

Multi-lobar resection for extensive epileptogenic lesions.



Submitted for MCh Neurosurgery

By

Dr. Bhaumik Prabhatsinh Thakor

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Department of Neurosurgery

Sree Chitra Tirunal Institute for Medical Sciences & Technology

Thiruvananthapuram – 695011

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CERTIFICATE

This is to certify that the thesis entitled “Multi-lobar resection for extensive epileptogenic lesions” is a bonafide work of **Dr.Bhaumik Prabhatsinh Thakor** and was conducted in the Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram (SCTIMST), under my guidance and supervision.

Dr. Suresh Nair N.

Professor and Head

Department of Neurosurgery

SCTIMST,

Thiruvananthapuram.

DECLARATION

This thesis titled “Multi-lobar resection for extensive epileptogenic lesions”, is a consolidated report based on a bonafide study of the period from January 2003 to December 2012, done by me under the Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

This thesis is submitted to SCTIMST in partial fulfillment of rules and regulations of MCh Neurosurgery examination.

Dr. Bhaumik Prabhatsinh Thakor,

Department of Neurosurgery,

SCTIMST,

Thiruvananthapuram.

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Introduction

Surgical treatment for medically intractable epilepsy is currently a well established treatment modality. The rationale of curative surgical procedures aiming at control of focal drug-resistant epilepsy is total inactivation (by resection or disconnection) of the epileptogenic zone (EZ), that is, the cortical region of onset and early spread of an ictal discharge. Considering the dynamic features of an ictal discharge, and therefore its spatial–temporal structure, it is not surprising that in a number of patients the EZ may not be localized within the anatomic limits that mark the boundaries between the cerebral lobes. Moreover, the extension of an anatomic lesion that may correlate with seizures does not necessarily correspond to that of the EZ. Indeed, lesions limited to a single lobe may be associated with a multilobar EZ; in addition, anatomic abnormalities as wide as an entire hemisphere may be observed in patients with an EZ involving only a portion of a single lobe.

Epilepsy involving more than one lobe is much more common in children than adults in whom lobar epilepsy dominates.

Multilobar resections are indicated for the control of pharmacologically refractory seizures in the presence of epileptogenic zones that affect more than one lobe of the brain in patients with some preserved neurologic function. The extent of the pathologic process responsible for the seizures or the wish to spare some function guides the extent of the resection and the decision between multilobar resection and hemispherectomy. Preserving residual functions while resecting the epileptogenic zone can be challenging. The objective was to study the effectiveness of such resections.

Review of literature

Resective extratemporal epilepsy surgery in general and multilobar resections in particular constitute a very small fraction of the total resective surgeries. The most recent multicenter source of information regarding current practice patterns of major epilepsy centers comes from a seven-center prospective observational study of resective epilepsy surgery. In this study, which included 355 patients at 1-year follow-up and 339 patients at 2-year follow-up, only 12% of the epilepsy surgery patients underwent extratemporal surgery^{1,2}.

In a review of 708 epilepsy surgeries at a major epilepsy surgery center in Germany, 429 of which were therapeutic, 35% of the therapeutic surgeries were extratemporal and consisted of frontal resection in 14%, parietal resection in 2%, occipital resection in 3%, multilobar resection in less than 1%, callosotomy in 8%, and hemispherectomy in 8%³.

Based on these and other studies, it is clear that temporal lobe epilepsy surgery, especially medial temporal lobectomy, is much more common than extratemporal lobe epilepsy surgery. There are several probable reasons for this discrepancy, including a higher incidence of medial temporal lobe epilepsy that is intractable, better seizure-free rates with medial temporal lobe resection than with extratemporal resection, and frequently, more diffuse or obscure extratemporal seizure foci necessitating a more tailored approach for extratemporal resection and requiring additional evaluation for determination of the exact seizure location, often with surgically implanted electrodes.

PATHOLOGIC SUBSTRATES

The pathologic substrates underlying multilobar epilepsy syndromes are important in planning surgery and also influence the seizure control outcomes of patients. It is clear that the presence of a defined lesion with a pathologic substrate signifies a better prognosis and that the so-called nonlesional extratemporal epilepsy presents a more difficult challenge in epilepsy surgery. Focal abnormalities, such as tumors, vascular lesions, and some cortical abnormalities, may have relatively distinct borders that can be differentiated more easily from normal brain tissue intraoperatively. Such differentiation facilitates identification of the epileptogenic substrate and complete removal of the entire abnormality.

Neoplastic lesions

Rani et al⁴ in their study including 63 patients undergoing multilobar resections had found neoplasms to be responsible for the syndrome in 8% of the patients.

In general, epileptogenic tumors occur in young people, are slow growing, and involve the cortical gray matter. These tumors can be addressed best with an extended lesionectomy in an effort to remove the tumor and its margins in the surrounding brain. As long as the entire lesion with margins is removed, the seizure-free outcome after resection of neoplasms is likely to be good. Surgical outcome depends on the extent of resection. Partial resections of neoplasms usually yield a poor seizure outcome, and the best results are achieved with initial complete resection of the lesion and surrounding margins⁵. There are differing opinions in the literature regarding the benefit of resection of additional contiguous tissue based on electrocorticography^{6,7}

Gliosis

Many of the gliotic lesions, including posttraumatic, postischemic, and postinflammatory pathologies are related to perinatal or birth trauma or anoxia. Improvements in obstetric care have contributed to the decreasing incidence of these pathologies in modern epilepsy surgery series. Gliotic lesions remain a significant cause of epilepsy, however, particularly in the pediatric population. Seizures resulting from gliotic lesions can be difficult to control surgically.

