients with epilepsy due to mutations in genes involved in channel function and synaptic transmission, whereas surgery was significantly more successful regarding seizure control in patients with epilepsy due to mutations in the mTOR pathway. Patients with a lesion on MRI tended to have higher seizure freedom rates than those who were MRI-negative. The authors concluded that although the evidence is still scarce, the findings of this systematic review suggested that studying genetic variations in patients with refractory epilepsy could help guide the selection of surgical candidates.

Furthermore, an UpToDate review on “Surgical treatment of epilepsy in adults” (Cascino, 2018) does not mention examination of genetic variants as part of surgical evaluation.

### CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by “+”:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>61534</td>
<td>Craniotomy with elevation of bone flap; for excision of epileptogenic focus without electrocorticography during surgery</td>
</tr>
<tr>
<td>61536</td>
<td>for excision of epileptic focus, with electrocorticography during surgery</td>
</tr>
<tr>
<td>61537</td>
<td>for lobectomy, temporal lobe, without electrocorticography during surgery</td>
</tr>
<tr>
<td>61538</td>
<td>for lobectomy with electrocorticography during surgery, temporal lobe</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>61541</td>
<td>for transection of corpus callosum</td>
</tr>
<tr>
<td>61543</td>
<td>for partial or subtotal hemispherectomy</td>
</tr>
<tr>
<td>61566</td>
<td>Craniotomy with elevation of bone flap; for selective amygdalohippocampectomy</td>
</tr>
<tr>
<td>61863</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of intraoperative microelectrode recording</td>
</tr>
<tr>
<td>61864</td>
<td></td>
</tr>
<tr>
<td>61867</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), with use of intraoperative microelectrode recording</td>
</tr>
<tr>
<td>61868</td>
<td></td>
</tr>
<tr>
<td>61880</td>
<td>Revision or removal of intracranial neurostimulator electrodes [covered for intractable seizures]</td>
</tr>
<tr>
<td>61885</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling</td>
</tr>
<tr>
<td>61886</td>
<td></td>
</tr>
<tr>
<td>95836</td>
<td>Electrocorticogram from an implanted brain neurostimulator pulse generator/transmitter, including recording, with interpretation and written report, up to 30 days [covered for intractable seizures]</td>
</tr>
<tr>
<td>95958</td>
<td>Wada activation test for hemispheric function, including electroencephalographic (EEG) monitoring</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>95970-95971</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of waveform, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements)</td>
</tr>
<tr>
<td>95976-95977</td>
<td>Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group, interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional</td>
</tr>
<tr>
<td>95978</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, battery status, electrode selectability and polarity, impedance and patient compliance measurements), complex deep brain neurostimulator pulse generator/transmitter, with initial or subsequent programming; first hour [covered for intractable seizures]</td>
</tr>
</tbody>
</table>
### Code | Code Description
--- | ---
95983 | Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group [s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with brain neurostimulator pulse generator/transmitter programming, first 15 minutes face-hyphen-hyphen face time with physician or other qualified health care professional [covered for intractable seizures]
95984 | Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group [s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with brain neurostimulator pulse generator/transmitter programming, first 15 minutes face-hyphen-hyphen face time with physician or other qualified health care professional [covered for intractable seizures]

**CPT codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>38232</td>
<td>Bone marrow harvesting for transplantation; autologous</td>
</tr>
<tr>
<td>38240</td>
<td>Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>38241</td>
<td>autologous transplantation</td>
</tr>
<tr>
<td>38242</td>
<td>Allogeneic donor lymphocyte infusions</td>
</tr>
<tr>
<td>61567</td>
<td>Craniotomy with elevation of bone flap; for multiple subpial transections, with electrocorticography during surgery [subpial transection surgery]</td>
</tr>
<tr>
<td>61798</td>
<td>Stereotactic radiosurgery (particle beam, gamma ray or linear accelerator); 1 complex cranial lesion</td>
</tr>
<tr>
<td>+ 61799</td>
<td>each additional cranial lesion, complex (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>61870</td>
<td>Craniectomy for implantation of neurostimulator electrodes, cerebellar; cortical</td>
</tr>
<tr>
<td>64553</td>
<td>Percutaneous implantation of neurostimulator electrode array; cranial nerve</td>
</tr>
<tr>
<td>77371</td>
<td>Radiation treatment delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; multi-source Cobalt 60 based</td>
</tr>
<tr>
<td>77372</td>
<td>linear accelerator based</td>
</tr>
<tr>
<td>77432</td>
<td>Stereotactic radiation treatment management of cranial lesion(s) (complete course of treatment consisting of 1 session)</td>
</tr>
<tr>
<td></td>
<td><strong>Other CPT codes related to the CPB:</strong></td>
</tr>
<tr>
<td>95961 -95962</td>
<td>Functional cortical and subcortical mapping by stimulation and/or recording of electrodes on brain surface, or of depth electrodes, to provoke seizures or identify vital brain structures</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>G0339</td>
<td>Image guided robotic linear accelerator-based stereotactic radiosurgery, complete course of therapy in one session, or first session of fractionated treatment</td>
</tr>
<tr>
<td>G0340</td>
<td>Image guided robotic linear accelerator-based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, second through fifth sessions, maximum 5 sessions per course of treatment</td>
</tr>
<tr>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td>L8681</td>
<td>Patient programmer (external) for use with implantable programmable implantable neurostimulator pulse generator</td>
</tr>
<tr>
<td>L8682</td>
<td>Implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td>L8683</td>
<td>Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver</td>
</tr>
<tr>
<td>L8685</td>
<td>Implantable neurostimulator pulse generator, single array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td>L8689</td>
<td>External recharging system for battery (internal) for use with implantable neurostimulator</td>
</tr>
<tr>
<td>L8695</td>
<td>External recharging system for battery (external) for use with implantable neurostimulator</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>S2142</td>
<td>Cord blood-derived stem cell transplantation, allogenic</td>
</tr>
<tr>
<td>S2150</td>
<td>Bone marrow or blood-derived stem cells (peripheral or umbilical), allogenic or autologous, harvesting, transplantation, and related complications; including; pheresis and cell preparation/storage; marrow ablative therapy; drugs, supplies, hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services; and the number of days of pre- and post-transplant care in the global definition</td>
</tr>
</tbody>
</table>

