

# Level 4 comprehensive epilepsy program in Malaysia, a resource-limited country

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## Abstract

**Background and Objective:** There is a great challenge to establish a level 4 epilepsy care offering complete evaluation for epilepsy surgery including invasive monitoring in a resource-limited country. This study aimed to report the setup of a level 4 comprehensive epilepsy program in Malaysia and the outcome of epilepsy surgery over the past 4 years. **Methods:** This is a retrospective study analyzing cases with intractable epilepsy in a comprehensive epilepsy program in University Malaya Medical Center (UMMC), Kuala Lumpur, from January 2012 to August 2016. **Results:** A total of 92 cases had comprehensive epilepsy evaluation from January 2012 till August 2016. The mean age was 35.57 years old (range 15-59) and 54 (58.7%) were male. There were 17 cases having epilepsy surgery after stage-1 evaluation. Eleven cases had mesial temporal sclerosis and 81% achieved Engel class I surgical outcome. Six cases had lesionectomy and 60% had Engel class I outcome. A total of 16 surgeries were performed after stage-2 evaluation, including invasive EEG monitoring in 9 cases. Among those with surgery performed more than 12 months from the time of data collection, 5/10 (50%) achieved Engel I outcome, whereas 2 (20%) had worthwhile improvement (Engel class III) with 75% and 90% seizure reduction.

**Conclusion:** Level 4 epilepsy care has an important role and is possible with joint multidisciplinary effort in a middle-income country like Malaysia despite resource limitation.

**Keywords:** Epilepsy surgery, intracranial monitoring, refractory epilepsy

## INTRODUCTION

*The role of epilepsy surgery in the overall epilepsy care*

Epilepsy is the most prevalent disabling neurological disorder. One-fourth of epilepsy patients will never attain seizure freedom with pharmacotherapy alone.<sup>1</sup> These patients experience significant morbidity with increased lifetime mortality. Epilepsy surgery is now an accepted practice of management in carefully selected patients with complex focal epilepsy with a chance of seizure freedom up to 66%.<sup>2</sup>

*Specialized epilepsy centers: level 3 and 4 of epilepsy care*

Four levels of epilepsy care was proposed by the Board of the National Association of Epilepsy

Centers and revised in 2010.<sup>3</sup> First level of epilepsy care occurs at emergency department or primary care clinic. It then proceeds to the second level of epilepsy care, which is a consultation with a general neurologist or possibly an epileptologist in a specialized epilepsy center. Level 3 and 4 centers provide interdisciplinary and comprehensive approach to the diagnosis and treatment of patients especially with intractable epilepsy. A level 3 center offers noninvasive evaluation for epilepsy surgery, whereas a level 4 center offers complete evaluation for epilepsy surgery including invasive monitoring and provides a broad range of surgical procedures for epilepsy.

*Epilepsy surgery in Malaysia*

Despite the high rate of pharmacoresistance, epilepsy surgery is still underutilized in Malaysia,

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ever since its first introduction in 1996 in National University of Malaysia Medical Center (UKMMC). The first report on epilepsy surgery in Malaysia was in year 2007<sup>4</sup>, whereby decision for surgery was based on non-invasive epilepsy pre-surgical evaluation including video-EEG monitoring (VEM) and 1.5T magnetic resonance imaging (MRI) of brain. Advanced evaluation such as interictal PET, ictal SPECT and invasive electroencephalogram (EEG) monitoring were not accessible in 2007. This level of epilepsy care is categorized as level 3 epilepsy care.

*Challenges of advanced epilepsy surgery service (level 4) in a resource limited setting*

Malaysia is a middle-income Asian county with a GDP per capita of USD 10,538.<sup>5</sup> There are three key challenges in setting up a level 4 epilepsy care service in a middle-income county. Level 4 care requires specific investigation modalities, e.g. single-photon emission computed tomography (SPECT) and positron emission tomography (PET). In addition, personnel specialized in implanting invasive EEG electrodes and interpreting the results are lacking. The last challenge is the high cost of performing these advanced investigations and procedures.

This study aimed to report the setup of a level

4 comprehensive epilepsy program in Malaysia and the outcome of epilepsy surgery over the past 4 years. It provides a concrete example of how higher level of epilepsy care can be established in a middle-income Asian country.