Rani et al⁴ in their study had observed encephalomalacia due to trauma or infarct in 24 of 63(38%) of the patients. Leiphart et al⁸ observed 30% of pathologies to be gliotic/atrophic in their series on pediatric patients

Developmental lesions

Abnormalities in neuronal migration and development are increasingly being recognized as a cause of intractable epilepsy. With modern neuroimaging, some of these lesions can be identified and treated surgically. The most common developmental abnormality underlying seizures is cortical dysplasia. Other common developmental abnormalities include polymicrogyria and other cortical gyral malformations. Tuberous sclerosis and heterotopias have also been reported as lesions underlying epilepsy. Developmental lesions are seen more commonly in pediatric epilepsy patients.

This group of pathologies does not demonstrate as high seizure-free rates as the other categories, and this can be attributed to the diffuse nature of developmental pathologies, which do not have distinct borders and often have more widespread subtle abnormalities in neuronal migration and neuronal activity throughout the brain⁹. In one epilepsy surgery series looking

only at outcomes after resection of focal cortical dysplasia, there was a high seizure-free rate of 72%, whereas multilobar patients with more widespread disease had worse outcomes¹⁰.

The most common etiologies for the epilepsy included MCDs in 46% in Rani et al's⁴ study including both adults and pediatric patients. The pathology for the multilobe resections was 55% cortical dysplasia in Leiphart et al's⁸ series.

Others

Other pathologies include vascular lesions, inflammatory and infective lesions, cryptogenic(normal tissue). Amongst the vascular lesions cavernoma, AVM, Sturge Webber syndrome are the most common causes of intractable epilepsy. Sturge Webber syndrome in particular tends to involve a large portion of the hemisphere.

LOBAR DISTRIBUTION OF MULTILOBAR EPILEPSY

The more common multilobar resection patterns are frontal-temporal, frontal-parietal, and temporal-occipital. In Leiphart et al's⁸ series temporo-parieto-occipital resections constituted 46 % of the resections. In Rani et al's⁴ series Occipital plus (TPO, PO, TO), FT,TP,FP resections constituted 57%,21%,17%,5% of the resections respectively.

PRE OPERATIVE EVALUATION

Because extratemporal lobe epileptic foci in general are difficult to localize by semiology or scalp EEG, other ancillary techniques are required to obtain a concordant assessment of localization of the seizure focus for resection, particularly in the absence of a

distinct structural abnormality on MRI. In many cases, invasive monitoring with intracranial electrodes is required. As part of the presurgical evaluation, three questions need to be answered:

- (1) is there a structural substrate for the disease?
- (2) are there physiologic markers for the zone that need to be removed?
- (3) are there functional constraints to removal of the epileptogenic focus?

History and physical examination

Specific auras such as experiential phenomena and somatomotor or somatosensory experiences may implicate specific areas of the brain. Symptoms at seizure onset, during progression, and after completion of the seizure can also offer lateralizing and localizing clues.

Important features found on physical examination may include stigmata of a neurocutaneous syndrome such as tuberous sclerosis or neurofibromatosis; asymmetry of the size of the face, hand, or fingernails, which implies an insult to the contralateral hemisphere early in life; focal findings on neurological examination.

Two or more fundamentally distinct semiologies should alert one to the possibility of multifocal epilepsy.

Scalp electroencephalography

Routine EEG findings are positive in 50% to 60% of patients with epilepsy, and the yield is increased by repeated or prolonged recordings that sample drowsiness and sleep. Even though focal slowing may signify an underlying structural abnormality, the major utility of routine EEG recordings is in the identification of interictal epileptiform discharges (IEDs) (sharp waves, spikes, or spike and wave complexes)¹¹

Video EEG

The goals of video-EEG recording are threefold:

- (1) to further characterize the interictal EEG recording;
- (2) to detect, characterize, and quantify the patient's habitual seizures¹² and
- (3) to acquire physiologic data regarding seizure localization that can be correlated and compared with anatomic data obtained from neuroimaging studies.

These investigations typically occur over a 5- to 7-day inpatient hospital stay (for adults) but are obviously dependent on seizure frequency and last as long as required to capture a satisfactory number of seizures^{13,14}

Characterizing the patient's seizures is crucial because it allows

- (1) correlation of the ictal behavior with the electrographic discharge,
- (2) establishment of whether a patient has more than one seizure type, and
- (3) lateralization (which hemisphere) and localization (which area of the hemisphere) of the onset of seizures and therefore identification of the EZ.

Typically, activating procedures such as sleep deprivation are used in addition to reduction or cessation of antiepileptic drugs in an attempt to increase the likelihood of seizure occurrence.

