**SURGICAL TREATMENT OF EPILEPSY**

**Rasul FT.1 Bal J.1 Pereira EA.2 Tisdall M.3 Themistocleus M.4 Haliasos N.1**

*Correspondence address:* [*nhaliasos@gmail.com*](mailto:nhaliasos@gmail.com)

1. *Essex Neurosciences Centre, Barking, Havering and Redbridge University NHS Trust, UK*
2. *Academic Neurosurgery Unit, St. George’s, University of London, UK*
3. *Department of Neurosurgery, Great Ormond Street Hospital for Children, UK*
4. *Department of Paediatric Neurosurgery, Agia Sofia Hospital, Greece*

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**ABSTRACT**

Surgery for epilepsy dates back to 1886 and has undergone significant developments to date. Today it is considered a key treatment modality in patients who are resistant to pharmacological intervention. It improves seizure control, cognition and quality of life. New technologies, advances in surgical technique and progress in scientific research underlie the expansion of surgery in epilepsy treatment. Effectiveness of surgical treatment depends on several factors including the type of epilepsy, the underlying pathology and the localisation of the epileptogenic zone. Timely referral to an experienced epilepsy surgery centre is important to allow the greatest chance of seizure control and to minimise associated mortality and morbidity in the patient. Following referral, patients undergo thorough presurgical investigation to evaluate their suitability for surgery. The commonest form of epilepsy treated by surgery is mesial temporal lobe sclerosis and there is Class I evidence for the medium-term efficacy of temporal lobe resection from two randomised control trials. Various other forms of epilepsy are now considered for resective and neuromodulatory surgical intervention due to favourable results. In this article the authors review the current status of surgical treatment for epilepsy including the presurgical evaluation of patients, surgical techniques and the future directions in epilepsy surgery.

*Key words: epilepsy, surgery, temporal lobe, deep brain stimulation, vagal nerve stimulation*

**INTRODUCTION**

Sir Victor Horsley is credited with performing the first operation for epilepsy in 1886 (1). The patient, James B, was a 22-year-old Scotsman, who as a child had been run over by an Edinburgh cab. This had caused a depressed skull fracture with injury to the underlying brain tissue. Focal seizures ensued and Horsley performed a resection of the ‘scarred cortex’ thereby curing the patient of his focal motor seizures. Since 1886 surgery for epilepsy has undergone significant expansion and has become an important intervention for various forms of the disease. Patients who remain refractory to medical therapy are referred to their neurosurgical colleagues for consideration of surgery.

From the first seizure, to the diagnosis of epilepsy and establishment of first, second or even third line of medication approximately 70% of patients would have a fair quality of life with modern antiepileptic drugs (2). Approximately 20-40% of patients with epilepsy remain resistant to pharmacological therapy (3) due to poor seizure control, side effect intolerance and other factors such as the potential for pregnancy related complications in women of child-bearing. This group of patients may be considered for surgical treatment of epilepsy as shown in Fig **(1)**. Surgery has a success rate of 60-70% depending on the type of surgery, site of surgery and underlying aetiology of seizures (4, 5). A multidisciplinary approach is important is optimising each patient’s treatment. The aim of surgery is to reduce the frequency of, or eliminate seizures, minimise neurological deficits and improve the patient’s quality of life.

There is high quality evidence from well-designed studies showing the value of surgery in epilepsy. In 2005 Spencer et al. published their results from a large multicentre prospective observational study of resective epilepsy surgery (5). Of 339 patients followed-up for two years a total of 223 patients experienced seizure remission (68%). Two large single centre studies have also reported beneficial results from epilepsy surgery. De Tisi et al. reported on the outcome of various surgical procedures for epilepsy in 615 adults (6). The authors reported that 52% of patients remained seizure free at 5 years and 47% were seizure free at 10 years. Patients who underwent extratemporal resections were more likely to have seizure recurrence compared to those patients who underwent anterior temporal lobe resections. Bien et al. studied 1721 patients in a single centre who had surgery for epilepsy. At a median follow-up period of 5.4 years, 586 (50.5%) patients were seizure free. Two randomised control trials (RCTs) and a large multicentre study are discussed in detail in the temporal lobe epilepsy section of this article. In 2015 a Cochrane review assessed the outcomes of epilepsy surgery using evidence from RCTs and non-randomised studies (7). 173 studies including four RCTs examined a total of 16,253 patients. Of these 10,518 patients (65%) had a good outcome following surgery with a range of 13.5%-92.5%. A recent systematic review investigated the long-term outcomes of surgical treatment for epilepsy in adult patients with regard to seizure control, antiepileptic drug treatment and employment (8). The authors found that 40-50% of patients were continuously free of seizures for ten years following resective surgery.

Though there is growing evidence to support the effect of epilepsy surgery on seizure frequency there is still a need for further well-designed trials to assess cognitive effects and quality of life outcomes in the long-term and to further define those groups of patients who will have the greatest benefit from surgery.

**PHYSICIAN GUIDELINES for REFERRAL to SPECIALIST**

In 2004 The National Institute for Health and Care Excellence (NICE) recommended that patients be referred to a tertiary referral centre for further treatment if patients met one or more of the following criteria (Fig. **2**): the epilepsy is not controlled by medication within 2 years, management if unsuccessful after two drugs, the child is aged under 2 years, there is a unilateral structural lesion, there is psychological and/or psychiatric morbidity or there is diagnostic doubt as to the nature of the seizures and/or seizure syndrome (9). Furthermore in 2003 the American Academy of Neurology (AAN) recommended that patients with temporal lobe epilepsy be referred for epilepsy surgery if they were refractory to pharmacological therapy (10). Sadly such guidelines have not always been well adhered to leading to delays in appropriate referral of up to 23 years (11). Such delays in referral may lead to preventable seizure-related deaths due to road traffic accidents, drowning and sudden unexpected death in epilepsy (SUDEP) (12). Timely referral is of paramount importance in the paediatric population as poor seizure control can affect cognitive and motor functions in the developing brain (13).

**HEALTH ECONOMICS and REFERRAL PATTERNS**

It is important to also understand the implications of a prompt referral to a specialist center from the point of view of the healthcare system and wider society. Epilepsy is a condition affecting 50 million people worldwide. It has an incidence of 68.8/100,000 person-years rendering it the most common neurological disorder after stroke with 6 million people affected in Europe. In a recent EU study, the total cost of epilepsy was estimated to be €15.5 billion in 2004, the total cost per patient – admission in a hospital setting – was €2000 - €11500 (14). If we look more in detail at patients with drug-resistant epilepsy, their healthcare costs account for 80% of the costs of epilepsy in society (15). Haneef et al. scrutinized referral patterns in the US from 2005 to 2008 ad showed that the average time of pharmacotherapy before an adult patient is referred to a specialist epilepsy center is 17-18 years (16). The average time of referral after failure of a second line drug treatment was 12-14 years implying that patients are left in a suboptimal state with two or three anti-epileptic medications for many years. It is also true that surgical treatment for this condition has been underutilized in both adult (17) and paediatric populations (18). In the past, this was thought to be mostly due to lack of Class I evidence favouring surgery and absence of widely publicized guidelines to aid referring physicians (19). The largest UK longitudinal study on the numbers of surgeries performed for adult and paediatric cases from 2000 to 2011 showed no increase in the numbers while there was a shift from MRI positive cases (lesion found) to MRI negative (no lesion found) and neuromodulation techniques (VNS, DBS) (20).

