STRATEGIC CANDIDATE SELECTION FOR INVASIVE MONITORING IN TEMPORAL LOBE EPILEPSY: ANALYSING PREDICTORS OF SURGICAL OUTCOME

Dr. Manisha K Yalapalli

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A THESIS SUBMITTED BY

Dr. Manisha K Yalapalli

TO

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IN PARTIAL FULFILMENT OF THE REQUIREMENTSFOR THE AWARD OF

Post-doctoral fellowship in Epilepsy

2024

DECLARATION BY THE STUDENT

CERTIFICATE

I, Dr. Manisha K Yalapalli. hereby certify that I had personally carried out the work depicted in the thesis titled "**STRATEGIC CANDIDATE SELECTION FOR INVASIVE MONITORING IN TEMPORAL LOBE EPILEPSY: ANALYSING PREDICTORS OF SURGICAL OUTCOME.**" No part of this thesis has been submitted for the award of any other degree or diploma prior to this date.

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The thesis entitled "**STRATEGIC CANDIDATE SELECTION FOR INVASIVE MONITORING IN TEMPORAL LOBE EPILEPSY: ANALYSING PREDICTORS OF SURGICAL OUTCOME**" was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma before this date.

*Clearance was obtained from the Institutional Ethics Committee for carrying out the study.



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APPROVAL OF THE THESIS

The thesis entitled

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Submitted by

Dr. Manisha K Yalapalli,

for post-doctoral fellowship in

Epilepsy

of

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

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SYNOPSIS

STRATEGIC CANDIDATE SELECTION FOR INVASIVE MONITORING IN TEMPORAL LOBE EPILEPSY: ANALYSING PREDICTORS OF SURGICAL OUTCOME

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BY

Manisha K Yalapalli

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SYNOPSIS

Invasive monitoring plays a crucial role in the surgical management of temporal lobe epilepsy by providing precise localisation of the epileptogenic zone. However, determining which patients should undergo this procedure remains a complex challenge. A multifaceted approach that considers neuroimaging, electrophysiological data, neuropsychological profiles, seizure semiology, and psychiatric evaluation is essential for optimising surgical outcomes.

AIMS:

- To evaluate the effectiveness of invasive EEG monitoring in identifying the epileptogenic zone in TLE
- To identify predictors of surgical outcomes for patients undergoing resective surgery

METHODOLOGY:

The Study design is a retrospective cohort study of prospectively maintained records and the data will be collected from electronic medical records. All the patients with TLE who underwent presurgical evaluation along with invasive EEG monitoring from 2002 until 2022 in SCTIMST will be included. The demographic, and electroclinical data including interictal and ictal patterns, imaging will be collected. All the patients underwent invasive monitoring.

The yield of invasive monitoring in TLE shall be ascertained. The seizure control is assessed at 2-year follow-up. The independent predictors of seizure freedom among patients with invasive EEG will also be determined.

RESULTS:

A total of 70 patients were included after applying the inclusion and exclusion criteria. The most common seizure semiology noted was focal seizures with impaired awareness noted in 67 patients (95.7%). All the patients underwent invasive monitoring. The most common cause for invasive monitoring was bitemporal epileptogenicity in 24 (40%), followed by non-lesional in 11 patients (18.3%), temporal plus in 7 (11.7%) patients. A definite epileptogenic zone was identified in 51 patients, of which 50 (79.4%) underwent resective surgery. Yield of invasive EEG monitoring in amounts to about 79.4%. Resective surgery was done in 50 (79.4%) patients; Good surgical outcome was noted in 22 (62.9%)

The presence of somatosensory aura($p=0.018$), a history of generalised seizures($p=0.042$), and status epilepticus($p=0.05$) were associated with poor surgical outcomes. In addition, the presence of a structural lesion was shown to be associated with good surgical outcomes ($p=0.036$), whereas the type of structural lesion did not show any association with surgical outcomes.

On analysing electrophysiological data on long-term VEEG, the ictal pattern of delta was associated with poor surgical outcome ($p = 0.029$). In the invasive data, the irritative zone pattern of high-amplitude polyspikes was shown to be associated with poor surgical outcomes ($p=0.036$).

CONCLUSION:

1. Invasive monitoring plays a critical role in the surgical treatment of temporal lobe epilepsy, particularly in patients with non-lesional or bitemporal epilepsy.