Imaging

MRI

The use of 3-T MRI and surface coils has made identification of a lesion underlying an epileptic focus 2.57 times more likely^{15,16}, and new quantitative techniques have made lesion characterization more accurate in terms of the underlying histopathology¹⁷. Localized, well-

circumscribed lesions on MRI, whether contrast-enhancing or signal abnormalities on T2-weighted or fluid-attenuated inversion recovery (FLAIR) images, delimit the target of resection, are associated with a higher occurrence of EEG focality¹⁸, and signify a greater possibility for postoperative seizure control. FLAIR imaging can be particularly useful and should be part of the routine epilepsy MRI protocol^{19,20}

More diffuse lesions have a lower chance for postoperative seizure control⁸ and the absence of a lesion on MRI denotes a poorer prognosis for seizure control with surgery (44% seizure free in one study^{21,22,23}).

Three-dimensional reconstructions of CT and magnetic resonance angiographic images can now be fused with three dimensional reconstructions of MRI in the frameless stereotactic system for more accurate representation of vascular structures in relation to cortical anatomy. Careful three-dimensional reconstructions of the cortical surface can reveal surface abnormalities associated with developmental lesions.

Imaging of the brain with invasive monitors in place can also be fused with the preoperative MRI to provide exact localization and verification of electrode placement²⁴.

Other Imaging modalities

Fluorodeoxyglucose F 18 PET

It identifies areas of cortex with abnormal metabolic activity. Interictally epileptogenic zones tend to be hypometabolic relative to normal cortex^{25,26}. PET has proved most useful in the evaluation of mesial temporal lobe epilepsy²⁷, but it can also help delineate extratemporal epileptic foci and verify the likely epileptogenicity of structural lesions seen on MRI.

SPECT

When used in the ictal state and compared with the interictal state, it may show a significant seizure focus in which enhanced neuronal activity results in increased blood flow^{28,29}. This technique has proved especially useful in tandem with coregistration to MRI (subtraction ictal SPECT coregistered to MRI [SISCOM])^{30,31,32}. Hypoperfusion on interictal SPECT can verify the epileptogenicity of certain foci identified on MRI, such as areas of cortical dysplasia³³. However, the disadvantage of ictal SPECT is that because of its inability to differentiate which region of activation occurred first, it can point to activated propagation pathways that do not need to be surgically removed to alleviate seizures³⁴. Although ictal SPECT has proved useful in the localization of extratemporal epileptic foci^{35,36}, interictal SPECT has not³⁷.

Magnetic source imaging

Magnetoencephalography

MEG uses superconducting quantum interference device magnetometers to detect the magnetic fields associated with intraneuronal electrical currents. The magnetic field, which can indicate the epileptic focus, is not attenuated or distorted by the overlying skull and scalp as in scalp EEG, thus increasing the accuracy of localization without resorting to invasive EEG monitoring. Magnetic source imaging is most useful for neocortical epilepsy³⁸ and correlates with intracranial recordings in the majority of cases³⁹. MEG can be helpful in identifying a seizure focus when MRI appears normal, and clustering of the MEG signal in the subsequently resected region can predict effective postoperative seizure control⁴⁰. In difficult cases requiring implantation of depth electrodes for evaluation of seizures, magnetic source imaging can be used

to focus placement of the intracranial electrodes in a particular region suspected of epileptogenesis.

MRS

It depicts the relative distributions of various chemicals in selected areas of the brain. MRS can be used to localize extratemporal seizure foci in patients with negative MRI findings⁴¹.

fMRI

fMRI is useful in the delineation of functional cortical anatomy for frontal lobe epilepsy resections that include motor and speech areas⁴². Although the clinical utility of fMRI activation outside the rolandic cortex is controversial⁴³, it provides a noninvasive preliminary to intraoperative mapping that can avoid craniotomy in patients in whom the deficits would be unacceptable. It is useful in determining hemispheric language dominance and it correlates well with results obtained by the Wada test⁴⁴.

Simultaneous EEG recording and event-related fMRI allow the linking of epileptiform activity with local hemodynamic changes in the brain.

Neuropsychological testing

It can be judiciously used as a confirmative tool in the presurgical evaluation. Preoperative neuropsychological testing is important to describe the current cognitive and behavioral functioning in the context of the seizure disorder and underlying neuropathology, to start interventions for cognitive and behavioral difficulties if present, and for postoperative prognosis, both for seizure-free outcome and for neuropsychological deficits^{45,46,47}.

Some epilepsy surgery centers use neuropsychological testing to aid in localization and lateralization⁴⁸, although neuropsychological findings alone are not reliable for the lateralization of seizure foci⁴⁹.

