

## Methods of epilepsy surgery

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### Pre-surgical evaluation

In order for any epilepsy surgery programme to be effective there has to be a critical mass of staff with the necessary expertise in order to carry out the appropriate evaluations in patients in the pre-operative period, and the post-operative follow up. In both adults and children, following pre-operative evaluation it is essential that the information acquired is critically appraised in a multidisciplinary meeting, not only to determine the suitability of the patient for surgical intervention, but also to attempt to assess the potential risks and benefits of surgery. The meeting should be structured to ensure that the information obtained is carefully assessed and any shortfall in the information identified.

A principal aim of pre-surgical evaluation is to determine the epileptogenic zone and the relationship of this zone to eloquent areas of the brain. The epileptogenic zone is the area of the brain which gives rise to seizures, and the removal of which results in the patient becoming seizure free. No single pre-operative investigation can determine the epileptogenic zone with complete reliability and even when various investigative modalities are combined there may be a variable degree of congruence. When pre-operative investigations have a high degree of concordance it may be possible to recommend immediate surgery with predictable levels of benefit and risk. However, if pre-operative investigations are discordant surgery may be rejected in favour of gathering further information using invasive studies.

### Intracranial EEG recording

The aim of invasive EEG recording is to acquire neurophysiological data to support or disprove a hypothesis regarding the site of onset of seizures. The type of intracranial recording depends on the suspected pathophysiological substrate of the epilepsy and its location. Invasive electrodes may be placed either within the brain parenchyma, in the subdural space, or in the extradural space. Electrodes may be used both for recording and for stimulation, allowing assessment of the relationship between the epileptogenic lesion and eloquent cortex.

The first brain electrode implantation took place in the early 1940s, followed in 1946 by the introduction by Spiegel and Wycis of the first stereotactic instrument for human use. Placement of electrodes was initially determined by pneumoencephalography. Angiography was also used in order to avoid major vascular structures when planning electrode trajectories. The additional use of contrast ventriculography allowed the positioning of multiple-depth electrodes in both hemispheres when a wide area needed to be sampled and this approach is still favoured in some centres.

Contemporary frame-based stereotaxy uses either CT or MRI to determine intracranial targets. For depth electrode implantation MRI offers the advantages of high anatomical

resolution and allows selection of trajectories that avoid crossing pial boundaries, thus reducing the risk of intracerebral haemorrhage. Depth electrodes may be placed either orthogonally or radially, the electrodes having between six and ten contact points at 1 cm intervals, to allow recording along the length of the electrode from both deep and superficial points.

In addition to using frame-based stereotaxy, depth electrodes may also be placed using image guidance systems. These have the advantage that the scan may be acquired pre-operatively, either with or without fiducials, at a time more convenient to the patient and the radiology department. It also obviates the need for the application of the stereotactic frame and therefore both simplifies the operation and reduces operating time. The insertion of the electrodes may then be either freehand following the trajectory delineated by the image guidance system, or alternatively they may be introduced using an electrode carrier stabilised to the Mayfield head holder.

In contrast to depth electrodes, subdural strips and grids do not breach the pial boundaries and potentially pose less risk of haemorrhage or cortical damage. Subdural strips can be placed through simple burr holes and used to localise and lateralise both temporal and extra-temporal epilepsy. Subdural grids can record from a larger area of contiguous cortex and are frequently used when epileptogenic lesions are adjacent to eloquent cortex. A wider area of cortex is covered by both strips and grids than by depth electrodes, however if the epileptogenic lesion is situated deep in the cerebral cortex the grid recordings need to be interpreted with care. Similarly, the disadvantage of using depth electrodes is that the area of the brain sampled is usually small and unless seizure onset is seen in a specific electrode or group of electrodes little conclusion can be made regarding the epileptogenic zone. This demonstrates the importance of having a clear plan and objective prior to implantation.

Implantation of a subdural grid over eloquent cortex allows an estimation to be made of the anatomical relationship between the epileptogenic zone and the functional cortex. This allows construction of a homunculus of motor and sensory cortex as well as the mapping of receptive and expressive speech areas. The paradigm for cortical stimulation needs to be adjusted in infants because the thresholds required differ when myelination is immature. As well as direct cortical stimulation, somatosensory evoked potentials can also be used to determine the central sulcus.