2. This study's findings suggest that seizure semiology, imaging results, and electrophysiological patterns all contribute to surgical decision-making.
3. We have demonstrated high yield of invasive monitoring in temporal lobe epilepsy constituiting about 80%
4. The study also demonstrated good surgical outcomes in patients who underwent resective surgery
5. Invasive data showed that irritative zone patterns like high amplitude polyspikes were associated with worse surgical outcomes , whereas ictal patterns like LVFA were associated with good surgical outcomes
6. The presence of structural lesion remains a key predictor of favorable surgical outcomes
7. Ultimately, invasive monitoring remains indispensable for refining surgical planning and improving outcomes in TLE patients

1 INTRODUCTION

Temporal Lobe Epilepsy (TLE) is the most prevalent form of **focal epilepsy**, accounting for approximately 60-70% of adult epilepsy cases (Engel, 2001). It is a neurological disorder that originates in the **temporal lobes**, the regions of the brain involved in **memory**, **emotion**, **auditory processing**, and other cognitive functions. TLE is particularly challenging due to its chronic, often drug-resistant nature, and it can lead to significant cognitive, emotional, and psychiatric comorbidities, severely affecting patients' quality of life.

TLE can be categorized into **mesial temporal lobe epilepsy** (MTLE) and **neocortical temporal lobe epilepsy** (NTLE), based on the seizure focus location. MTLE typically involves the **hippocampus** and **amygdala**, and it is often associated with **hippocampal sclerosis** (HS), which is thought to be a major pathological correlate of the disorder. NTLE, on the other hand, arises from the lateral temporal neocortex and may present with a distinct clinical and electroclinical profile (Thom, 2009).

The mechanisms of epileptogenesis in TLE are multifactorial, involving structural damage, dysfunctional neuroplasticity, altered neurotransmission, and abnormal brain network interactions. Despite extensive research, **drug-resistant epilepsy** remains a major clinical challenge in TLE, prompting the exploration of **surgical**, **neuromodulatory**, and **genetic** therapeutic approaches.

REVIEW OF LITERATURE

TLE is responsible for 60-70% of all cases of drug-resistant epilepsy in adults. It is most commonly diagnosed in patients between the ages of 18 and 40, and it can result from both structural brain lesions and genetic predisposition. The incidence of drug-resistant TLE varies across populations, but estimates suggest that approximately 30-40% of individuals with epilepsy suffer from drug-resistant forms of the disorder, making surgical intervention a critical option for many.

Clinical Presentation of Temporal Lobe Epilepsy

The clinical presentation of TLE is often highly variable, but it is typically characterized by **focal seizures** originating in the temporal lobes. These seizures may progress to **generalized tonic-clonic seizures** in some patients. The hallmark feature of TLE is the **seizure aura**, a phenomenon that occurs prior to the onset of a more significant seizure and is thought to reflect **abnormal neuronal activity** in the temporal lobe.

1. **Focal Seizures with Auras**: The most common form of TLE is **MTLE**, which involves seizure foci in the medial temporal structures, such as the **hippocampus**, **amygdala**, and **entorhinal cortex**. Auras often consist of unusual **memories**, **deja vu**, or **jamais vu**, **gustatory** or **olfactory hallucinations**, **fear**, or **epigastric rising sensations** (Bancaud & Halgren, 1975). These auras are indicative of focal onset seizures that may evolve to more generalized manifestations.
2. **Automatisms**: As the seizure spreads, patients may exhibit **automatisms**, such as lip-smacking, chewing, or repeated hand movements. These symptoms reflect **involuntary motor behavior** that arises due to abnormal activity in the temporal

lobe and connected limbic structures, including the **amygdala** (Halgren et al., 2009).

3. **Secondary Generalized Seizures**: In more severe cases, the seizure may propagate to both hemispheres, leading to **secondary generalized tonic-clonic seizures**. These seizures are often followed by **postictal confusion**, which can persist for minutes to hours, depending on the duration and severity of the seizure.
4. **Cognitive and Emotional Manifestations**: Patients with TLE, especially MTLE, may report cognitive disturbances such as **memory loss**, particularly in the domains of **verbal** and **spatial memory**. In addition, the chronic nature of TLE can contribute to **emotional instability**, anxiety, and **depression**, which often coexist with the seizures.
5. **Psychiatric Comorbidities**: TLE has a high incidence of **psychiatric disorders**, including **depression**, **anxiety**, **psychosis**, and **irritability**. The presence of these disorders complicates the clinical picture, and addressing them requires careful management (Thompson et al., 2005).

Pathophysiology of Temporal Lobe Epilepsy

The pathophysiological mechanisms underlying TLE are complex and involve **structural abnormalities**, **neuroplasticity**, **network dysfunction**, and **genetic** predisposition. The primary focus of much of the research into TLE has been on the **hippocampus**, which plays a central role in both **memory formation** and **seizure generation**.

1. **Hippocampal Sclerosis (HS)**: One of the key pathological features of MTLE is **hippocampal sclerosis**, which is characterized by **neuronal loss**, **gliosis**,

and the **reorganization** of neural networks within the hippocampus (Blumcke et al., 2012). HS leads to **increased excitability** in the affected area, which enhances the likelihood of seizure initiation. This is particularly evident in the **CA1** and **CA3** subfields of the hippocampus, which are heavily involved in the generation of **epileptiform activity** (Thom, 2009). The presence of HS correlates with a more severe form of epilepsy that is often **drug-resistant**.