Wada test

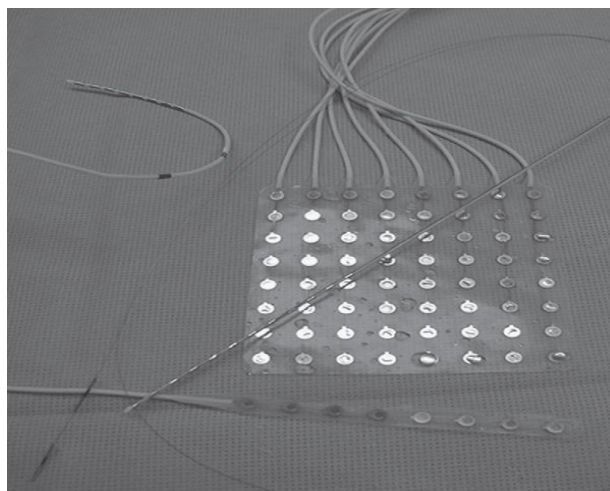
The patient's language and memory functions are tested during injection of a barbiturate into one cerebral hemisphere to block function on that side, and the test is sometimes repeated with injection on the other side. A review of 1421 Wada tests suggested that the test has high reliability and validity for language lateralization but does not have as high reliability or validity for memory lateralization⁵⁰. For extratemporal epilepsy, the memory part of the Wada test is less important. Establishing the side of language dominance is crucial, however, in planning frontal lobe and parietal lobe epilepsy surgery.

Invasive electrode monitoring

Invasive monitoring with surgically implanted electrodes is frequently necessary for more accurate localization of the epileptic focus than can be provided by scalp EEG, especially with extratemporal lobe epilepsy⁵¹. They are especially helpful in the evaluation of mesial temporal lobe epilepsy syndromes or when patterns of spread from an extratemporal focus may involve the mesial temporal lobe rapidly⁵². The use of depth electrodes in patients with suspected extratemporal lobe epilepsy is supported by a study showing that 25% of these patients will be found to have mesial temporal foci rather than extratemporal foci⁵³. Depth electrodes have a remarkably low complication rate, with a 2.4% infection rate, a 0.6% hemorrhage rate, no neurological deficits, and no deaths in one series in which there was an 85% rate of determining

a surgically amenable seizure focus⁵⁴. Subdural grid and strip electrodes are surgically placed in direct apposition to the cortex, either through bur holes or by craniotomy. Grid electrodes are especially useful in extratemporal lobe epilepsy because they provide sampling of cortical activity over the cerebral convexities and make recording from more extensive territories possible. The advantage of subdural grids is that they enable detailed sampling of a cortical region in terms of seizure activity, along with functional mapping via electrical stimulation⁵⁵. Subdural electrodes alone appear to be preferable for the evaluation of frontal or multilobar seizure onset, whereas combined subdural and depth electrodes seem to be better for the evaluation of patients with dual pathology consisting of epileptic foci in both a neocortical region and the mesial temporal lobe⁵⁶.

Invasive monitoring can also be performed in the epidural space with the use of grid or peg electrodes. Epidural peg electrodes are surgically implanted in small holes drilled into the skull such that they rest against the dura mater. They do not provide the same level of sensitivity or accuracy as depth and subdural electrodes, but they are useful in situations with significant subdural scarring in patients who have had previous surgery or trauma.



Intracranial monitoring hardware

SURGERY

Goals of surgery

Multilobar resection aims at achieving complete cessation of seizures or significant improvement in seizure frequency without producing neurologic deficits. Most widespread lesions responsible for seizure disorders are static and thus do not require surgery to alter their natural course. Atrophic, porencephalic, and dysplastic lesions are not by definition progressive disorders. However, these static lesions may indirectly interfere with brain function through mechanisms of secondary epileptogenesis⁵⁷

On the basis of these mechanisms, another goal of multilobar resections may be to prevent further brain damage. The ultimate goal of the surgery should be to improve psychosocial functioning and thereby promote a better quality of life.

Surgical technique

Rasmussen⁵⁸ stressed two important technical aspects of the resection strategy:

- (a) Subpial removal along sulci to leave the removal cavity lined by untraumatized pial-covered gyri and
- (b) Avoidance of movement of the underlying white matter during the cortical excision to minimize risk of injury.

The supine position is usually preferred even when surgery is performed on the posterior portions of the hemisphere, with the operating table being tilted and the head rotated to obtain comfortable access to the surgical field. The prone position is used mainly when surgery involves the mesial aspects of the parietal or occipital lobes. Both skin incision and bone flap are

designed to fully expose the region to be removed, as well as the surrounding cortical areas. In some instances, when a two-step procedure is likely, the surgeon must take into account the possible subsequent step when fashioning skin and bone flaps. While opening the dura mater, if an SEEG has been previously performed, care should be taken to separate the adhesions between the inner aspect of the dura and the cortical surface at the electrode entry points.

Neuronavigation is helpful in optimizing accuracy and safety of the procedure, and it is routinely used in some centres. With the aid of the surgical microscope, resection is accomplished according to a few simple rules:

- Vessels that cross the region of resection but are tributaries of, or draining from, regions outside its borders must be identified on the stereoscopic angiograms, isolated, and left intact.
- Subpial dissection should be preferred, especially in mesial regions and along the main fissures, to protect vascular and extra-axial nervous structures (e.g., those in the prepuncular cistern during mesial temporal removal).
- Suction and bipolar coagulation should be avoided to obtain as many unaltered tissue specimens as possible available for histopathologic evaluation.

Unlike the case of hemispherectomy, intraoperative attention to preservation of function is essential. When a less than maximal hemiparesis is present, the arm and leg area of the sensorimotor gyri should be preserved. If a useful visual field is present, the posterior parietotemporal and occipital regions should also be preserved. During surgery, somatosensory evoked potentials and motor-evoked potentials can be used to delineate the sensorimotor cortex, which can then be left intact. Preoperative investigations localizing the epileptogenic area should be available in the operating room, so that the intraoperative findings can be correlated with

those obtained preoperatively. Some surgeons have also used intraoperative electrocorticography to further define the margins of the multilobar resection.