**THE EPILEPSY PATIENT “SURGICAL WORKUP” PATHWAY**

This review is divided into two parts, the first giving a brief overview of the problem, the referral guidelines, summary of evidence and an overview of the patient pathway from diagnosis to treatment (Fig. **3**). The second part details more surgical techniques applicable to adult and paediatric patients.

**PRESURGICAL EVALUATION IN EPILEPSY**

After diagnosing a patient with drug resistant epilepsy and assuming that the appropriate referral is made to the Epilepsy Surgery Center then a series of investigations and multidisciplinary “decision tree” is put in place in order to identify whether the patient is a candidate for surgery or not and also to quantify as far as possible the risk benefit ratio.

A multidisciplinary approach to presurgical evaluation in epilepsy patients is fundamental. There are many invasive and noninvasive investigations that can be performed to assess a patient’s suitability for surgery. In addition the presurgical evaluation phase can help determine where the focus of seizure arises and what operation is best for the individual. Neuropsychological assessment allows better understanding of the patient’s baseline cognitive status and is an important tool to understand language dominance and lateralisation of cognitive deficits. There is no single investigation that comprehensively assesses all the patient’s needs. Therefore a number of complementary investigations are performed that together allow the clinician to make an informed decision about how to surgically treat each individual patient’s epilepsy.

There are two phases in the presurgical work-up. Phase I involves investigations that localise the epileptogenic zone and assess the patient’s suitability for surgery. Phase II involves improved delineation of the epileptogenic zone if required (21).

**Phase I** includes high resolution MRI, video scalp EEG monitoring and neuropsychological/neuropsychiatric assessment. High-resolution MRI confirms the location of any underlying brain lesion including the anatomical location. Video scalp EEG telemetry allows collection of semiological information with time-locked EEG to determine the epileptic nature of events and localisation of ictal and interictal electrographic changes. Neuropsychological assessment allows better understanding of the presence and nature of cognitive deficits and their relationship with MRI and EEG findings (22). During this multidisciplinary approach significant information is also gathered with regards to the patient’s social background, family and carers/parents support as this would impact the quality of life outcome and the social circle stress after surgery. Typical examples are patients that would want to know if they could return to work after surgery (8) be able to have a family in the future or parents that need to understand that epilepsy surgery may not improve other long-term disabilities these children may have (23). The management of expectation either at the level of adult or paediatric patients is a key priority of a multidisciplinary team offering epilepsy surgery treatments.

**Phase II** investigations include single-photon emission CT (SPECT), positron emission tomography (PET), functional MRI (fMRI), Magnetoencephalography (MEG), EEG-based Electrical Source Imaging localization(ESI) analysis, EEG-fMRI and ultimately invasive intracranial EEG recordings.

SPECT can provide data on the changes of cerebral perfusion before, during or after the seizure event. Timing of injection and duration of the seizure are important so this process is operator and patient dependent for correct interpretation of results. During the ictal period SPECT shows an area of hyperperfusion in the epileptogenic region, surrounded by an area of hypoperfusion. Ictal SPECT could guide the investigation process when dealing with focal seizures that do not correlate with MRI data and/or EEG results in order to aid the localization of the area of ictal onset (24).

PET or 18FDG-PET has been used in epilepsy surgery workup for many years as a tool of inter-ictal activity of the cerebral cortical activity which is actually one of its advantages in relation to the more time-restricted SPECT. The concept of PET imaging is based on identifying areas of cerebral hypometabolism which usually correlate with that of the seizure focus however many times the specificity is low so it could include projection areas of seizure activity as well (25). This absence of specificity makes surgical decisions on the extent of resections difficult. However, in a study of postoperative outcomes, the extent of resection correlated positively with the hypometabolic areas shown on PET imaging (26).

In many occasions the epileptogenic area can be close or on to eloquent cortex. Mapping the functions of eloquent cortical activity like speech, motor and episodic memory is crucial when making decision about surgical resections. fMRI has become a major contributor in non-invasive mapping of cortical functions. Various speech tasks have been refined to activate the Broca’s area and Wernicke’s language areas (27). Verbal fluency, verb generation, and semantic decision tasks are used commonly for assessment of language lateralization N29. For motor function assessments, finger and foot tapping tasks can be used to identify the primary motor cortex, which is important when planning intracranial EEG implantations and resections. Due to the low spatial resolution of fMRI resections close to motor cortex still need direct electrophysiological stimulation mapping or techniques of awake surgery to minimise the risk of causing an ongoing deficit (27). With regards to verbal memory it is shown that there is a considerable decline in a third of patients undergoing left temporal lobe resection and visual memory declines in a third of those who have right temporal lobe resection N29. Asymmetry of activation on fMRI for verbal and visual memory is a useful tool in predicting this decline together with preoperative memory ability, age at onset of epilepsy, language lateralisation. It is also noted that verbal memory declines predominantly after left anterior temporal lobe resection while visual memory declines after right anterior temporal lobe resection although the evidence is less robust (28, 29).

The techniques of MEG, ESI and EEG-fMRI which share common a mathematical background were developed with the aim to try and refine the temporal and spatial localization of the seizure activity. Simultaneous recording of intracranial EEG and fMRI can show haemodynamic alterations occurring before the first detected EEG changes, suggesting the presence of a “distributed network” which can help interpreting or planning the implantation of invasive electrodes (30). Also simultaneous scalp EEG-fMRI recordings can be used to map haemodynamic changes associated with interictal epileptic discharges with 30–40% sensitivity, which, especially in cases with widespread activity could predict poor outcomes of surgery (31). ESI techniques are based on reconstruction of electrical activity derived from high-density scalp EEGs. A large number of channels (eg, 128) are needed for high-quality ESI. The probability map of the electrical activity is fused with the MRI data and a model is made to aid surgical planning. Resection base on ESI models has been associated with a good surgical outcome (32) and the concordance of an ESI focus with an MRI lesion has been associated with a 92% chance of good seizure outcome after resection (33). MEG is a less widely used technique due to cost and technical limitations. MEG is based on detecting the magnetic field changes produced by the neuronal electrical activity. The advantage is that this activity can be measured at a temporal resolution of millisecond-by-millisecond. In retrospective studies conducted so far, MEG has been used to map interictal activity and aid in localizing the epileptogenic zone. Clinical outcomes of seizure freedom seem to correlate with the use if MEG data (34, 35).