2. **Neuroplasticity and Network Reorganization**: Chronic seizure activity in TLE can lead to maladaptive **neuroplastic changes**, including **synaptic reorganization** and **neurogenesis**. Over time, this may result in the development of **abnormal neuronal networks** that promote **seizure propagation**. Changes in **synaptic density** and **glutamatergic neurotransmission** (increased **NMDA** receptor activity) have been observed in animal models of TLE (Pitkänen & Lukasiuk, 2009). These alterations in neuronal communication play a critical role in **epileptogenesis**, the process by which normal brain tissue becomes prone to seizures.
3. **Network Dysfunction and Hyperexcitability**: TLE is also marked by the disruption of **brain networks** that mediate **memory**, **emotion**, and **cognitive functions**. The **limbic system**, which includes the hippocampus, amygdala, and entorhinal cortex, is particularly involved in the emotional and memory aspects of TLE. **Functional imaging** studies have revealed that seizures often spread to **prefrontal regions**, **parietal cortices**, and even the **contralateral temporal lobe**, contributing to a broader dysfunction in brain networks (Liu et al., 2015).
4. **Increased Glutamatergic Activity**: Alterations in the **glutamate system** have been implicated in the pathogenesis of TLE. Glutamate, the primary

excitatory neurotransmitter, plays a key role in neuronal excitability. In TLE, excessive glutamatergic activity can promote the **hyperexcitability** of neurons, a hallmark of seizure activity. On the other hand, **GABAergic dysfunction** (reduced inhibitory neurotransmission) has been noted as a factor contributing to seizure onset (Liu et al., 2019).

Cognitive and Psychiatric Comorbidities in TLE

Cognitive dysfunction and psychiatric disorders are common in TLE, contributing significantly to the disability associated with this epilepsy type. These comorbidities often coexist and complicate both diagnosis and treatment.

1. **Memory Deficits**: The **hippocampus** plays a central role in memory processing, and **hippocampal damage**, particularly in MTLE, often leads to significant **memory impairments**. These deficits primarily affect **episodic memory**—the ability to recall personal experiences or events—and **verbal memory** (Hermann et al., 2007). Additionally, **working memory** and **attention** may be impaired in TLE patients, reflecting broader cognitive dysfunction.
2. **Psychiatric Disorders**: **Depression**, **anxiety**, and **psychosis** are common psychiatric disorders observed in TLE. Research has shown that patients with TLE have higher rates of **depression** and **anxiety** compared to the general population (Bussmann et al., 2004). The **emotional dysregulation** that often accompanies TLE may be linked to **amygdala dysfunction**, which affects the processing of fear and emotional responses (Bremner et al., 1995).
3. **Emotional Instability**: In addition to mood disorders, emotional instability, such as **irritability** and **aggression**, is also common in TLE. These emotional

disturbances are thought to arise from altered neural regulation of the limbic system, which mediates emotional responses.

Genetic Factors in Temporal Lobe Epilepsy

While TLE is primarily considered an **acquired** disorder, genetic factors play an increasingly recognized role in its development, particularly in cases without identifiable structural causes.

1. **Familial Aggregation**: Some studies have suggested a **genetic predisposition** to TLE, especially in patients with a family history of epilepsy. Several **genetic loci** associated with TLE have been identified, although the specific genes responsible remain elusive (Heron et al., 2007).
2. **Ion Channel Mutations**: Research into **genetic epilepsies** has revealed that mutations in genes encoding ion channels (e.g., **SCN1A**,**KCNQ2**, and **GABA-A receptor** genes) can increase the risk of developing epilepsy, including TLE (Catterall, 2012). These mutations often result in **channelopathies**—alterations in ion channel function that increase neuronal excitability and predispose individuals to seizures.

3. **Epigenetic Mechanisms**: There is growing interest in the role of **epigenetic modifications**, such as DNA methylation and histone modification, in TLE. These processes may contribute to **neuroplasticity** and the **epileptogenesis** that occurs in response to injury or prolonged seizures (Baraban et al., 2016).

Pre-Surgical Evaluation of Temporal Lobe Epilepsy:

A typical pre-surgical evaluation for TLE patients includes a combination of clinical semiology, neuroimaging (primarily MRI), functional imaging (e.g., PET, SPECT), and electrophysiological monitoring, including scalp EEG and VEEG. When non-invasive tests fail to accurately localize the SOZ, invasive monitoring with intracranial electrodes (e.g., subdural grids, depth electrodes) is employed (Engel, 1996). The goal of invasive monitoring is to identify the epileptogenic zone (EZ), which is the brain region responsible for initiating seizures, and to assess the seizure propagation network.