At dural closure, intravenous phenytoin (10-15 mg per kilogram of body weight) is administered over a 20-minute period. At the end of surgery, the patient is moved to the intensive care unit (ICU) and anesthesia is progressively tapered. Habitual oral antiepileptic medicaments are given as soon as the patient can safely swallow

Complications

The anatomofunctional basis of morbidity in multilobar resections does not differ substantially from that of unilobar resections, and it strictly depends on the site of surgery. Morbidity may include transient motor impairment, akinesia and mutism after removal of the supplementary motor area⁵⁹, transient speech disturbances following resections involving the neocortex of the dominant temporal lobe, and contralateral superior quadrantoanopia in anterior temporal lobectomies. The risk of larger contralateral visual field defects is higher following resections in the posterior portion of the hemisphere. When removal is contiguous to the rolandic region, the risk of motor–sensory impairment is usually increased, and functional mapping by either intracerebral electrical stimulations at SEEG or functional MRI or intraoperative cortical and subcortical electrophysiologic evaluation is helpful to minimize the chances of unwanted postoperative deficits.

OUTCOME

Results on seizures of multilobar surgery are far less gratifying if compared to other unilobar resections^{10,60,61,62,63,64,65,66}.

Slightly better results are observed in multilobar resections, including the temporal lobe. However, it must be stressed that, despite a complex epileptologic situation that could hardly be improved by further drug regimens, a substantial number of patients can be cured or improved by surgical treatment.

Aims and objective

Neurologic function can coexist with extensive epileptogenic zones within an affected hemisphere. Preserving residual functions while resecting the epileptogenic zone can be challenging. The outcome and effectiveness of such resections are studied.

Material and methods

Patient selection

A retrospective data review of consecutive patients undergoing multi-lobar resections at Sree Chitra Tirunal Institute for Medical Sciences and Technology from 2003 until 2012 was performed. Hemispherectomies and hemispheric disconnections were excluded from this study. Only patients who had at least one year follow up were included.

Preoperative evaluation

Routine preoperative work up included detailed history and neurological examination, neuropsychological and speech assessment, neuro-imaging studies, scalp EEG, video EEG, and visual field charting. In addition functional imaging and the Wada test were performed in a select group of patients. Invasive monitoring with subdural and intra-parenchymal electrodes was reserved of patients who had dual pathology, extension of the lesion into eloquent cortex, or who had an unclear ictal onset zone.

Post operative follow up

Patients were followed up in the outpatient department at regular intervals.

Seizure outcome

Seizure outcome was assigned according to Engel⁶⁷ classification scheme.

Class I: Free of disabling seizures

Class II: Rare disabling seizures (“almost seizure free”)

Class III: Worthwhile improvement

Class IV: No worthwhile improvement

Engel score I and II were considered good outcome.

Statistical analysis

Fischer's exact test was used for statistical analysis. A p value of less than 0.05 was considered significant.

Results

Patient characteristics

Of a total of 60 consecutive patients who underwent multi-lobar resections from 2003 until 2012, one patient was excluded for statistical analysis, as the patient had expired before completion of one year of follow up.

Of the 59 patients in the study sample, 39 were male and 20 were female. The mean age of the patients at surgery was 17 years.

The average duration of seizures before surgery was 12 years and 6 months. Seizure semiology consisted of complex partial seizures in all the patients. Seizures were lateralized to the right hemisphere in 32 patients and to the left hemisphere in 27 patients.

On examination 8(13.55%) patients had baseline visual field deficits, while 23(38.98%) patients had motor or sensory deficits. (Table 1)

Table 1. Patient characteristics

Variable	No.(%)
Total	59
Male	39
Female	20
Mean age(years)	17
Mean duration of seizures(years)	12.5
Seizure lateralization	
Right	32
Left	27
Pre-operative deficits	
Visual field	8(13.55)
Motor/sensory	23(38.98)

Follow up

The mean follow up was 41 months with a range of one year to 9 years. All the patients had at least one year follow up, while 18 patients reached a follow up period of 5 years or more. None of the patients were lost to follow up.

Antecedents

18 out of 59(30.5%) patients had antecedents, which would have contributed to their syndrome. Five patients had a history of intracranial hemorrhage, five patients had hypoxic insult, two patients had suffered encephalitis, two patients had history of febrile seizures, two patients suffered neonatal hypoglycemia. There was one case of meningitis, while one patient had a family history of seizures .

Surgery

31 patients (52.54%) underwent posterior resection defined as behind the sensory cortex, 9 patients (15.25%) underwent anterior resection defined as anterior to motor cortex, while 17 patients (28.81%) underwent combined resection preserving the central area(Table 2). Two patients (3.39%) underwent centro-parietal (motor sensory) resection.(Images1-3).