The invasive investigations of Phase II include Intracranial EEG recording +/- cortical stimulation and postprocessing analyses (*high-frequency oscillations, epileptogenicity index*). Subdural electrodes can be placed as a grid or strip. To place a grid a craniotomy must be performed over an area of the brain and the grid of electrodes is placed over the cortex. Strips can be inserted via a burr hole (burr hole strip electrocortigography EcoG), and directed in in the direction of interest under the burr hole. Multiple strips can be inserted in different directions. Insertion of electrodes in this method is not under direct vision (36). The subdural grid is typically made up of an array of contacts. It is placed over the cortical surface and is able to examine areas of functional brain. The areas measured are limited to where the craniotomy is placed. Once the readings have been performed cortical resection is performed once the electrodes are removed. This means the data must be interpreted immediately. The main complications of this procedure are infection (2.3% CNS and 3 % superficial) and intracerebral haemorrhage (4%). Hader et al performed a systematic review, which showed over an 18 year period that there was a reported 0.6% major or permanent complication rate and a 7.7% minor complication rate. The subdural strips suffer in terms of their topographic accuracy. In addition as they are not placed under direct vision there is a risk they may overly or damage underlying cerebral veins. This can result in scarring / adhesions / haemorrhage which can cause neurological morbidity (37).

Stereo-electroencephalography (SEEG) refers to depth electrodes placed stereotactically within the brain parenchyma for the purpose of intracranial monitoring. Using this technique almost any part of the brain can be targeted and monitored. These electrodes can also be in place for up to 14 days. Their main role is for obtained diagnostic data but they can also be used for treatment. If thermocoagulation is used with the depth electrode epileptogenic foci can be targeted and lesioned. In comparison to subdural electrodes it is relatively well tolerated (38). The risk of infection is lower than that of subdural electrodes (1%) with a 1 to 3 % risk of brain haematomata (39). Those patients who are favoured for SEEG over subdural electrodes are those with epilepsy suspected to be bitemporal, insular or multifocal. Those patients who have had a previous craniotomy are not ideal candidates for subdural electrode monitoring as there is an increased risk of infection and haemorrhage in these patients due to post-operative adhesions (40). SEEG offers some clear advantages over subdural electrodes. Targets deep to the cortex can be monitored. The procedure does not require a craniotomy so in a sense is less invasive but it does require complex planning and specialized equipment such as a stereotactic frame. Due to the significant number of sEEG electrodes that need to be placed, robotic technology has come to aid in order to reduce length of procedure and reproducibility (41) (Fig. 4). sEEG has the advantage that it can record data over a period of days; this allows data collection and planning. Unlike subdural electrode recording where resective surgery is normally performed at implantation, thus mandating immediate data analysis, SEEG allows a period of reflection on the data and discussion with the patient / family prior to resection. Conversely high-density functional mapping may be more easily achieved with a subdural grid.

To date there is no high-quality evidence that the adjunctive investigative techniques are clinically effective or diagnostically accurate (42). As such most epilepsy surgeons perform phase I assessment and the use of phase II assessment is centre and patient dependent. Recent advances in presurgical evaluation and future directions in this area are discussed later in this article.

**OUTOMES OF PRESURGICAL ASSESSMENT**

We can therefore identify the following subgroups of patients arising from our “decision-tree” (Fig. 3). If a clear surgical option is available with concordant MRI, EEG and seizure semiology data and the risk is acceptable then the surgical option is offered. If there is no clear MRI target or the EEG and rest of semiology data as discordant most centers would offer “Phase II” investigations. If after these tests the risk of resective surgery is acceptable again this can be offered to the patient. For the ones that either from the beginning or after the “Phase II” tests are not good candidates for surgery then there is the option of either palliative procedures or in the recent 5 years more focus is given to neuromodulation techniques. If none of these options are available then the patient would be deemed unsuitable for any invasive procedure and would be treated with other drugs and/or ketogenic diet.

We will now elaborate on the main surgical techniques of the three treatment modalities – resective surgery, palliative procedures and neuromodulation

**SURGERY FOR TEMPORAL LOBE EPILEPSY**

Mesial temporal lobe epilepsy (MTLE) is the commonest and best-defined focal epilepsy syndrome, it is also the most likely to be refractory to pharmacological intervention (10) and is the most frequent indication for surgery. In a subset of patients with MTLE an anterior temporal lobectomy can give patients a seizure-free life. It is a safe and effective procedure supported by class I evidence.

A common contemporary technique in performing an anterior temporal lobe resection is a two-part procedure whereby the lateral neocortex is first resected followed by resection of the mesial hippocampal structures (43). In some patients there is a very well defined area of focus in the mesial temporal lobe causing seizures. In these patients the lateral neocortical structures can be preserved and a selective amygdalohippocampectomy (SAH) may be performed. Variations on SAH exist mainly differing in the approach to the mesial temporal structures. The overall aim is to resect the uncus, a portion of the amygdala, the anterior 2-3 cm of hippocampus, and the adjoining parahippocampal gyrus.

Post-operative complications are relatively rare. Several studies with hundreds of patients have reported a mortality rate of zero (44-47). However with the removal of functional brain tissue there are a number of possible, subtle neurological deficits that may occur. Perhaps the most commonly described is the contralateral superior quadrantanopia (‘pie in the sky’ visual field deficit) which may ensue following surgery (48). This is due to disruption of optic radiation fibres (Meyer’s loop) that course over the temporal horn of the lateral ventricle. Injury or manipulation of the middle cerebral artery or the anterior choroidal artery may produce a hemiparesis but this is rare (<1%). Psychiatric effects have been observed in up to 50% of patients (49). New depression may occur post-operatively, however, a seizure-free outcome can improve pre-existing depression in some patients. Memory deficits may occurs with verbal memory more affected especially in left temporal lobe resections than visuospatial memory which is more affected in right temporal lobe and there is a risk to language function (30, 43). Cognitive effects are also seen in epilepsy surgery patients. Intellectual ability and IQ may improve post-operatively if seizure remission is achieved (50).

Class I evidence shows positive outcomes in patients following surgery for temporal lobe epilepsy. Two RCTs have investigated the role of temporal lobe resection compared to medication for medication refractory epilepsy (51, 52). Both RCTs showed a superior efficacy in the surgical arm. In 2001 Wiebe et al. randomised 40 patients to each arm of their trial - medical therapy vs. temporal lobe resection in patients with medication resistant epilepsy. The follow-up period was 1 year and the group found that the cumulative proportion of patients who were free of seizures was 58% in the surgical group compared to 8% in the medical group (p<0.001). One patient in the medical group died. In 2012 Englot et al. published their multicentre randomised trial Early Randomised Surgical Epilepsy Trial (ERSET). At a follow-up period of two years the authors reported that 11 of 15 patients in the surgical arm were seizure free compared to zero of 23 patients in medical arm being seizure free. Three patients in the medical group developed status epilepticus. In 2005 Spencer et al. published their results from a large multicentre prospective observational study of respective epilepsy surgery (53). Of 339 patients followed-up for two years a total of 223 patients experienced seizure remission (68%).