Invasive Monitoring in Temporal Lobe Epilepsy:

Rationale for Invasive Monitoring

Invasive monitoring allows clinicians to precisely localize the seizure onset zone (SOZ) and delineate the epileptogenic zone (EZ). It is crucial for patients who are candidates for epilepsy surgery, such as lobectomy or laser ablation. Invasive methods are typically used when non-invasive methods (EEG, MRI) fail to provide clear localization, or when there is discordance between imaging and clinical findings.

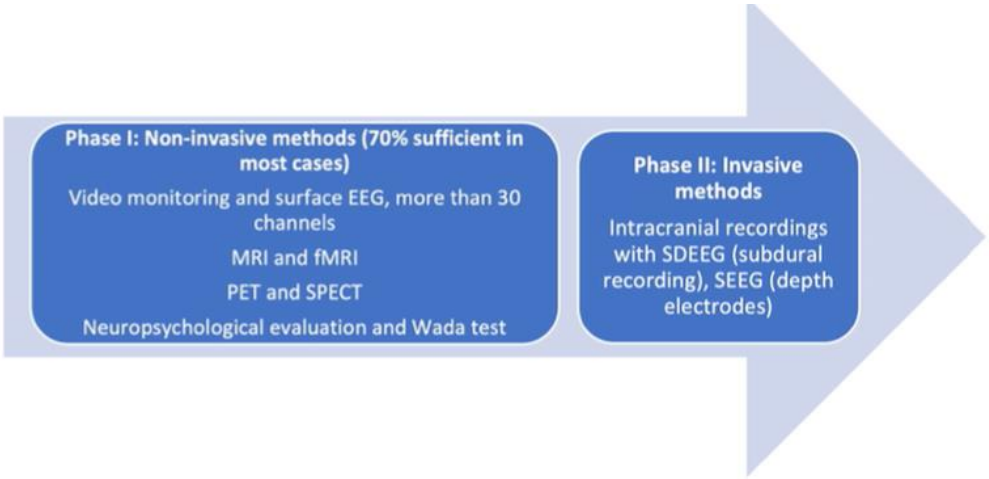


Figure 1 – Presurgical evaluation in epilepsy- Phases (Paredes-Aragon E, et al)

Techniques for Invasive Monitoring

The primary techniques for invasive monitoring in TLE include:

1. *Intracranial EEG (iEEG):* Electrodes are placed directly on the cortical surface or within the brain (subdural, depth electrodes).
2. *Stereo-electroencephalography (SEEG):* A minimally invasive technique where depth electrodes are implanted in deep brain structures, including the temporal lobe, to record seizure activity.
3. *Functional mapping:* Direct cortical stimulation to map eloquent areas (e.g., language, motor) during surgery.

Indications for Invasive Monitoring

1. Differentiating mesial from neocortical involvement in EZ
2. Extension of the EZ beyond the temporal region
3. The bitemporal onset of epilepsy requires exploring mesial temporal structures that may or may not include the hippocampus (although most centers cover this area) for bilateral intracranial recording to determine the laterality of seizures.

Invasive Monitoring: Role in Surgical Planning

Invasive monitoring (IM) is performed when non-invasive methods, such as MRI, video-EEG, or PET, fail to identify the epileptogenic zone adequately or when there is ambiguity regarding the localization of the seizure focus. This technique involves implanting electrodes either subdurally (subdural grids and strips) or intracranially (depth electrodes) to record brain activity and identify the origin of seizures more precisely (Zangiabadi et al., 2019).

IM provides several advantages over non-invasive methods. It offers a direct, real-time assessment of brain activity, enabling the localization of both the seizure onset zone (SOZ) and any eloquent cortical regions that must be preserved during surgery. Furthermore, it allows for identifying subtle or difficult-to-detect epileptogenic areas that may not be visible on conventional MRI or SPECT imaging. As such, IM is considered a crucial tool in the surgical evaluation of patients with drug-resistant epilepsy (Engel, 2013).

The decision to proceed with IM, however, is not straightforward. It involves a risk-benefit analysis that considers the procedure's invasiveness and the potential

for adverse effects, such as infection, bleeding, or cognitive deficits. Moreover, IM has inherent challenges, including technical difficulties in electrode placement, limited spatial resolution in some electrode systems, and the need for specialized expertise in interpreting the data (Owen et al., 2019).