Table 2. Types of Surgery

Surgery	n(%)
Posterior resection	31(52.54)
Anterior resection	9(15.25)
Combined anterior and posterior	17(28.81)
Centroparietal	2(3.39)

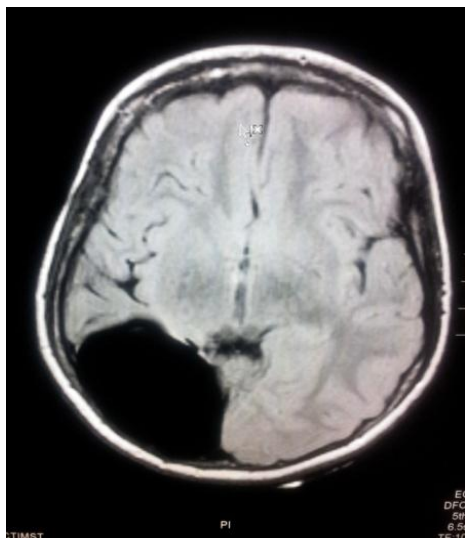


Image 1. Right posterior quadrantectomy

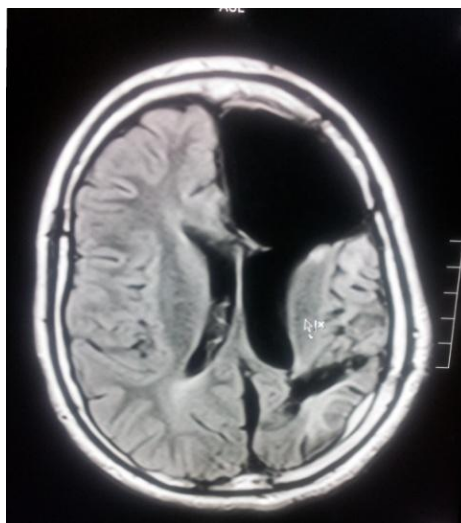


Image 2. Left frontotemporal lobectomy

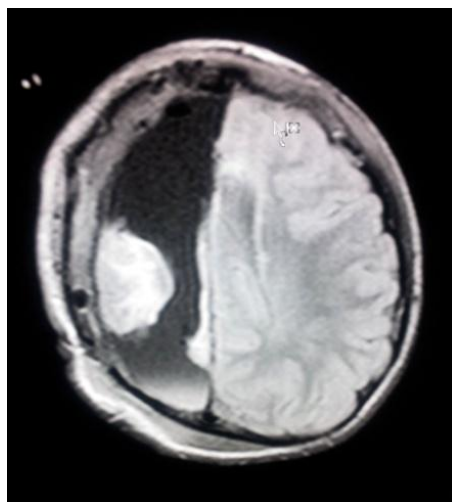


Image 3. Motor sensory cortex preserving combined resection

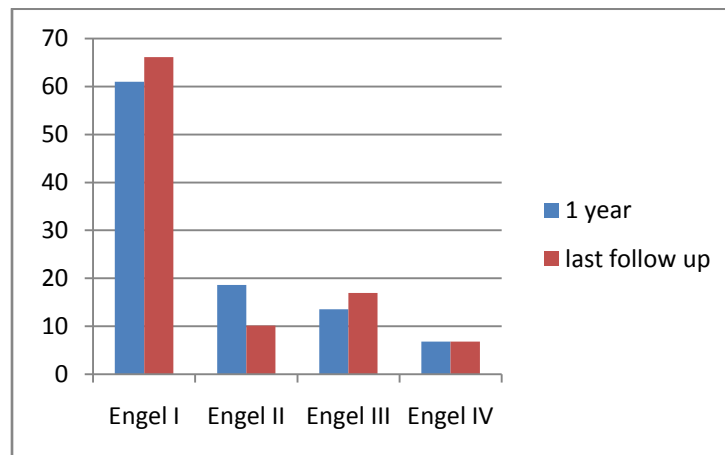
Seizure outcome

Seizure outcome was measured at 1 year and at last available follow up.. At one year follow up good outcome (Engel I and II) was achieved in 79.66 percent of patients. At their last follow up good outcome was achieved in 76.27% patients. 10(16.94%) patients had Engel score III , while 4(6.78%) patients had Engel score of IV at their last follow up. Table 3 and figure 1 show the seizure outcome.

Table 3. Seizure outcome

Engel class	1 year n(%)	Last follow up n(%)
I	36(61.01)	39(66.1)
II	11(18.64)	6(10.16)
III	8 (13.55)	10(16.94)
IV	4 (6.78)	4(6.78)

Figure 1



Good seizure outcome was achieved in 77.77% of patients aged 18 years or less compared to 73.91% of those aged above 18 years (Table 4).

Table 4. Age wise outcome

Age	Good outcome	<i>p</i>
<18 years	28/36(77.77)	0.9689
>18 years	17/23(73.91)	

10(16.94%) patients were off anticonvulsants at their last follow up, 24(40.67%) patients had reduced anticonvulsants, 16(27.11%) patients remained on same number of anticonvulsants, while 9(15.25%) patients were on increased number of anticonvulsants.

Reexploration

Five patients underwent reexploration due to poor seizure outcome. One patient with a right parieto-occipital focal cortical dysplasia underwent a repeat surgery. Imaging studies had shown a suspicious residual lesion. The patient had an unfavorable (Engel IV) seizure outcome following second surgery.