**METHODS**

This is a retrospective study analyzing cases with intractable epilepsy in a comprehensive epilepsy program in University Malaya Medical Center (UMMC), Kuala Lumpur, from January 2012 to August 2016. Inclusion criteria are age 12 years old and above during VEM, epilepsy diagnosed for a minimum of one year, intractable to at least 2 antiepileptic drugs as defined by ILAE definition<sup>6</sup>, and have had VEM and MRI brain performed in our center.

*Comprehensive epilepsy program in UMMC (Figure 1)*

1. Case identification: Diagnosis of intractable focal epilepsy was made based on clinical and drug history, routine EEG and MRI brain findings, by a epileptologist. MRI brain was performed using a specific epilepsy protocol developed in house.<sup>7</sup> Those who fulfilled the inclusion criteria were counselled for comprehensive epilepsy evaluation.

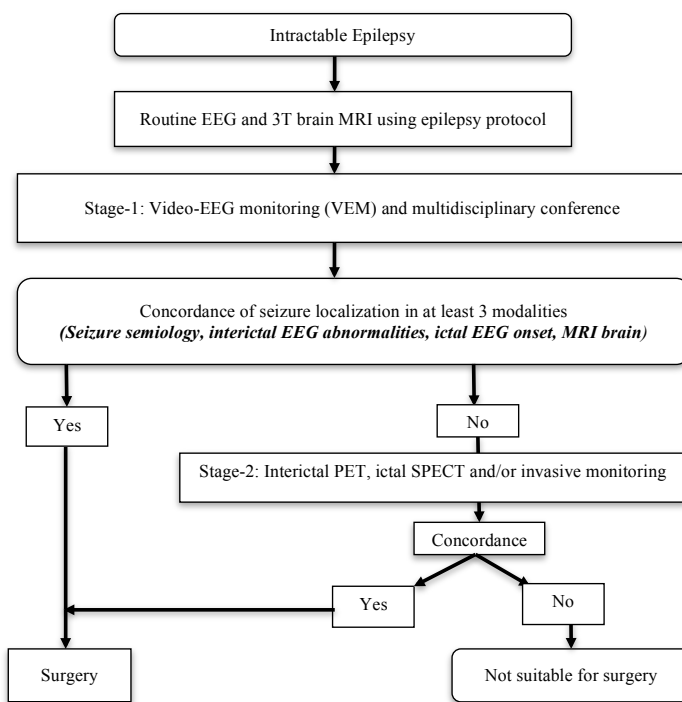


Figure 1. Comprehensive epilepsy program in University Malaya Medical Centre.

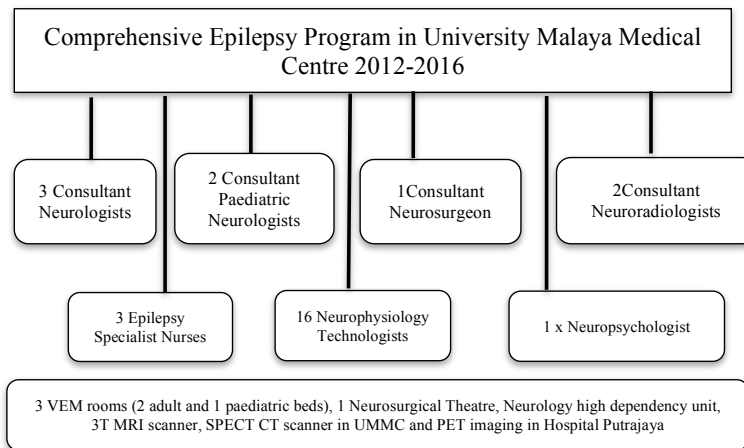


Figure 2. Members of the multidisciplinary team in the comprehensive epilepsy program in University Malaya Medical Centre.