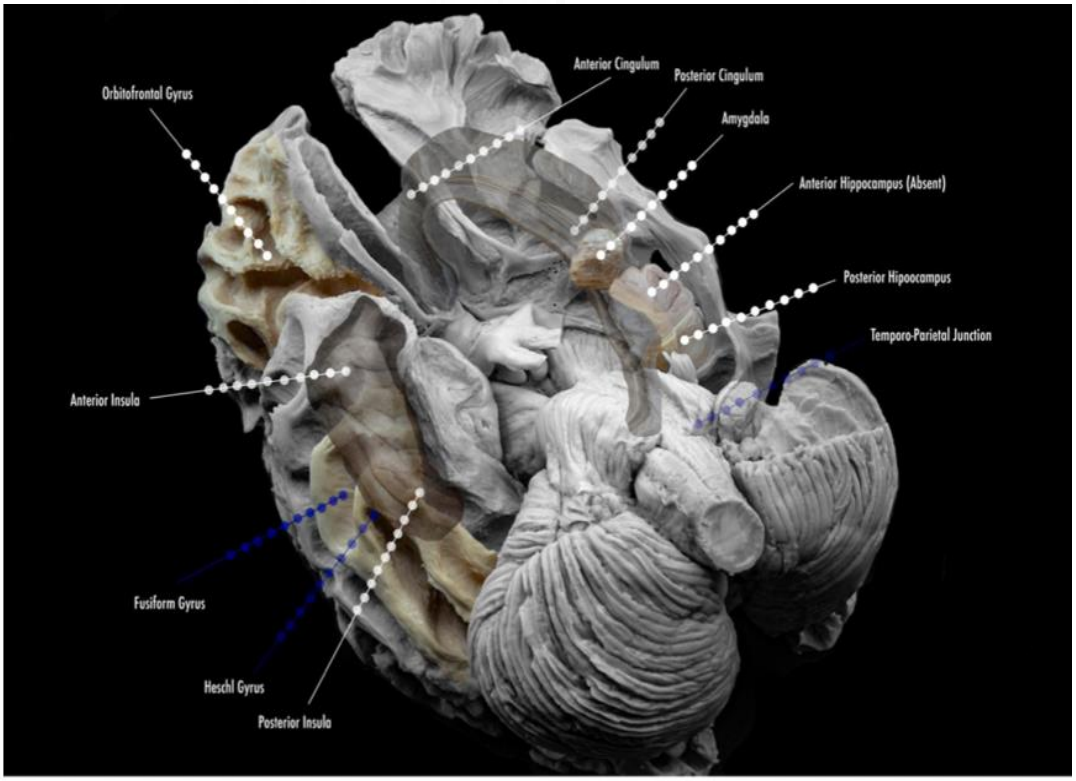


Figure 2: Proposed scheme of implantation in temporal lobe epilepsy

(Paredes-Aragon E, et al)

Invasive monitoring aims to achieve precise localisation of the seizure onset zone (SOZ) and to differentiate it from the functional areas of the brain. This is crucial for deciding whether the patient is a suitable candidate for resective surgery, such as temporal lobectomy

Techniques for Invasive Monitoring

There are several techniques for invasive monitoring in TLE, each with specific applications and limitations:

Intracranial EEG (iEEG): To record seizure activity, intracranial electrodes are placed directly on the cortical surface (subdural electrodes) or within deep brain structures (depth electrodes). iEEG is invaluable for identifying the epileptogenic zone (EZ).

Subdural Electrodes: These are placed over the cortical surface, allowing direct monitoring of cortical activity.

Depth Electrodes: These electrodes are inserted into deep brain structures like the hippocampus or amygdala to monitor activity in the deeper temporal lobe structures.

Stereo-electroencephalography (SEEG): SEEG involves the implantation of depth electrodes through small burr holes into deep structures like the hippocampus and amygdala. It provides high-resolution temporal and spatial data and is particularly useful for patients with multiple seizure foci or when the SOZ is difficult to identify on scalp EEG.

Functional Mapping: This includes cortical stimulation (e.g., via subdural electrodes) to identify eloquent areas (e.g., language, motor areas) before resection to prevent functional impairment.

ELECTROPHYSIOLOGICAL PATTERNS:

Ictal and interictal EEG patterns are crucial in this process. While VEEG provides the advantage of correlating seizure activity with clinical manifestations, invasive EEG allows for higher spatial resolution and direct recording from deeper brain structures such as the hippocampus and amygdala, which are often involved in TLE (Engel, 2001).

Interictal Patterns in Video-EEG and Invasive EEG:

Interictal epileptiform discharges (IEDs) represent abnormal brain activity occurring between seizures and are one of the primary features used in the localization of the epileptogenic zone. These discharges can manifest as spikes, sharp waves, or slow waves, and their location, frequency, and morphology provide valuable information about the nature and extent of the epileptogenic network.

1. Interictal Patterns in Video-EEG:

In video-EEG (VEEG), interictal discharges are typically recorded during periods of wakefulness or sleep between seizures. VEEG is a non-invasive method and can provide important localization information when used in conjunction with other imaging modalities (Engel et al., 2003).