Three other patients had shown residual lesion on imaging. Of the three, one patient had low grade tumor, one had residual focal cortical dysplasia, while the third patient had a residual cavernoma. Following second surgery all three had a good seizure outcome.

The fifth patient had undergone excision of low grade tumor during the first surgery. Post operative imaging done after seizure recurrence had shown an adjacent area of encephalomalacia. Following the second surgery the patient had a favourable seizure outcome.

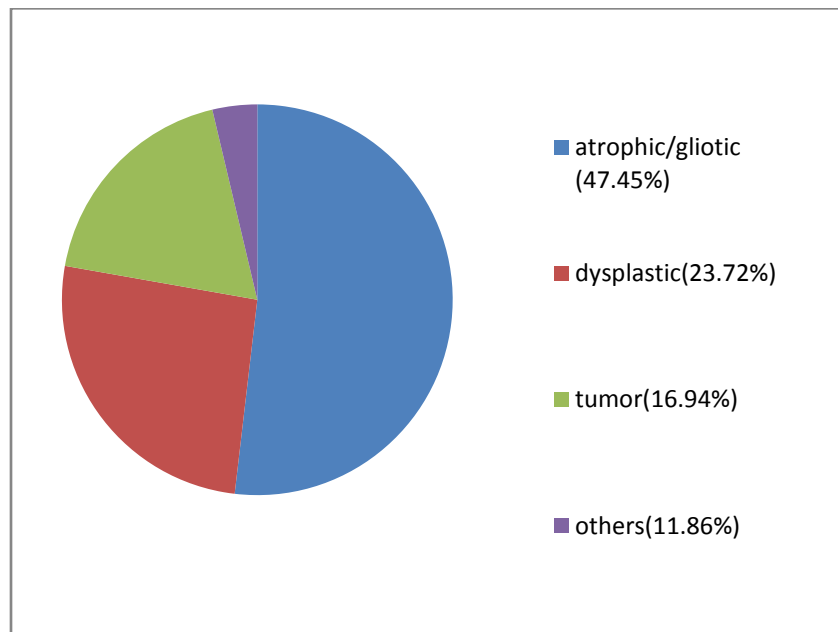
Pathology

Twenty eight(47.45%) lesions were atrophic or gliotic. There were 14(23.72%) dysplastic lesions. Ten(16.94%) patients had low-grade neoplasm. There were 2(3.39%) granulomas and 5(8.47%) vascular lesions in the series. The seizure outcome by pathology is shown in table 5. The pathology wise distribution is shown in figure 2.

Table 5. Seizure outcome by pathology

Pathology	Good outcome (%)	<i>p</i>
Atrophic/gliotic	71.42	0.5996
Dysplastic	71.42	0.8719
Tumor	90	0.4965
Granuloma	100	1.0000
Vascular	80	1.0000

Figure 2.Pathology



Seizure outcome by type of surgery

Type of surgery did not make a significant difference to the seizure outcome, as shown in table 6.

Table 6. Seizure outcome by type of surgery

Surgery type	Good outcome(%)	<i>p</i>
Posterior resection	74.19	0.9322
Anterior resection	77.77	1.0000
Combined resection	76.47	1.0000
Centroparietal resection	100	1.0000

Early post operative seizures

Early post operative seizures were defined as those within the first month of surgery. 23 patients (38.98%) had early post operative seizures, of which 7 patients (30.4%) were seizure free at their last follow up. Of those who did not suffer early post operative seizures , 88.9% were seizure free at their last follow up.(Table 7)

Table 7. Early post operative seizures

	Seizure free(%)	<i>p</i>
Early post op seizures (n = 23)	30.4	0.00001
No early seizures (n = 36)	88.9	

Invasive monitoring

Eight patients underwent invasive monitoring prior to surgery. Four patients had a good seizure outcome while 4 had unfavourable outcome.

Post operative complications

One patient died at a local hospital six months after the surgery. None of the patients developed new or worsened motor or sensory deficit. One patient suffered motor aphasia which had improved significantly at the last follow up. Twelve (20.33%) patients developed fresh visual field deficits. There was one case of wound infection, one case of CSF leak through the wound, one case of deep vein thrombosis and one instance of meningitis which resolved with adequate treatment.

Discussion

The burden of disease experienced by patients with drug resistant epilepsy may be due to the direct effects of the seizures, epileptic encephalopathy or side effects of antiepileptic medications.

Very often the ictal onset zone spans more than one lobe. Seizure outcome following temporal lobectomies, and extratemporal unilobar resections have been well described in the literature. Studies on multilobar resections have been rare, and the majority of the available data is derived from series on extratemporal resections. The focus of our study is solely on multilobar resections in both children and adults.

Seizure outcome

Good seizure outcome (Engel class I and II) of 76% at the last follow up seen in this series is comparable to 73% good outcome in series with a similar follow up period⁶⁸ though its cohort consisted of children and adolescents alone. Total seizure freedom (Engel class I) of 66% noted in this study is comparable or better than that achieved in other similar studies^{4,61,66,69,70,71}. Wyllie et al.⁶⁸ achieved a seizure free outcome in 54% of children and adolescents with multilobar resections. Hemb et al.⁷⁰ achieved a similar seizure free outcome of 55% at 2 years follow up. Rani et al.⁴ achieved a seizure free outcome of 52% in their series which included both adults and pediatric patients. Table 8 summarises the seizure outcome of some of the recent studies.