**EXTRATEMPORAL LOBE EPILEPSY**

In contrast to temporal lobe techniques and strategies, in extratemporal neocortical epilepsies the boundary of resection is not always defined by precise anatomy but is mostly guided by the MRI / invasive recording. We can also divide these epilepsies into lesional or non lesional depending on whether there is a clear MRI abnormality that correlates with EEG and semiology of the ictal activity. Most of these patients, will undergo the into “PHASE II” investigations including PET, ictal SPECT, MEG, fMRI. Depending on the center 50% of them will undergo also invasive recordings in the form of subdural grids/sEEG. The aim is to try to define as best as possible the epileptogenic focus in relation to functional eloquent cortex such as speech and motor areas of the hemisphere.

Understandably the presence of a positive lesion on the MRI predicts a better outcome in patients with neocortical epilepsy. Seizure freedom is achieved in 67% and seizure reduction in 22% of these cases, whereas only 11% do not improve at all with respect to seizure frequency (54)In a review of patients with lesional frontal lobe epilepsy, freedom from disabling seizures and nondisabling daily seizures can be achieved in 72% of patients, whereas this is achieved in only 41% of the patients with nonlesional frontal lobe epilepsy (55).

In contrast nonlesional extratemporal lobe epilepsy surgery is less successful (29%–56% success rate) (55-59) than nonlesional temporal lobe epilepsy surgery (41%–65% success rate) (60-63). Approximately 60% of patients with nonlesional temporal lobe epilepsy are rendered seizure free after an anterior temporal lobectomy (60, 62). It should also be recognized that this is a highly select group of patients undergoing surgery. In a series published by Noe et al. (64), only 29% (9 of 31) of patients undergoing long-term intracranial EEG and only 11% (9 of 85) of the original study population were candidates for surgery and had excellent outcomes. The large number of patients who must undergo an extensive and costly evaluation to identify good nonlesional epilepsy surgery candidates is in marked contrast to temporal epilepsy, for which the number needed to treat to achieve an excellent outcome is only two (52). A possible explanation for this is that the neural networks involved in epileptogenesis and seizure generation in nonlesional extratemporal lobe epilepsy are less clearly defined, and creating a surgical plan for these patients presents a significant challenge.

***HEMISPHERECTOMY AND HEMISPHERIC DISCONNECTION***

Hemispherectomy / hemispherotomy is a procedure that is performed for unilateral, diffuse hemispheric epileptic syndromes refractory to pharmacological intervention. Such syndromes can be caused by a variety of pathologies. Congenital causes include Sturge-Weber syndrome, hemimegalencephaly, diffuse hemispheric cortical dysplasia, and prenatal vascular insults. Rasmussen encephalitis is an acquired cause. Walter Dandy first described the anatomical hemispherectomy procedure in 1928 but this was for a patient with glioma. It was not until 1938 that McKenzie used this technique to treat refractory epilepsy. Since then several differing techniques have been described including functional hemispherectomy and hemispherotomy. These procedures have been modified by individuals further so today the hemispherectomy procedure is heterogeneous amongst surgeons.

The classical anatomical hemispherectomy involved resection of the entire hemisphere sparing the basal ganglia after ligation of the major blood vessels. However this procedure has now become obsolete and other techniques that ‘disconnect’ the hemisphere are now more commonplace as they reduce morbidity.

The functional hemispherectomy first described by Rasmussen (65), a form of ‘disconnective’ surgery, consists of the following steps (66):

* The temporal gyrus, the supramarginal gyrus, and the suprasylvian opercula are removed
* The white matter of the temporal stem is incised
* The basolateral portion of the amygdala and the uncus are removed, and the uncinate fasciculus is sectioned, thus interrupting the connections of the anterior part of the temporal lobe.
* The parahippocampal gyrus and the fornix are incised, leaving the branches of the posterior cerebral artery intact.
* The splenium of the corpus callosum is incised, then the suprasylvian white matter consisting of fibers of the long connection tracts, is incised
* The callosotomy is then performed.
* The insula, according to the indications, may be separately removed

In 1995 Schramm et al. and Villemure and Mascot simultaneously described a modified version of the functional hemispherectomy known as the hemispherotomy (67, 68). Today, most epilepsy surgeons perform this, or a variation of this. Schramm described his procedure as

*‘…it starts with either hippocampectomy alone or with hippocampectomy and anterior temporal lobectomy. After this, deafferentation of the white matter of the temporal, occipital, parietal, and frontal lobe, using either a transcortical transventricular approach along the outline of the lateral ventricle or a sylvian key hole approach, is performed. The technique includes a transventricular callosotomy, and it leaves in place only a small portion of the suprainsular cortex and the insular cortex.’*

The outcomes following hemispheric surgery, either resective or disconnective, were assessed in a recent systematic review and meta-analysis by Hu et al. (69). The authors investigated the outcomes of studies reporting on hemispheric surgery dating back to 1970. 1528 patients from 56 studies had a pooled seizure-free rate of 73%. They commented that the aetiology of the epilepsy had an impact on the effects of surgery, specifically, those patients with developmental disorders, generalized seizures, non-lateralisation on EEG, and contralateral MRI abnormalities had reduced odds of being seizure-free after surgery. There is good evidence that disconnective techniques are superior to resective procedures (70-72).

Overall, hemispheric surgery is an efficacious therapy for specific indications in refractory epilepsy with a preference for disconnective surgery due to favourable results.

**NEUROMODULATION TECHNIQUES**

Electrical neuromodulatory approaches to extratemporal epilepsy are indicated where epilepsy persists despite resection of epileptogenic foci or in the palliative circumstance where no seizure focus is demonstrated using scalp recording, non-invasive neuroimaging and invasive recording described elsewhere. Vagus nerve stimulation (VNS) has been approved in many countries for partial seizures with or without secondary generalisation based upon trials showing differences in seizure frequency reduction between high frequency (25-30% reduction) and low frequency (6-15% reduction) stimulation groups(73). Median seizure reductions in 454 patients was 44% from baseline after 3 years, with 43% of patients having at least 50% seizure frequency reduction, although 20% had persisting hoarseness at two years’ follow-up(74). Trigeminal nerve stimulation has also recently been reported, 12 patients having a median 66% seizure frequency reduction at three months with occasional side-effects of orbicularis oculi twitching and dental discomfort and paraesthesia. The results augur well for larger trials given its advantage over vagus nerve stimulation of transcutaneous test stimulation.(75)

DBS for epilepsy is almost as old as human stereotactic surgery, having first been attempted acutely in 1952 by Heath. He recorded interictal spikes from the septum in a patient with complex partial seizures and then stimulated him. *“Almost instantly, his behavioural state changed from one of disorganisation, rage and persecution to one of happiness and mild euphoria”(76).* Cooper first treated epilepsy with implantable DBS throughout the 1970s, targeting the superomedial cerebellar cortex and reporting seizure reduction first in 6 of 7 then later 18 of 32 patients(77). Eleven unblinded case series have reported benefits in 88 of 116 patients (76%)(78), but two small double-blinded studies comprising 14 patients have shown no benefit(79). Cerebellar stimulation therefore fell out of favour, with the exception of one recent report of five patients with generalised tonic-clonic seizures showing mean seizure frequency reduction of 59% at six months after surgery.(80) Current deep brain targets under evaluation for epilepsy are the anterior thalamic nucleus, centromedian thalamus, subthalamic nucleus, posterior hypothalamus, hippocampus caudate, corpus callosum and brainstem(81-83).