The duration of invasive monitoring depends very much on the seizure frequency, the success of any planned stimulation, and patient compliance. In current clinical practice depth electrode implantation is used mainly to determine laterality in seizures of temporal lobe origin and in MRI negative frontal lobe cases, whereas subdural grids are most commonly used for MRI-positive extra-temporal epilepsy and in cases where the presumed seizure onset zone is close to eloquent function. Several weeks of depth electrode recording may be necessary to build a true picture of the patient's seizures and to establish the number of seizures. In contrast, subdural grid recordings seldom extend beyond 10–14 days as the seizure frequency is often higher in these patients, as are the inherent risks of infection.

Invasive monitoring may be terminated at any stage if a clinically significant adverse event is recorded. The risks from monitoring procedures are intracranial haematoma formation as a result of the primary procedure and infection as a consequence of the wires passing through the scalp. These risks can be reduced by careful intra-operative technique and appropriate post-operative nursing care. The use of antibiotics during invasive recording is controversial.

At the end of the invasive monitoring period the data collected are evaluated and the suitability for surgery reassessed. Regrettably a certain percentage of patients will undergo invasive recording but not be deemed suitable for resective surgery, either because the

epileptogenic zone could not be satisfactorily determined, because multiple sites were found, or alternatively because the epileptogenic zone was situated in eloquent cortex. If neither a resective nor a functional procedure is thought possible then the electrodes are removed and the epilepsy is then managed medically.

Invasive intracranial EEG studies are time consuming, expensive, have an inherent complication risk and require numerous personnel. Despite this, the number of patients undergoing these procedures is increasing in recent years. This is being driven by newer imaging modalities such as PET (positron emission tomography), SPECT (single-photon emission computed tomography), MEG (magnetoencephalography) and EEG-fMRI, suggesting possible focal targets for patients with epilepsy. At this time the sensitivity and specificity of these investigations is still to be ascertained and intracranial EEG is needed to prove or disprove the suggested seizure onset zone.

### **Surgical resection**

Epilepsy surgery may be divided into two major categories: resective and functional. The aim of resective surgery is to remove the epileptogenic zone and render the patient seizure free. Based on the discussions at the presurgical meeting, a risk:benefit analysis for each individual patient is determined and the exact nature of the surgical procedure is explained and discussed with the patient in detail. Patients and their families or carers are given both verbal and written information, as well as counselling, so that they are fully informed before written consent is obtained. Once consent is given the surgeon can embark on surgery with a clear clinical objective and surgical strategy.

The surgical techniques employed in epilepsy surgery are relevant to all branches of neurosurgery, with newly-developed technology being particularly useful in this type of surgical intervention. In addition to the basic principles of resection to preserve pial boundaries first described by Sir Victor Horsley a century ago it is also essential to respect the anatomical planes in both the deep and superficial cortex. Stereotaxy or image guidance assists with localisation while accurate tissue removal is facilitated by high quality operating microscopes and the use of the ultrasonic aspirator. At low power the aspirator allows removal of gliotic, tumour and dysplastic tissues while at the same time preserving the pia. The newly available use of interventional MRI allows documentation of lesion resection prior to the termination of any surgical procedure and also allows the surgical navigation software to be recalibrated during the operation, making the procedure more accurate.

#### *Lesionectomy*

The increased anatomical resolution afforded by MRI means that many more cortically-based lesions, which give rise to epilepsy, are identified. Small lesions such as cavernomas, focal areas of cortical dysplasia, and indolent tumours such as dysembryoplastic neuroepithelial tumours are recognised as highly epileptogenic and resection of these lesions, particularly when they are extra-temporal, is associated with a high rate of freedom from seizures. As with all resective surgery, success depends on the complete resection of the epileptogenic zone. What may not be clear purely from imaging is the extent to which the tissues surrounding an area of structural abnormality may be contributing to the epileptogenic zone. The extent of perilesional resection is determined by visual inspection and intra-operative electrocorticography and may be further facilitated by the use of image guidance or intra-operative imaging.