2. Stage 1 evaluation included a 3-to-4-day video-EEG monitoring and a multidisciplinary team (MDT) conference. In the case conference, the clinical history, neuroimaging and EEG findings were reviewed and discussed by multidisciplinary team members, including neurologist, neurosurgeon and neuroradiologist, neuropsychologist, neurophysiology technologists, and epilepsy specialist nurses. (Figure 2) Patient management decision included:
  - Patient eligibility as a surgical candidate,
  - The type of surgery, i.e. curative or palliative,
  - The need for stage-2 evaluation, such as ictal SPECT, interictal PET and invasive monitoring, OR
  - Further consideration of medical therapy or ketogenic diet for non-surgical candidates
3. Stage 2 evaluation was mostly required for those with normal MRI (MRI-negative focal epilepsy) or discordant results. Stage 2 MDT conference was carried out after further evaluations, such as ictal SPECT, interictal PET and invasive monitoring, were performed. If invasive monitoring with subdural or depth electrodes was performed, there would be two additional case conferences to discuss the initial implantation plan, followed by the surgical plan post invasive monitoring. Some cases only underwent intraoperative electrocorticography (ECoG) to delineate the seizure foci.

#### Outcome measurement

Surgical outcome was determined at 12-month

post-surgery. Engel classification was used to classify surgical outcome.<sup>8</sup> Engel class I was defined as free of disabling seizures, Engel class II as rare disabling seizures, III as worthwhile improvement and IV as no worthwhile improvement. For MRI-negative cases, percentage of seizure reduction was also calculated.

## RESULTS

### *Comprehensive epilepsy program*

A total of 92 cases were identified from January 2012 till August 2016. (Figure 3) The mean age was 35.57 years old (range 15-59) and 54 (58.7%) were male. There were 33/92 (35.9%) cases identified as eligible surgical candidate after stage 1 evaluation, of which 17 were operated. A total of 43 (46.7%) were planned for stage 2 evaluation, of which 16 cases were operated.

### *Epilepsy surgery after stage 1 evaluation*

There were 17 cases having epilepsy surgery after stage 1 evaluation. (Table 1) Fourteen cases had temporal lobe epilepsy, and 3 extra-temporal lobe epilepsy. Of those, eleven had temporal lobe epilepsy (TLE) secondary to mesial temporal sclerosis (MTS), and 81% (9/11) achieved Engel class I surgical outcome. The percentage of Engel class I surgical outcome was higher with anterior temporal lobectomy (100%), as compared with selective amygdalo-hippocampectomy (60%). Six cases had lesionectomy and 3/5 (60%) had Engel class I outcome.