- **Sharp waves and spikes** are the most common interictal patterns seen in TLE. These are most often localised to the temporal lobes, particularly the mesial structures such as the hippocampus and amygdala (Lhatoo et al., 1999). Sharp waves can indicate a high likelihood of involvement of the mesial temporal lobe in the epileptogenic network. The amplitude and latency of spikes also help in differentiating between focal and generalised epilepsy. More prominent, localised spikes suggest a focal epileptogenic zone, while generalized spikes might indicate bilateral involvement or a more diffuse epileptic network (Morrell, 2006).

- **Bilateral interictal discharges** are not uncommon in TLE and are typically found in patients with bilateral epileptogenic foci (Stefan et al., 2000). Bilateral IEDs can complicate surgical decision-making, as resecting tissue from both temporal lobes might be necessary to achieve a seizure-free outcome. In such cases, the decision to proceed with surgery may depend on whether the interictal discharges are purely spatially coincident or synchronously active, as the latter suggests more complex, widespread epileptic networks (Tellez-Zenteno et al., 2005).
- **Low-voltage fast activity (LVFA)** is another interictal pattern observed in TLE patients, and its presence may reflect a more diffuse epileptogenic network. LVFA is typically seen in more refractory cases, where the epileptic network is not confined to a single region of the brain. Its association with poor surgical outcomes is well-documented, as it suggests that the epileptogenic zone may be multifocal or involve deep brain structures (Thom et al., 2010).

2. Interictal Patterns in Invasive EEG

Invasive EEG offers several advantages over VEEG, primarily its ability to record from deeper brain regions such as the hippocampus and amygdala, which are often involved in TLE but are difficult to localize with scalp EEG alone. Invasive EEG can be obtained using subdural grid electrodes or depth electrodes, the latter being particularly useful for recording from the hippocampus and other deep brain structures.

- **Sharp waves and spikes** recorded in mesial temporal structures, such as the hippocampus and amygdala, are common interictal findings in TLE patients. These discharges are often used to localize the epileptogenic zone (Lhatoo et al., 1999). The presence of interictal spikes in the hippocampus, especially when they occur in the same region where ictal onset is observed, strongly suggests that the hippocampus is part of the epileptogenic zone.
- **Bilateral interictal discharges** are also observed in invasive EEG recordings, especially in cases of **bitemporal epilepsy**. Bilateral spikes are more likely to be seen in patients with a diffuse epileptogenic network, where both temporal lobes contribute to seizure generation. Identifying bilateral involvement through invasive EEG is crucial in surgical planning, as it may necessitate a more extensive resection or even a decision to avoid surgery (Stefan et al., 2000).
- **Interictal discharges** recorded from subdural electrodes placed over the lateral temporal cortex can provide insights into the extent of the epileptogenic network. These lateral temporal interictal spikes may indicate the involvement of the **neocortex** in the seizure process, suggesting that the EZ extends beyond the mesial temporal structures (Iwasaki et al., 2013).

Ictal Patterns in Video-EEG and Invasive EEG

Ictal patterns represent the electrical changes observed during a seizure. In TLE, ictal patterns can help identify the location of the seizure onset zone (SOZ) and the pathways through which the seizure propagates.

1. Ictal Patterns in Video-EEG:

Video-EEG plays a vital role in identifying ictal patterns and correlating them with clinical semiology, which helps determine the onset and spread of seizures. In TLE, seizures typically start in the temporal lobe, often with **rhythmic theta** or **alpha activity** in the initial stages. These patterns are seen in focal-onset seizures with impaired awareness, which is the most common semiological presentation in TLE (Moran et al., 2001).

- **Rhythmic theta activity** is commonly observed at the onset of seizures originating in the mesial temporal lobe. It typically begins in the hippocampus and spreads to the amygdala and other temporal regions (Iwasaki et al., 2013). This pattern is seen in the early ictal phase and reflects the initiation of seizure activity within the epileptogenic focus.
- **Low-voltage fast activity (LVFA)** during ictal events is also seen in TLE, particularly in patients with a more widespread epileptogenic network. LVFA can signify the propagation of seizures to other regions of the brain or the involvement of a broader epileptogenic network, including the neocortex or contralateral temporal lobe (Iwasaki et al., 2013).
- **Generalized spike-and-wave activity** may occur in patients with secondary generalization, where the seizure spreads from the temporal lobe to other brain regions. Secondary generalization is a common feature in TLE and

often presents with generalized tonic-clonic seizures (Tellez-Zenteno et al., 2005). The detection of generalized spike-and-wave activity on VEEG is important for distinguishing TLE from generalized epilepsies.

2. Ictal Patterns in Invasive EEG:

Invasive EEG provides more detailed information about the dynamics of seizure onset and propagation, especially in the mesial temporal structures, which are frequently involved in TLE. The advantage of invasive EEG lies in its ability to record from deeper brain structures, such as the hippocampus, amygdala, and parahippocampal gyrus, where seizures often originate in TLE.