Outcome studies have shown that, when the cortical lesion lies within the temporal lobe, resection of the lesion alone results in a significantly poorer outcome than in extra-temporal cases. It is probable that this inferior outcome is a result of the proximity of the cortical lesions to the mesial temporal structures and associated dual pathology, i.e. the presence of

hippocampal sclerosis alongside the structural lesion. When lesions occur in the temporal lobe a careful preoperative assessment of hippocampal size and signal, as well as the patient's neuropsychological function, should be carried out. Careful consideration has to be given to the potential benefits and risks of lesionectomy and the removal of the mesial temporal structures, particularly when the lesion lies within the dominant temporal lobe. It may be worth considering a staged approach to resection, whereby a lesionectomy is performed initially in the knowledge that, should this fail, a subsequent wider procedure may be performed.

#### *Temporal lobe resection*

Penfield was the first to recognise that, in patients with seizures of temporal lobe origin, the temporal lobe together with the hippocampus and amygdala could be removed safely and effectively. This procedure now accounts for approximately 50% of operative procedures carried out in specialist epilepsy centres. This is primarily due to the stereotypical semiology of seizures arising from the temporal lobe, and in particular the mesial temporal structures. It is also due to the ease with which the diagnosis can be made electrographically and the tremendous contribution made by MRI in the pre-operative diagnosis of hippocampal sclerosis.

In the 1950s, Falconer at the Maudsley Hospital described anatomical temporal lobe resection. This standardised procedure involved the removal of a large amount of temporal neocortex 'en bloc' with the mesial temporal structures. The resection of a large amount of temporal neocortex has the disadvantage of producing significant neuropsychological deficits as well as a superior quadrantanopia. For this reason there has been a tendency to reduce the size of the neocortical resection, either according to the method described by Spencer or by carrying out one of the variously described forms of selective amygdalohippocampectomy. Selective amygdalohippocampectomy may be performed anatomically or by using intra-operative image guidance. When the causative pathology is hippocampal sclerosis it is likely that the extent of mediobasal resection, rather than the neocortical resection, is the determinate factor in outcome. Despite this there is still controversy about the different approaches adopted although this is probably due more to the surgeon's preference than scientific study. Nonetheless, the familiarity of a specific approach or technique does improve outcome and lower morbidity and this should therefore be a serious consideration when determining surgical strategy.

Despite the dramatic advances in pre-operative diagnosis the outcome from temporal lobectomy has only slowly improved. In the case of hippocampal sclerosis our seizure-free rate at the National Hospital for Neurology and Neurosurgery is approximately 75–80% while for lesions it is approximately 70–75%. In dominant temporal resections deterioration in verbal memory is most common in patients with a preserved memory pre-operatively. Quadrantanopia occurs in approximately 10% of patients and in 5% this is severe enough to render the patient ineligible for a driving licence. Post-operative depression is seen in many patients and although commoner in patients with a previous history of psychiatric problems it may occur *de novo*.

#### *Extra-temporal resections*

This category includes single and multi-lobar resection, either for diffuse pathology or in patients in whom the MRI is negative. In order to determine the extent of a lobar or multi-lobar resection it may be necessary either to carry out chronic invasive recording or alternatively to use a combination of electrocorticography and evoked potentials intra-operatively. Depending on the pathology, large resections may be necessary to effectively remove the epileptogenic zone and, under these circumstances, care must be taken not to impinge on eloquent cortex, unless the pre-operative discussions have determined that neurological deficit is preferable to persistent seizures.

The outcome and morbidity in these cases is determined by the pathology and anatomical position of the epileptogenic zone. The extent of the resection may also influence the neuropsychological sequelae of a resection, but in many cases is predictable.

### *Hemispherectomy*

Hemispherectomy was first described in the management of malignant cerebral tumours. This established the surgical technique but quickly demonstrated that the indications were inappropriate. In 1938 McKenzie described the application of the procedure in a patient with medically intractable seizures and behavioural problems. Over the next 25 years the procedure was widely used in patients with intractable seizures. The inevitable consequence of a hemispherectomy is a profound neurological deficit, including hemiplegia and hemianopia, however many of the patients considered for surgery already have these neurological deficits. In the 1960s the original anatomical procedure fell into disrepute as the procedure caused long-term complications in many patients such as hydrocephalus, and in some cases resulted in death.