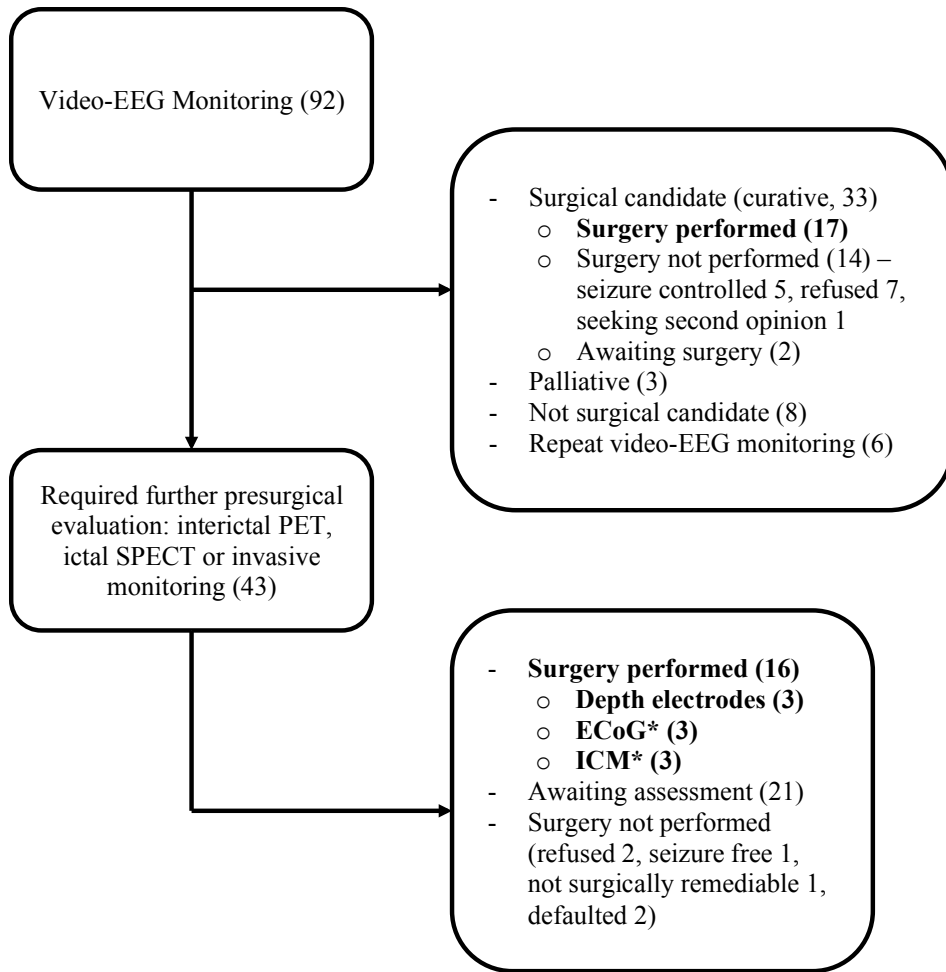


Figure 3. Cases in University Malaya Medical Centre comprehensive epilepsy program from January 2012 till August 2016.

\*ECoG, intraoperative electrocorticography; ICM, intracranial monitoring with subdural±depth electrodes

**Table 1: Characteristics and outcome of epilepsy surgery after stage-1 evaluation (N=17)**

Epilepsy syndrome (n)	Pathology (n)	Type of surgery (n)	Engel class I, n (%)	Complications
TLE (14)	MTS (11)	SAH (5)	3/5 (60%)	Monoparesis (1)
		ATL (6)	6/6 (100%)	
	Non-MTS (2 FCD, 1 DNET)	Lesionectomy	1 (33.3%)	
Extra-TLE (3)	FCD (3)	Lesionectomy	2/2 (100%) *(1)	

TLE, temporal lobe epilepsy; MTS, mesial temporal sclerosis; FCD, focal cortical dysplasia; DNET, dysembryoplasticneuroepithelialtumours; SAH, selective amygdalo-hippocampectomy; ATL, anterior temporal lobectomy  
\*Surgery was performed <12 months from the time of data collection and thus outcome is not determined

### Epilepsy surgery after stage-2 evaluation

A total of 16 surgeries were performed after stage 2 evaluation. Invasive EEG monitoring, including ECoG, subdural and depth EEG implantation, was performed in nine cases. Among those with surgery performed more than 12 months from the time of data collection, 5/10 (50%) achieved Engel I outcome, whereas 2 (20%) had worthwhile improvement (Engel class III) with 75% and 90% seizure reduction. (Table 2)

### Reasons for not undergoing surgery

After stage 1 evaluation, out of 33 cases

concluded to benefit from curative surgery, 16 did not undergo surgery. Seven refused surgery because concern about surgical risk and complications, and lack of family support. Two cases decided for surgery after multiple discussion sessions with family members. Five cases had improved seizure control with antiepileptic drugs adjustment. Of which, some might claim good seizure control to avoid surgery, but this possibility was unable to be verified. One case decided to seek second opinion.

After stage 2 evaluation, 6 cases out of 22 did not undergo surgery, because one case was thought to be not surgically remediable, 2 refused

**Table 2: Characteristics and outcome of epilepsy surgery after stage-2 evaluation (N=16)**

Additional evaluation, (n)	Epilepsy syndrome, (n)	Pathology, (n)	Engel class, (n)	Seizure reduction (%)	Complications
PET only (7)	TLE (5)	FCD (2)	III (1) * (1)	75% seizure reduction	
		Bilateral MTS (1)	I (1)		
		Cavernoma (1)	I (1)		
		Non-specific (1)	IV (1)		
	OLE (2)	Ulegyria (1)	III (1)	90% seizure reduction	Hemianopia
		FCD (1)	IV (1)		Hemianopia
PET and ECoG (3)	FLE (3)	FCD (1)	* (2)		
		Desmoplastic infantile ganglioglioma	* (1)		
Depth electrodes only (3)	Bilateral TLE	MTS (3)	I (1) * (2)		
PET and ICM (3)	PLE	FCD (2)	I (1) IV (1) <sup>®</sup>	GTC resolved	
		Non-specific gliosis (1)	I (1)		
<i>Total</i>			<i>I (5/10, 50%)</i>		

PET, positron emission tomography; TLE, temporal lobe epilepsy; OLE, occipital lobe epilepsy; FCD, focal cortical dysplasia; MTS, mesial temporal sclerosis; ECoG, intraoperative electrocorticography; ICM, intracranial monitoring with subdural=depth electrodes; GTC, generalized tonic-clonic seizure

\*Surgery was performed <12 months from the time of data collection and thus outcome is not determined

<sup>®</sup>The resection was incomplete because of eloquent area involvement.

intracranial monitoring, 1 became seizure free with pharmacological treatment and 2 defaulted follow-up.