- **Rhythmic theta activity** is the most common ictal pattern in invasive EEG recordings from mesial temporal structures. Theta waves are typically the first electrical sign of seizure onset and often begin in the hippocampus, spreading to other temporal lobe structures (Iwasaki et al., 2013). This rhythmic theta activity is crucial for identifying the epileptogenic zone in TLE patients.
- **Gamma activity** is also frequently observed during seizure propagation. As the seizure spreads from its initial focus, higher frequency gamma waves may appear. Gamma activity reflects more widespread cortical involvement and can provide additional information about the networks involved in seizure spread (Jacobs et al., 2012).
- **Low-voltage fast activity (LVFA)** can also be observed during seizures, especially in patients with more complex, multifocal seizure patterns. LVFA during seizures is often associated with poor surgical outcomes, as it suggests a more diffuse epileptogenic network that is difficult to resect effectively (Thom et al., 2010).
- **High-amplitude polyspike patterns** can also be seen during seizures and are

typically associated with more refractory forms of epilepsy. These polyspikes may reflect a more widespread epileptic network and are less likely to be amenable to resective surgery (Morrell, 2006).

Clinical Implications and Surgical Planning:

Analyzing ictal and interictal patterns in VEEG and iEEG has significant implications for surgical decision-making in TLE patients.

1. **Localizing the Epileptogenic Zone (EZ)**: Interictal and ictal patterns provide essential information about the localization of the EZ. The identification of mesial temporal spikes or rhythmic theta activity during seizures strongly suggests that the mesial temporal structures (hippocampus and amygdala) are involved in the epileptogenic network (Lhatoo et al., 1999).
2. **Predicting Surgical Outcomes**: The presence of specific ictal and interictal patterns can predict surgical outcomes. Well-localized seizures with rhythmic theta activity and interictal spikes in mesial temporal structures are associated with good surgical outcomes (Engel, 2001). In contrast, patients with multifocal or generalized ictal patterns (e.g., LVFA) may have poorer outcomes due to the difficulty in achieving complete resection of the epileptogenic network (Thom et al., 2010).
3. **Bilateral Epileptogenicity**: Identifying bilateral ictal or interictal activity is critical for surgical planning. In cases of bitemporal epilepsy, bilateral temporal lobectomy may be considered, although the presence of bilateral epileptiform activity is often associated with less favorable outcomes (Stefan et al., 2000).

Multidisciplinary Approach:

Invasive monitoring decisions are best made through a multidisciplinary approach involving neurologists, neurosurgeons, neuropsychologists, and radiologists. This collaborative approach ensures that all clinical, cognitive, and structural factors are considered when selecting candidates for invasive procedures.

Invasive monitoring plays a pivotal role in the management of drug-resistant temporal lobe epilepsy. The decision to proceed with invasive techniques is influenced by a combination of clinical, radiological, and electrophysiological factors. Although the use of invasive monitoring can significantly enhance seizure localization and improve outcomes for surgical candidates, careful consideration of patient factors, ethics, and emerging technologies is necessary. As research in this area progresses, non-invasive methods may become more reliable, but invasive techniques will likely remain indispensable for many patients with TLE

Treatment Strategies:

Treatment for TLE focuses on controlling seizures, alleviating cognitive and psychiatric symptoms, and improving quality of life. Treatment approaches include **pharmacological**, **surgical**, and **neuromodulatory** interventions.

1. **Pharmacotherapy**: **Antiepileptic drugs (AEDs)** remain the first-line treatment for TLE. Common AEDs include **carbamazepine**, **lamotrigine**, **valproate**, and **levetiracetam**. However, many patients with TLE, especially those with MTLE, remain **drug-resistant**, with approximately 30-40% of patients failing to achieve adequate seizure control with medications (Brodie et al., 2009).
2. **Surgical Intervention**: **Temporal lobectomy** remains the gold standard for treating **drug-resistant MTLE**, especially when there is

hippocampal sclerosis. The success rate of this surgery in achieving seizure freedom is **60-80%**, and it significantly improves quality of life for many patients (Engel et al., 2003). However, surgery carries risks, including **memory loss** and cognitive deficits, particularly if the hippocampus is removed.

3. **Neuromodulation**: **Vagus nerve stimulation (VNS)** and **deep brain stimulation (DBS)** are promising treatments for patients with **drug-resistant TLE**. Both techniques aim to modulate abnormal brain activity. Studies show that DBS, particularly in the **anterior thalamus** or **hippocampus**, can reduce seizure frequency and improve cognitive function (Kringelbach et al., 2007). **Responsive neurostimulation (RNS)** is another emerging technique involving a brain implant that detects seizures and provides real-time electrical stimulation to disrupt their progression (Jobst & Cascino, 2015).