As a result alternative techniques for either obliteration of the surgical cavity or disconnection of the hemisphere were developed. First, Rasmussen described a functional hemispherectomy in which the temporal lobe and central cortex were removed and the corpus callosum and frontal and occipital cortex disconnected. This procedure was subsequently made less invasive by Delalande and Villemure who described different techniques of hemispherectomy. The consensus view of these alternative techniques is that, when properly performed, the outcomes are very similar if disconnection and not resection is performed.

The success of hemispherectomy depends on the underlying pathology, with excellent outcomes expected for pathologies such as Rasmussen's encephalitis and focal infarcts, and a poorer outcome expected in patients with hemi-megalencephaly.

### **Functional procedures**

The objective in functional epilepsy surgery is to palliate rather than to cure the epilepsy. Functional procedures should only be considered once resective surgery has been deemed inappropriate, or to carry too great a risk.

### *Corpus callosotomy*

Corpus callosotomy was first developed in the 1940s following the observation that in patients undergoing transcallosal exploration of tumours, seizures were reduced in frequency. The primary indication for corpus callosotomy is atonic drop attacks, although it has been used to good effect in other epilepsy types and syndromes. The major concern with corpus callosotomy is the risk of either immediate or delayed symptoms of disconnection. In order to prevent or minimise the risk of a disconnection syndrome the callosotomy should be carried out in two stages, with the anterior two-thirds of the corpus callosum being divided at the first operation and the posterior third divided if and when the callosal section is completed. In children under the age of 12 years there is no evidence to suggest that long-term disconnection syndrome occurs and for this reason a one-stage complete callosotomy is carried out whenever possible in this younger age group.

Careful surgical technique is essential for this procedure and great attention needs to be paid to preservation of the vascular anatomy, particularly the bridging veins, and retraction should, as always, be kept to the minimum.

### *Stimulation*

Since the introduction of deep brain stimulation there has been a continuing quest to determine its efficacy in the management of epilepsy. The numbers of patients who have undergone deep brain and cerebellar stimulation for epilepsy are small and results to date have not been dramatic. However, with the continuing advancements in stimulator technology and the improved accuracy of implanting electrodes, this may be a continuing source of development in the future. A recently reported randomised trial of the anterior nucleus of the thalamus has shown efficacy comparable with vagal nerve stimulation (VNS).

Peripheral stimulation in the form of VNS has attracted considerable interest since it received FDA approval in the United States in 1997 and is used as a palliative procedure in patients for whom resective surgery is not suitable. Although not wholly elucidated, the pathophysiological basis of periodic vagal nerve stimulation seems to be stimulation of autonomic nervous pathways. Besides intermittent stimulation, on demand stimulation can be achieved by the patient or companion.

At surgery the left vagal nerve is used in order to avoid cardiac side effects, and the electrode is placed on the nerve in the neck between the common carotid artery and the internal jugular vein. Side effects include hoarseness and coughing during stimulation and discomfort in the neck. The median reduction of seizures from vagal nerve stimulation is 45% at one year. While relatively few patients become seizure free with VNS, there are suggestions that efficacy and quality of life further improve over time. An extensive patient registry and ongoing clinical evaluation to provide a growing database of information will ultimately allow a cost:benefit analysis of this therapy.

### *Multiple subpial transection*

This technique was first described following animal research by Morel in which he demonstrated that superficial incisions in the cortex could reduce seizure propagation while preserving function. This followed recognition that the anatomical organisation of the cortex was vertically oriented, while spike propagation occurred horizontally. In addition, intragyrus incisions in the cortex had been shown to preserve the vascular supply, thus preserving function. A critical volume of cortex was also shown to be necessary for spike generation.

Multiple subpial transection is a technique advocated for the palliation of seizure generation and propagation within eloquent cortex, with the objective of maintaining anatomical function while reducing epileptogenesis. It is frequently used in conjunction with wider resections which makes an accurate assessment of outcome following multiple subpial transection difficult. There are a few specific indications including Landau-Kleffner syndrome in children in whom, following demonstration of a predominant epileptogenic focus following a methohexital suppression test, multiple subpial transection may result in improvement in both language, communication and behaviour.