## DISCUSSION

This report presents the surgical outcome for patients with intractable focal epilepsy requiring level 4 epilepsy care. A total of 33 epilepsy surgeries were performed in 4 years and 8 months duration in UMMC, which included invasive monitoring such as ECoG, depth and subdural electrodes implantation in 9 patients. The surgical outcome was compatible to previous published studies, i.e. 66% seizure freedom with temporal lobe resections, 46% with occipital and parietal resections, and 27% with frontal lobe resections.<sup>2</sup>

### *Practicality and role of level 4 epilepsy care in a middle-income country like Malaysia*

Level 4 epilepsy care is useful especially in those with lesion-negative focal refractory epilepsy or failed initial epilepsy surgery. Invasive EEG monitoring was judged to have greatest utility in resolving discordant data and localizing extratemporal and multilobar epileptogenic zones.<sup>9</sup> In temporal lobe epilepsy, invasive EEG monitoring was reported to be necessary in 14% of the operated cases.<sup>10</sup> In our series, we were able to operate on 17 patients at level 3 assessment; whereas at level 4, we were able to extend the operation to another 16 patients, close to double the number of patients operated, with reasonable results and morbidity. This indicates a strong need to have level 4 epilepsy care despite multiple challenges, even in a middle-income country.

### *Barriers in developing level 4 epilepsy surgery program*

The challenges in upgrading the epilepsy care from level 3 to level 4 include high medical costs, lack of facilities, expertise and financial support. Despite published recommendations by various leading neurological organisations that support comprehensive epilepsy evaluation, studies on epilepsy surgery have shown long delay of comprehensive epilepsy evaluation and potential curative epilepsy surgery.<sup>11</sup>

In Malaysia, with a population of 31.7 million, the challenge is greater with only about 80 neurologists in the country (with a ratio of 400,000 population per neurologist), of which half are in private practice. Most EEGs were used for routine daytime assessment and could not

be spared for long-term video-EEG monitoring. In addition, most EEG head boxes available are limited to 10-20 EEG recording, not enough for intracranial monitoring. There is only one PET scanner available in the government hospitals, for which some patients need a long travel to have a PET done. Cost remains the main challenge, for example, intracranial electrodes are not within the government subsidy scheme and the cost is borne by the patients.

Cultural perception of brain surgery is also a key barrier, for which most Malaysians perceived brain surgery as a major surgery with high morbidity and mortality. A significant number of our patients, despite multiple discussions, refused to have the surgery because of the concern of surgical complications. Of which, some decisions were made by the family members against the patients accepting surgery. This is compatible to a report stating African Americans had a 60% less chance to receive surgery than non-Hispanic whites.<sup>12</sup>

### *Overcoming challenges*

These challenges can be overcome with joint effort and perseverance. In UMMC, a multidisciplinary epilepsy team was formed in 2012 with the help of various experts in this field, upon which, a video-EEG monitoring unit was established. Ictal SPECT was first explored in 2012 using 99mTc-HMPAO tracer, which has a shorter radioactive duration but was cheaper than 99mTc-ECD. The ictal SPECT protocol was developed and modified with the assistance of nuclear medicine experts that allowed early ictal injection of SPECT tracer. PET imaging, though available in Hospital Putrajaya since 2006, was mainly used for oncological assessment. Interictal PET for epilepsy, using an epilepsy specific protocol, was performed two years ago as a supportive service for other government hospitals.

With these advancements in neuroimaging and the presence of a multidisciplinary team, a total of 16 surgeries were performed after stage 2 evaluation, with a 50% Engel class I outcome and 20% achieved worthwhile improvement.

In conclusion, level 4 epilepsy care has an important role and is possible with joint multidisciplinary effort in a middle-income country like Malaysia despite resource limitation. The more expensive and invasive monitoring, though available and useful, should be limited to patients who definitely require it. This patient selection can be achieved by careful assessment and joint discussion in the MDT.



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