***ANTERIOR THALAMIC NUCLEUS STIMULATION***

Bilateral DBS of the anterior thalamic nuclei has been undertaken by several groups and is currently being investigated in a multicentre, double-blind, randomized clinical trial – stimulation of the anterior nucleus of the thalamus for epilepsy (SANTE), the first results of which were published in 2010 (84). SANTE recruited 110 patients with medically refractory partial or secondarily generalized seizures(84). Bilateral DBS (Fig 5) was standardized to monopolar stimulation at a frequency of 145 Hz, pulse-width of 90 µs and cycle time on for 1 minute then off for 5 minutes using quadripolar electrodes (Medtronic Inc., Minneapolis, MN, USA). Significant seizure reduction from a median baseline of 19.5 seizures per month was seen in the group stimulated at an amplitude of 5V compared to the placebo implanted group stimulated at 0V, with a 29% seizure reduction in the last month of a three month blinded phase. After three months, all patients were transferred to 5V DBS. Median seizure frequency reduction continued to improve with DBS throughout three years of the trial, with a 41% median seizure frequency reduction at one year, 56% reduction in 102 patients at two years and 68% reduction in 57 patients at three years, 54% of patients having a seizure reduction of at least 50% and 14 patients being seizure free at 6 months. No surgery related symptomatic haemorrhage or deaths were reported although two participants had transient, stimulation induced seizures. The follow-up of the SANTE study at 5 years (85) showed a 69% median seizure reduction.  The responder rate (≥50% reduction in seizure frequency) was 68% at 5 years while 16% of subjects were seizure-free for at least 6 months. There were no reported unanticipated adverse device effects or symptomatic intracranial haemorrhage. They also demonstrated Quality of Life in Epilepsy measure showing statistically significant improvement over baseline at 5 years. In a most recent analysis of the study (86) the most important finding was that no statistically significant cognitive declines or worsening of depression scores were observed. Actually higher scores were observed at 7 years on measures of executive functions and attention.

The mechanisms of anterior thalamic nucleus stimulation remain unclear. Animal models have shown seizure reduction in drug induced seizure models, postulating current dependent and serotonin-mediated effects.(87, 88) Anatomical evidence suggests widespread limbic system sclerosis in epilepsy, including projections to and from the anterior thalamic nucleus to cingulate cortex and hippocampus(89). Concurrent thalamic and scalp EEG recording studies after surgery suggest a recruiting rhythm, elicited with low frequency stimulation, correlating with clinical improvement(90). The nucleus is small and projects to and from many limbic and cortical structures, yet is less deep and proximal to subarachnoid vessels and the mammillary bodies, enabling safer targeting. Stereotactic ablation of the target demonstrated seizure reduction four decades ago (91), motivating its intensive experimental and clinical study.

***CENTROMEDIAN THALAMIC STIMULATION***

Wilder Penfield first postulated that the centromedian thalamic nucleus could be modulated to ameliorate seizures, noting its diffuse projections from brainstem to cerebral cortex.(92) Targeting the parvocellular division of the centromedian nucleus bilaterally, Velasco and colleagues have found seizure frequency reduction in 13 patients with Lennox-Gastaut syndrome(93). Low frequency (6-8Hz) bipolar stimulation was delivered through pairs of adjacent quadripolar electrode contacts while assessing responses in concomitant scalp EEG. Implanted DBS settings were low frequency or high (130 Hz), pulse-width 450 μs and amplitude 6-10V. Their results from unblinded case series showed significant improvements in generalised seizures, less so in complex partial seizures, and seizure frequency increases with depleted battery life of implanatable pulse generators (94). The results have, however, not yet been replicated by others for this brain target. A double-blinded, crossover design, trial in seven patients by Fisher et al. revealed no clinical improvement in seizure frequency with centromedian thalamic stimulation,(95) nor did a recent report of two patients with longer term follow-up.(96)

***SUBTHALAMIC NUCLEUS STIMULATION***

The subthalamic nucleus has been established of late as the surgical target of choice in DBS for Parkinson’s disease and is therefore appealing as functional neurosurgeons should have most experience in targetting it. A mechanistic rationale for its stimulation has arisen from observations that the substantia nigra pars reticulata may act as a gate to seizures through inhibitory nigrotectal projections to the superior colliculi, and its inhibition suppresses seizures in animal models.(97) Subthalamic nucleus inhibition has also been shown to suppress seizures in animals.(98) Clinically, Chabardès et al. demonstrated mean 64% seizure frequency reduction in 4 of 5 patients.(99) Other small studies have also shown improvements, two of five patients reported by Loddenkemper et al. as having 80% improvement in their partial seizures and two patients having their seizures mildly reduced according to Handforth et al.(100, 101) Despite this evidence and Benabid’s promising case report of a child showing 81% seizure improvement at 30 months,(102) larger, blinded trials are required to demonstrate efficacy.

***OTHER DEEP BRAIN TARGETS***

The posterior hypothalamus has been targeted by DBS based upon observations that the mammillary bodies show epileptiform activity with depth electrode recording.(103) A report of two patients by Franzini et al. showed seizure frequency reduced by up to 80% from baseline after nine months follow-up.(104) The mammillothalamic tract has also been stimulated to relieve gelastic seizures secondary to hypothalamic hamartomas with improvements in seizure frequency.(105) Growing case series of DBS for cluster headache targeting the posterior hypothalamus increase our experience and confidence of this challenging deep brain target adjacent to the circle of Willis,(106) with initial evidence pointing towards specific indications of epilepsy with concomitant aggression or gelastic seizures.

DBS of the head of the caudate has been studied as an epilepsy treatment after non-human primate studies showing reductions in induced seizures with stimulation.(107) Sramka et al. have published a study of 74 patients showing reduced interictal EEG activity with both caudate and dentate nucleus stimulation.(108) Chkhenkeli et al. have stimulated the ventral caudate head at low frequency (4-8 Hz) in 38 patients, impressively eliminating seizures in 21 patients and improving 35 patients overall (92%).(109) These results both encourage further, more controlled, clinical trials of caudate DBS.

The corpus callosum has been stimulated in ten patients, perhaps unsurprisingly without benefit,(110) and the locus coeruleus has been stimulated unilaterally in two patients, seemingly improving seizure frequency.(111)

*CLOSED-LOOP STIMULATION*

Closed-loop also known as demand-driven or ‘smart’ stimulation describes devices that respond to and terminate epileptiform activity. They have potential advantages not just in terms of efficacy but also in increased efficiency prolonging device and battery longevity and reduced adverse effects.(112) A recent trial of automated seizure detection equipment delivering stimulation to the anterior thalamic nucleus and cortex reduced seizure frequency in three of four cortically stimulated and two of four thalamically stimulated patients.(113) A multi-centre trial of a closed-loop stimulator also known as   
responsive neurostimulation(RN) has shown reduction in the frequency of medically intractable partial onset seizures from 44% at 1 year to 60% to 66% over 3 to 6 years of treatment. The trial has also shown improvements in quality of life with responsive stimulation and no negative effects on mood or cognition, and some patients experienced improvements in aspects of language and memory. Such technology holds much promise and seems naturally suited to ameliorating epileptic attacks.