## **Exploratory and future techniques**

### *Gamma knife surgery*

Following on from the 'proof of concept' that selective procedures on the medial temporal lobe could be effective in the surgical management of epilepsy, Regis has pioneered the concept of creating a stereotactic radiosurgical lesion to the amygdala and hippocampus instead of performing a resection. Increase in efficacy comparing doses of 20 and 24 Gy has been demonstrated, with a two-year seizure-free outcome similar to resection reported in a carefully selected cohort. The theoretical benefits are that the patient avoids an open surgical procedure and that the psychological/psychiatric consequences may be less. These must be balanced against the risk of post-procedure swelling, delay to seizure freedom, increase in

simple seizures one year following treatment, and reported increase in visual field deficits and the unknown long-term risk of radiation. The ROSE study, a randomised multicentre trial, is presently taking place comparing surgery and gamma knife in medial temporal lobe epilepsy. Other forms of anatomical lesioning, such as with a laser, are presently being investigated. The advantage of these techniques is their immediate effect.

#### *Neuropace RNS™*

The RNS neurostimulator is a programmable, battery powered, microprocessor-controlled device that delivers a short train of electrical pulses to the brain through implanted leads. The stimulator is designed to detect abnormal electrical activity in the brain and respond by delivering electrical stimulation to normalise brain activity before the patient experiences seizure symptoms. The neurostimulator is implanted in the cranium and connected to one or two leads that are implanted near the patient's seizure focus. The device monitors the patient's electrical activity by connection to an implanted strip electrode on the brain surface. In theory the device can be taught to recognise the onset of a patient's seizure and the data from its phase III study is presently under review by the FDA.

### **Paediatric epilepsy surgery**

The role and importance of the multidisciplinary meeting in determining surgical suitability and surgical strategy has already been stressed. In the case of children this means that neurophysiologists, neuropsychologists, neuropsychiatrists, and neurologists must have specific experience in managing children with intractable epilepsy. A dedicated paediatric service is also vital in the peri and post-operative periods. Surgery should be carried out in a paediatric centre and, to ensure the safety and well-being of the patient, the services of a paediatric neuro-anaesthetist are paramount. There are very specific anaesthetic requirements, particularly when electrocorticography is required, and the anaesthetic technique employed should be carefully selected.

Furthermore, when dealing with cortical dysplasia, blood supply to the dysplastic area may be extremely abnormal with intra-operative blood loss becoming a critical issue. This is the case particularly in patients with hemimegalencephaly, in whom the dysplastic hemisphere may have a grossly disorganised blood supply and venous blood loss during the procedure can pose a very significant hazard.

Many patients with severe, refractory epilepsy suffer from delayed neurological development and also impaired psychosocial adaptation and behaviour. For this reason many patients undergoing epilepsy surgery remain in the care of the paediatric epilepsy services despite being above the age of sixteen. The skills of the paediatric team are therefore also of benefit to young adults. Sympathetic management from a medical and nursing standpoint is essential to ensure that the experience of the hospital admission and surgical intervention is as smooth and as atraumatic as possible.

### **Surgical follow-up**

There are many facets of outcome from epilepsy surgery; seizure control, neuropsychological development, neurological deficits, quality of life and psychosocial adjustment. It is regrettable that many publications address the outcome following surgery after only a very short time. Long-term studies of all patients are required, with a follow-up of at least two years. It is also important to realise that seizure status may not necessarily indicate a good outcome, and quality of life measurements are increasingly used to determine the efficacy of surgical intervention. Some patients with long-standing epilepsy will have few improvements in their quality of life. Over time epilepsy affects a patient's pattern of behaviour and also their social interaction; and these effects may be irreversible. This would suggest that earlier

surgical intervention may be beneficial. Since we are increasingly able to detect epileptogenic lesions in children and predict patterns of clinical progress, this will without doubt lead to increasing emphasis on surgery in childhood.

### **Suggested reading and reference books**

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