ICD-10 codes covered if selection criteria are met:

- G40.011 - G40.019
- G40.111 - G40.119
- G40.211 - G40.219
- G40.311 - G40.319
- G40.A11 - G40.A19
- G40.B11 - G40.B19
- G40.411 - G40.419
- G40.811 - G40.812
- G40.911 - G40.919

ICD-10 codes not covered for indications listed in the CPB:

- Epilepsy, intractable
<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G40.001-</td>
<td>Epilepsy, not intractable</td>
</tr>
<tr>
<td>G40.009</td>
<td></td>
</tr>
<tr>
<td>G40.101-</td>
<td></td>
</tr>
<tr>
<td>G40.109</td>
<td></td>
</tr>
<tr>
<td>G40.201-</td>
<td></td>
</tr>
<tr>
<td>G40.209</td>
<td></td>
</tr>
<tr>
<td>G40.301-</td>
<td></td>
</tr>
<tr>
<td>G40.309</td>
<td></td>
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<tr>
<td>G40.A01-</td>
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<tr>
<td>G40.A09</td>
<td></td>
</tr>
<tr>
<td>G40.B01-</td>
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</tr>
<tr>
<td>G40.B09</td>
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<tr>
<td>G40.401-</td>
<td></td>
</tr>
<tr>
<td>G40.409</td>
<td></td>
</tr>
<tr>
<td>G40.501-</td>
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<tr>
<td>G40.509</td>
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<tr>
<td>G40.801-</td>
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<tr>
<td>G40.804</td>
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<tr>
<td>G40.901-</td>
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<tr>
<td>G40.909</td>
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</tbody>
</table>

**NeuroPace:**

**CPT codes covered if criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>61850</td>
<td>Twist drill or burr hole(s) for implantation of neurostimulator electrodes, cortical</td>
</tr>
<tr>
<td>61860</td>
<td>Craniectomy or craniotomy for implantation of neurostimulator electrodes, cerebral, cortical</td>
</tr>
<tr>
<td>61863</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array in subcortical site (e.g., thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of intraoperative microelectrode recording, first array</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>----------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>61864</td>
<td>each additional array (List separately in addition to primary procedure)</td>
</tr>
<tr>
<td>61880</td>
<td>Revision or removal of intracranial neurostimulator electrodes</td>
</tr>
<tr>
<td>61885</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array</td>
</tr>
<tr>
<td>61886</td>
<td>with connection to 2 or more electrode arrays</td>
</tr>
<tr>
<td>61888</td>
<td>Revision or removal of cranial neurostimulator pulse generator or receiver</td>
</tr>
<tr>
<td>95836</td>
<td>Electrocorticogram from an implanted brain neurostimulator pulse generator/transmitter, including recording, with interpretation and written report, up to 30 days</td>
</tr>
<tr>
<td>95970</td>
<td>Electronic analysis of implanted neurostimulator pulse generator system (eg, rate, pulse amplitude, pulse duration, configuration of waveform, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (ie, cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without programming</td>
</tr>
<tr>
<td>95971</td>
<td>simple spinal cord, or peripheral (ie, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>-------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>95977</td>
<td>Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group [s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with complex cranial nerve neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional</td>
</tr>
<tr>
<td>95983</td>
<td>Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group [s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with brain neurostimulator pulse generator/transmitter programming, first 15 minutes face-to-face time with physician or other qualified health care professional</td>
</tr>
</tbody>
</table>
### Code | Code Description
--- | ---
95984 | Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with brain neurostimulator pulse generator/transmitter programming, each additional 15 minutes face-to-face time with physician or other qualified health care professional (List separately in addition to code for primary procedure)

**HCPCS codes covered if criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1767</td>
<td>Generator, neurostimulator (implantable), non-rechargeable</td>
</tr>
<tr>
<td>L8687</td>
<td>Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension</td>
</tr>
<tr>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension</td>
</tr>
</tbody>
</table>

**ICD-10 codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G40.011 - G40.019</td>
<td>Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable</td>
</tr>
<tr>
<td>G40.111 - G40.119</td>
<td>Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable</td>
</tr>
<tr>
<td>G40.211 - G40.219</td>
<td>Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable</td>
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<tr>
<td>Code</td>
<td>Code Description</td>
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<td>Magnetic resonance-guided laser interstitial thermal therapy (e.g. the NeuroBlate and the Visualase Thermal Therapy System - no specific code)</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:

9. Elwes RD, Dunn G, Binnie CD, Polkey CE. Outcome following resective surgery for temporal lobe epilepsy:


70. Heck CN, King-Stephens D, Massey AD, et al. Two-year seizure reduction in adults with medically intractable partial onset epilepsy treated with responsive


89. Waseem H, Vivas AC, Vale FL. MRI-guided laser interstitial thermal therapy for treatment of medically


100. Cascino GD. Surgical treatment of epilepsy in adults. UpToDate Inc., Waltham, MA. Last reviewed December 2018.
AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0394 Epilepsy Surgery

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania

annual 06/01/2020