***VAGAL NERVE STIMULATION***

There are various hypotheses on the mechanism of vagal nerve stimulation (VNS). It is known that stimulation of the cervical vagal nerve has effects on EEG synchronicity and sleep cycles. The visceral afferents from the vagal nerve return signals to cortex and subcortical regions, particularly the thalamus, via the medial reticular formation. These signals are returned via the nucleus of the solitary tract (NST). Inhibition of the NST has been shown to increase the threshold to limbic motor seizures in animals (114, 115) It has been shown there are regional changes in cerebral blood flow (116) during VNS and SPECT studies have shown deactivation of the thalamus and activation of the limbic system during stimulation (117). VNS has been traditionally an open loop system but recently a system has been developed which triggers in response to tachycardia (118).

There is no benefit to bilateral stimulation and it is usually performed via the left side to potentially reduce cardiac effects . The generator is inserted in the left sub-clavicular region with an electrode around left vagus nerve.

Englot et al. (119) presented a meta-analysis of 3321 patients who had been treated with VNS. The reduction in seizure frequency was shown to be 51 % (obtained > 50 % seizure reduction) and control rates increased the longer the duration of therapy. VNS is currently FDA approved for children above the ages of 12 but also has been used in the wider paediatric population. Murphy et al (120) showed a 31% and 34 % seizure reduction at 6 and 12 months respectively in children aged between 3 and 18 years. It has also been shown that long-term outcomes show improving rates of seizure control over time (121). This was also shown by the American Academy of Neurology who analysed the literature of patients younger than 12. The evidence shows VNS to have a 55% seizure reduction in the cohort 470 children. An increase of 7 % occurs from 1 to 5 years after implantation. Namgung et al (122) present the outcomes of 31 patients (18 children and 13 adults). They found a 59 % reduction in seizure frequency in the children compared to 27 % in the adults. This may indicate VNS has better outcomes in children. A Cochrane review (123) in 2015 which compared five trials of 439 patients showed VNS was over 1.5 times effective at reducing seizure frequency at high frequency stimulation compared to low frequency.

***TRIGEMINAL STIMULATION***

Similar to VNS it is hypothesised that trigeminal stimulation affects the afferent pathways to the reticular activating system. Unlike VNS it is not an implantable device and instead it is placed over the skin. The supra-orbital, supra-trochlear and infra-orbital nerves have all been used as targets. Various studies have indicated a superior effect of bilateral stimulation compared to unilateral stimulation (75, 124, 125). Soss et al. (126) in 2015 performed a long-term prospective follow up of patients who had received external trigeminal stimulation. They found that at 6 months 27% seizure reduction and 37% reduction at 12 months.

**PALLIATIVE PROCEDURES**

***CORPUS CALLOSOTOMY***

This procedure dates back to 1940 when it was introduced by van Wagenen and Herren (127). The theory leading to its use as a palliative treatment for severe epilepsy is that the corpus callosum is the most important pathway for interhemispheric spread of epileptiform activity. It has varied in popularity over the years mainly due to the possible supremacy of emerging techniques. However it has remained a useful palliative procedure for severe epilepsy. The most common current indication is ‘drop-attacks’. In a small group of patients the corpus callosotomy (CC) is performed as a first stage procedure for patients who will eventually undergo hemispherotomy to aid determination of seizure lateralisation.

The modern technique involves resection of the anterior two-thirds of the corpus callosum. The anterior portion of the corpus callosum carries fibres connecting the two frontal cortices. It contains the anterior cingulate, premotor, motor and anterior insular areas. Secondary generalisation of seizures is dependent on the anterior motor callosal fibres in tonic-clonic attacks. The posterior fibres transmit somatosensory and visual information from the parietal and occipital lobes. In addition it transmits information from association cortices. The splenium is preferentially kept intact during CC due to the possibility of a perceptual disconnection syndrome. Severing the posterior corpus callosum is reserved for patients who are refractory to anterior sectioning alone or in children with developmental delay in whom complete corpus callosotomy is often the initial procedure of choice

Malmgren et al. recently reviewed the evidence for CC (128). In total 289 patients from nine single-centre series and one multi-centre series have undergone CC. Seven of ten series were retrospective and the largest series included 50 and 58 patients in total. Up to 20% of patients were seizure-free at short-term follow-up with the greatest effects being seen in patients with drop attacks (Lennox Gastaut syndrome (LGS)) and in children. One group published a population-based, multi-centre, prospective study with long-term follow-up data (129). Only 31 patients were studied but the results showed a sustained reduction in seizure frequency at five and ten years and this appeared to improve with time. With such a small sample size, however, it is difficult to draw general conclusions from this data.

There is also some evidence that it may be superior to VNS in LGS. A recent meta-analysis compared CC with VNS for LGS (130). 17 VNS studies and 9 CC studies were analysed. CC had a significantly better outcome than VNS for >50% and >75% atonic seizure reduction. Another recent review (131) focused on techniques of CC showing 88.2% of total corpus callosotomy patients had a worthwhile reduction in seizures compared with 58.6% of patients who underwent anterior corpus callosotomy. Drop attacks improved from corpus callosotomy more than other generalized seizure types. Improvements in quality of life, behavior, and intelligence/development quotient, as well as parental satisfaction, were generally correlated with seizure outcome. There was no postcallosotomy change in the number of antiepileptic drugs.

In summary CC is an effective palliative procedure for adults and children who suffer from LGS drop attacks.

**PAEDIATRIC EPILEPSY SURGERY**

The paediatric group of patients present a unique challenge for the epilepsy surgeon. A significant proportion of paediatric patients with epilepsy suffer from neurodevelopmental disorders such as autism and ADHD and/or neuropsychological problems including behavioural problems, depression and anxiety (132, 133). In fact, comorbidities such as depression and anxiety can be more of a burden to the patient than the seizures themselves (134). A recent systematic review analysing children’s experiences of epilepsy suggested that these patients suffer from vulnerability, disempowerment and discrimination (135). Compliance with anti-epileptic medications can be a particular problem in this cohort (136). Hence there is a need to ensure appropriate and efficient referral of medication refractory children to epilepsy surgeons for consideration of operative intervention. Before performing surgery there are some other important factors to be aware of in children. Early surgery may improve cognitive development and quality of life in children (137). In addition developmental delay or psychiatric morbidity are not contraindications to paediatric epilepsy surgery (138). In 2006 the Paediatric Epilepsy Subcommission of the International League Against Epilepsy (ILAE) published guidelines that defined the principles that differentiate epilepsy surgery in children from that in adults (18). They emphasised the importance of the unique care required for children with epilepsy due to the complex issues they face.