Table 8. Comparison between studies

	SCTIMST	Wyllie⁶⁸	Rani⁴	Hemb⁷⁰
Number	59	48	63	51
Follow up(yrs)	3.5	3.6	4.6	2
Engel I(%)	66.1	54	52	54.9
Engel II(%)	10.16	19		
Cohort	Pediatric and adults	Pediatric and adolescents	Pediatric and adults	Pediatric

Early post operative habitual seizures have been associated with a worse outcome in our study. Twenty three out of 59 patients had early post operative seizures, of which 7 patients (30.4%) were seizure free at their last follow up. Of those who did not suffer early post operative seizures , 88.9% were seizure free at their last follow up. Similar observation was made by Rani et al.⁴ in their study. The occurrence of early post operative seizure may be proposed to be linked to incomplete resection of the epileptic focus. Progression of the epileptic syndrome may be the cause of some of the late recurrences.

Seizure outcome did not differ significantly between pediatric and adult patients in our series. Longer duration of seizures and the use of anticonvulsants contribute to development deficits in children, hence an early surgery may be justified. Cossu et al⁷² compared outcome in children younger than 12 years and above 12 years .They did not find age to be an outcome determining factor, though their cohort included both uni-lobar and multi lobar resections.

Need for preoperative invasive monitoring did not make any difference in the seizure outcome in our study. Because invasive monitoring is usually reserved for cases where seizure localization is ambiguous, one might expect that the eventual outcome of epilepsy surgery in

these patients would be worse than in patients who did not require invasive monitoring as part of their work up. Good results from eventual resective surgery can be achieved in patients needing invasive recordings as shown by Keith et al⁷³.

Majority of the patients in this series underwent posterior resection(52.54%). However the type of resection did not influence the seizure outcome, in contrast to the observation made in Rani et al⁴ study, in which results following occipital plus resections were significantly better than the other resections.

Gliosis was the major histological substrate in both children and adults in this series. Rani et al⁴ and Cossu et al⁷² in their study found malformations of cortical development as the major histological subgroups. The outcome in our series is best for tumors(90% good outcome). The same was observed by Cossu et al⁷².

Collin C. Tebu et al⁷⁴ in a recent meta-analysis observed 5.2% rate of persistent neurological deficits among patients undergoing extratemporal and multilobar resections during the period from 1996 to 2012. Persistent neurological deficit was observed in thirteen(22.03%) patients out of fifty nine in our series. Twelve patients had visual field deficits while one had dysphasia. However we have not considered unilobar extra-temporal resections, and have focused solely on multi-lobar resections.

Predictors of outcome

Occurrence of early post operative seizures is the only factor predictive of unfavourable seizure outcome in our study. The type of resection does not affect the seizure outcome, in contrast to observation by Rani et al⁴. Multilobar resections are equally effective in both pediatric and adult age groups, irrespective of the pathology.

Limitations

One of the limitations of our study is its retrospective nature which could add to observation bias. Also a longer follow up is desirable to assess the sustainability of seizure freedom following surgery. We have not evaluated the neurocognitive aspects of the surgery, which remain an important outcome.

Conclusion

Multi-lobar resections are innovative surgical strategies to resect extensive seizure correlates while preserving neurological function in their close proximity. They are both safe and effective across all age groups and pathologic substrates.

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Annexure 1

Abbreviations

AED	:	Anti epileptic drugs
AVM	:	Arterio-venous malformation
CT	:	Computed Tomography
EEG	:	Electroencephalography
EZ	:	Epileptogenic zone
FLAIR	:	Fluid attenuated inversion recovery
fMRI	:	Functional MRI
FP	:	Fronto-parietal
FT	:	Fronto-temporal
MEG	:	Magnetoencephalography
MRI	:	Magnetic resonance imaging
MRS	:	Magnetic resonance spectroscopy
PET	:	Positron emission tomography
PO	:	Parieto-occipital
SPECT	:	Single photo emission computed tomography
TP	:	Temporo – parietal
TPO	:	Temporo – parieto – occipital
TO	:	Temporo-occipital
VEEG	:	Video Electroencephalography

Annexure 2

Proforma

1. General information

- a. Name
- b. Age
- c. Sex
- d. Address
- e. Hospital number

2. Seizure history

- a. Age of onset
- b. Frequency
- c. Duration
- d. Number of AED
- e. Antecedent history

3. MRI findings

4. VEEG localization

5. Preoperative deficits

- a. Visual field
- b. Sensory
- c. Motor

6. Invasive monitoring
 - a. Yes
 - b. No
7. Surgery
 - a. Date
 - b. Type
 - i. Anterior resection
 - ii. Posterior resection
 - iii. Combined resection
 - iv. Centroparietal
8. Post operative complications
9. Post operative deficits
 - a. Visual field
 - b. Sensory
 - c. Motor
 - d. Language
10. Histopathology report
11. Seizure outcome
 - a. One year
 - b. Five years
 - c. Last follow up
12. Number of AED at last follow up