In the presurgical work-up phase there are some specific considerations to make for children. They should be assessed in a specialist epilepsy unit and presurgical assessment should be done as soon as possible. Advances in technology over the past decade have aided presurgical evaluation and the ILAE published a report concerning standardisation of the utilisation of diagnostic tests at the pre-operative stage (139). The global panel of experts reviewed the literature to date, of which there is a lack of class I and II evidence, and made expert recommendations. All patients should have through clinical history, video EEG telemetry (-ictal and interictal), 3D volumetric MRI and neuropsychology assessment. Following this a preliminary review is undertaken and further testing is performed if indicated.

Some patients do not require additional testing as the preliminary review identifies all the important information required to make an informed decision about the next stage of treatment. This occurs in the group where there is clear convergence of clinical and scalp EEG data. If there is some divergence then false localisation on scalp EEG may have occurred and thus further testing may be indicated. In pathologies such as hippocampal sclerosis, arterio-venous malformations and other vascular lesions no further testing is required prior to performing surgery although some ancillary testing may be needed to evaluate the lesional penumbra. For focal cortical dysplasia and nonlesional cases FDG-PET is advocated as the next investigation following MRI. For hemispheric patients with preserved function, tuberous sclerosis or patients that have previously undergone surgery then ictal-SPECT is suggested even though it is technically challenging to perform. It does also require that the seizures are frequent enough and last long enough for data capture. MEG can be useful in MRI-negative case where the seizure source is suspected to be tangential, interhemispheric foci or in postoperative failures due to likely distortion of EEG fields. 3D-EEG is complementary to MEG and cheaper and so this can be used as first line though some centres with adequate resources may wish to utilise both modalities if possible. When the initial investigations suggest an epileptic focus that is close to eloquent cortex then either fMRI or MEG can be used to definitively localise eloquent cortex. Wada testing or electrocortical stimulation mapping confirmation can be performed in older, compliant children in whom memory functions are a concern. These investigations inform the MDT meeting in allowing clinician’s to decide both the likely benefit vs cost ratio of surgery and the type of surgery that should be performed.

Specific pathologies that are frequently encountered in paediatric epilepsy surgery:

* **Focal cortical dysplasia (FCD):** This is the commonest malformation of cortical development encountered in epilepsy surgery. It can be focal, multifocal and even hemispheric. It usually occurs in the frontal and temporal lobes although it may occur anywhere in the cortex. Structural MRI often identifies the abnormal lesion although abnormal cortex has been observed outside the area defined by non-invasive imaging.
* **Tuberous sclerosis**: Patients with medication refractory tuberous sclerosis with identified epileptogenic cortical tubers are considered for surgery. Multiple tubers are not a contraindication if a single resectable epileptogenic focus can be identified. Ictal-SPECT may be useful in helping to identify the primary seizure focus.
* **Hemispheric syndromes:** This group of pathologies includes hemispheric malformations of cortical development (including extensive polymicrogyria and hemimegalencephaly), meningeal angiomatosis in Sturge-Weber syndrome, infantile hemiplegia with unilateral cortical atrophy or porencephaly from single/multiple vascular territories, and Rasmussen encephalitis. These patients undergo either resection or disconnection of the affected hemisphere. It is crucial to exclude seizure formation from the contralateral hemisphere.
* **Hypothalamic hamartomas:** In this rare congenital disorder patients suffer from precocious puberty and frequent gelastic fits. Developmental delay and behavioural disorders are often present. These patients may undergo resective surgery and some are considered for radiosurgery.
* **West syndrome and Lennox-Gastaut syndrome (LGS)**: In West syndrome patients suffer from infantile spasms and partial seizures. These are often due to focal epileptogenic pathology which may require resection. In LGS patients suffer from drop attacks and this may be amenable to partial or complete disconnection of the corpus callosal fibres (as previously described).

There is variation in the reported clinical outcomes in paediatric epilepsy surgery owing to the numerous pathologies that necessitate surgery and the multiple techniques employed by surgeons. Research suggests a reduction of seizure frequency between 40 and 80% (140).

In patients with FCD surgical resection offers an overall seizure freedom rate between 40 and 73 %, at approximately two years follow-up (141). Most studies report a 50-55% success rate. The most important variable predictive of postoperative seizure freedom is complete resection of the epileptogenic lesion. Hemispheric surgery, whether it is resective/disconnective and/or anatomical/functional, has a reported success rate of 52-90% in achieving complete seizure freedom (142). After corpus callosotomy for drop attacks seizure freedom from drop attacks is observed in up to 57% of patients and those who are not seizure free experience less disabling seizures and less falls (143). In general the rate of seizure freedom in paediatric epilepsy surgery is variable but a recent meta-analysis indicated that patients with a lesion on imaging or histopathology are more likely to experience seizure freedom than those undergoing nonlesional epilepsy surgery (144).

There is a paucity of literature pertaining to outcome measures other than seizure freedom in paediatric epilepsy surgery. One group performed a study investigating the IQ in children with temporal lobe epilepsy following surgery (145). The authors reported a six-year follow-up series in which they found that 41% of patients had an increase in IQ of at least 10 points. Other studies also suggest that there may be some improvements in memory and other neuropsychological measures following temporal lobectomy (146, 147). In extra-temporal lobe epilepsy patients who underwent frontal lobe resection had occasional improvement in attention, language and executive functioning (148). Similarly, behavioural outcomes have been poorly investigated following epilepsy surgery in children. To date, only four studies having reported on the behavioural and emotional effects of surgery using standardized testing (149-152). The limited available data suggests that there may be some improvement in these areas although the small numbers of patients in each study limit the generalisation of the data. There is also a lack of high quality data regarding quality of life outcomes. Titus et al. reported on the health-related quality of life (HRQOL) of 28 patients. Their results showed improvements in overall HRQOL after surgery, particularly in physical and social activities. Children with better seizure outcome had more improvement in HRQOL.

**FUTURE DIRECTIONS IN EPILEPSY SURGERY**

Epilepsy surgery has come a long way since Horsley’s first operation in 1886. Major technological advances over the years have expanded the epilepsy surgeon’s armamentarium. Improved understanding of various epilepitogenic pathologies and better utilisation of available investigative modalities together with the development of existing and new surgical techniques underlie the journey that epilepsy surgery has made to date. However, despite such advances there has been no significant improvement in the outcomes for seizure freedom over the last 20 years (3).

The future of epilepsy surgery is exciting and there is much on the horizon that promises to aid surgeons in the pursuit of improved outcomes for patients with epilepsy. Here we discuss some of the newer techniques that have not been previously mentioned in the text of this article.

**Advanced imaging techniques**

As in most neurosciences fields, advances in imaging will enable to improve the preoperative workup and the outcomes especially in the group of patients suffering from extratemporal and/or nonlesional epilepsy where the results are still suboptimal (ref 11 De Tisi). It would either enable to localize architectural abnormalities only visible in high field MRI scanners (above 7T) or give additional information to the multidisciplinary team refining techniques already used like fMRI, DTI, voxel-based morphometry analysis and postprocessing algorithms (153, 154). Considerable work is also done in enabling IT platforms that can easily visualize all this information and be of real use when putting together multi-modal imaging techniques (155). It may not be long before machine learning and big-data analytics can provide insights into architectural abnormalities of MRI scans of epilepsy patients (156).

**Stereotactic radiosurgery**

Stereotactic radiosurgery (SRS) is a potential option for patients with temporal or extratemporal lobe epilepsy. A multi-centre, randomised, prospective pilot study investigated the safety and efficacy of radiosurgery in mesial temporal lobe epilepsy (157). The authors reported a 67% seizure free rate at 3-year follow-up. A more recent meta-analysis investigated 13 studies that reported on the outcomes of SRS for temporal lobe epilepsy (158). Approximately half of the patients were seizure free at a variable length of follow-up (6 months – 9 years). However, to date there has been limited data comparing open surgery with SRS.

The radiosurgery or open surgery for epilepsy (ROSE) trial is a phase III clinical trial that aims to compare radiosurgery with temporal lobectomy for temporal lobe epilepsy. The study has a 3-year follow-up period and its primary outcome measure is seizure freedom. The results of this trial will provide high quality evidence to better define the role of radiosurgery in temporal lobe epilepsy.

**Laser interstitial thermal therapy**

Laser interstitial thermal therapy (LITT) is a percutaneous, stereotactically guided procedure that delivers light energy to a target tissue. It results in thermal ablation of the target tissue. It is used in the treatment of deep-seated brain tumours and is an emerging technique in medication-refractory epilepsy treatment. It is performed under MRI guidance allowing monitoring of tissue ablation in real time.

Several reports have investigated the efficacy of LITT in epilepsy. Curry et al. were the first group to describe the outcome in a group of five paediatric patients (159). One patient was seizure free at a one-year follow up period. Willie et al. reported the first series of 13 patients who underwent MRI guided LITT for mesial temporal lobe epilepsy (160). 30.8% of patients were seizure free at last follow-up with 54% of patients achieving freedom from disabling seizures. More recently Kang et al. prospectively assessed 20 patients who underwent LITT for mesial temporal lobe epilepsy (161) 3 of 5 patients were seizure-free at 2 years. Such small series do not provide sufficient evidence for the safety and/or efficacy of such treatment.

There are currently two commercially available MRI guided LITT systems in use: Visualase and NeuroBlate.

Visualase *(Visualase Inc, Houston, TX, acquired by Medtronic Inc, Minneapolis, MN in 2014)* is an FDA approved MRI guided LITT system. It uses a saline-cooled catheter to deliver fibre optic thermal coagulation via a 3 or 10 mm diffusing tip. Laser energy is delivered through a 15 W, 980 nm diode laser, which is controlled *via* a user monitoring station that provides user-defined safety limits that trigger automatic laser shutoff when exceeded. The laser fibre is implanted through a plastic or titanium anchor bolt that is stereotactically implanted in the bone using either frameless or frame based stereotactic techniques. After insertion of the cooling-cannula/laser fibre a pre-operative planning MRI is performed to select the target volume for ablation. The extent and temperature of the thermal delivery is assessed in near real time by MR thermography. By specifying temperature thresholds and their associated geometric volumes with real-time MRI imaging, they were able to define both a target for thermal ablation and critical structures that would be protected from high temperatures.

NeuroBlate *(Monteris Medical, Inc, Plymouth, MN)* is a MRI guided LITT that achieved FDA approval in 2009. It uses a CO2-cooled catheter with a 12 W, 1064nm Nd:YAG laser. The software (M-Vision) allows preoperative targeting of the area for thermal ablation. The ablation process is performed on a slice-by-slice basis. Once the laser is place an intraoperative MRI is acquired and ablation is performed. The surgeon can monitor this process. Then the laser goes to the next ‘slice’ via a robotic system before performing thermocoagulation there, this repeats until the entire volume has been coagulated.

 The LITT systems have a relatively low risk/complication rate. Perhaps the most likely complication is failure to position the stereotactic probe in the exact correct location hence causing thermocoagulation to adjacent structures. MRI guidance for targeting and trajectory planning greatly reduces this risk.

 MRI guided LITT is an important emerging technique used in the treatment of refractory epilepsy. As yet there is paucity of literature to support its widespread use, however, in centres that have sufficient experience it is a genuine alternative to open surgery. Further studies are required to properly test its safety, efficacy and compare it to the more common epilepsy surgery treatments.

**Focused ultrasound**

Magnetic resonance-guided focused ultrasound surgery (MRgFUS) allows the delivery of high doses of ultrasound energy to a specific target area of the brain. It is performed stereotactically. The main drawback is the possibility of causing overheating to critical structures including cranial nerves and parts of the skull base. This technique has been used in various pathologies including medial thalamotomy for chronic neuropathic pain and essential tremor. There is a current study that is currently recruiting patients (A Feasibility Study to Evaluate Safety and Initial Effectiveness of MR-Guided Focused Ultrasound Ablation Therapy in the Treatment of Subcortical Lesional Epilepsy) that aims to evaluate the feasibility, safety and initial effectiveness of the ExAblate transcranial system to produce multiple sonications targetting the lesion of interest (162).

**CONCLUSIONS**

Epilepsy surgery has made considerable steps over the last 25 years. It clearly the testing ground for advanced imaging techniques that improve and refine patient selection. Neuromodulation treatments have started to give us insights into neural networks and mechanisms of action and are advancing our knowledge of connectivity analysis of the brain. It is important to understand that follow-up of surgically treated epilepsy patients is a lifelong process as seizure recurrence is a common theme and outcomes can change over an extended period of time. This applies also to the design of clinical trials where long follow-ups are necessary to elucidate the true value of each of the treatments proposed. Despite our best efforts epilepsy surgery is still failing in a number of patients especially in extratemporal nonlesional epilepsy where there can be inability to localize the epileptogenic focus, multiple foci or a very widespread epileptogenic zone. These are areas where advances must be made.

Finally, epilepsy surgery remains underutilized with referring times to specialist centers exceeding 18 years for adult patients despite the fact that it is a cost-effective treatment able to reduce hospital admissions, antiepileptic medication burden and social stigma. Probably the most important message for non-specialist professionals and the public is to increase the awareness and visibility of epilepsy surgery interventions as a safe and effective tool to use as early as possible in the population in need.

**CONFLICT OF INTEREST**

FTR: Nil

JB: Nil

EACP: Nil

MT: Nil

MTh: Nil

NH: Nil

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Fig **(1).** Epilepsy care pathway. Almost 70% of patient would be able to lead a fair quality of life on modern antiepileptic medication. The 30% with intractable seizures should undergo a referral to a specialist center for evaluation

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Fig **(2).** National Institute of health and Clinical Excellence (NICE) recommendations as to the criteria fulfilled in order to refer the patient to a specialist center to discuss further options of treatment

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Fig **(3).** Surgical patient pathway from referral to epilepsy center to possible treatment options

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Fig **(4).** Robotic Arm and head clamp for implantation of sEEG electrodes

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Fig. **(5)**. Targeting the right anterior thalamic nucleus planning for bilateral deep brain stimulation.