Key Predictors of Surgical Outcome

1. Neuroimaging and Structural Changes in TLE

Neuroimaging plays a fundamental role in the presurgical evaluation of TLE. High-resolution MRI remains the gold standard for identifying structural abnormalities, such as hippocampal sclerosis or tumours, that may underlie the epileptogenic zone (Bernasconi et al., 2011). In particular, hippocampal volumetry—measuring the size of the hippocampus on MRI scans—has proven to be a reliable predictor of surgical outcomes. Studies have shown that patients with unilateral hippocampal sclerosis (HS) on MRI are more likely to experience favourable outcomes after temporal lobectomy, with seizure-free rates of up to 70-80% (Engel, 2013).

In MRI-negative cases, where no structural abnormality is detected, other imaging techniques such as functional MRI (fMRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT) can provide complementary data to localize the epileptogenic focus. PET and SPECT, in particular, can identify areas of hypometabolism or altered temporal lobe perfusion, which may suggest the epileptogenic zone (Hermann et al., 2015). When combined with electrophysiological data from video-EEG and invasive monitoring, these imaging modalities help refine surgical planning and improve the chances of achieving seizure freedom post-surgery.

2. Electrophysiological Monitoring: Video-EEG and Invasive Recording

Video-EEG monitoring is commonly used to record the onset and spread of seizures in TLE patients. It is especially helpful in lateralizing the focus of seizures and determining whether the seizures are truly originating from the temporal lobes or if there is a secondary spread to other areas of the brain (Téllez-Zenteno et al., 2005). In cases where video-EEG is inconclusive, invasive monitoring provides more precise localization of the seizure onset zone, enabling the surgical team to make better-informed decisions regarding the extent of tissue resection required.

Invasive monitoring has shown its utility in patients with complex or non-lateralizing seizures, particularly when the non-invasive tests provide ambiguous results. For example, a study by Bouthillier et al. (2015) found that invasive monitoring was able to localize the epileptogenic zone in patients who were otherwise non-lateralized on scalp EEG, improving surgical outcomes and reducing the risk of postoperative seizures.

3. Neuropsychological Assessment

A comprehensive neuropsychological assessment is crucial in the presurgical

evaluation of TLE patients, as it can provide insights into baseline cognitive function and predict postoperative changes. Memory deficits, particularly in the context of hippocampal sclerosis, are common in TLE patients and may affect postoperative recovery and long-term outcomes. Several studies have found that pre-surgical memory dysfunction is associated with poorer surgical outcomes and a higher likelihood of postoperative cognitive decline (Hermann et al., 2015).

Moreover, neuropsychological testing can help identify patients at risk of cognitive deterioration following surgery. For example, a study by Wilson et al. (2016) demonstrated that patients with lower cognitive reserve, a concept referring to the brain's ability to compensate for injury or pathology, were more likely to experience cognitive decline after surgery. Therefore, assessing cognitive reserve is essential when selecting candidates for surgery, particularly in older patients or those with long-standing epilepsy.

4. Seizure Semiological Features

Seizure semiology, or the clinical manifestation of seizures, is another predictor of surgical success in TLE patients. The semiology of a patient's seizures can provide valuable information regarding the lateralization and localization of the epileptogenic focus. For instance, patients with simple partial seizures or those with motor involvement often demonstrate more lateralized seizure foci, which can be accurately localized with non-invasive or invasive monitoring (Téllez-Zenteno et al., 2005). Conversely, patients with generalized or complex semiologies may present greater challenges in localizing the seizure onset zone, requiring more extensive monitoring and a multidisciplinary approach.

A recent study by Lüders et al. (2020) emphasized the importance of seizure semiology in predicting the likelihood of seizure freedom after surgery. Patients with simple partial seizures originating from the mesial temporal lobe were found to have

higher rates of postoperative seizure freedom compared to those with complex or non-lateralizing seizures.

5. Psychiatric Comorbidities

Psychiatric comorbidities, such as depression and anxiety, are common in patients with drug-resistant epilepsy and can influence surgical outcomes. Depression, for example, has been shown to affect both preoperative cognitive function and postoperative recovery (Baker et al., 2016). Furthermore, untreated psychiatric conditions can complicate the management of epilepsy and increase the risk of postoperative complications. A thorough psychiatric evaluation, therefore, should be part of the candidate selection process for invasive monitoring and surgery.

6. Age and Epilepsy Duration

Age and the duration of epilepsy are well-established predictors of surgical outcomes in TLE patients. Younger patients, particularly those with a shorter duration of epilepsy, tend to have better postoperative outcomes, including higher rates of seizure freedom and less cognitive decline (Lüders et al., 2001). On the other hand, older patients, especially those with long-standing epilepsy, may have lower chances of achieving seizure freedom post-surgery due to cumulative neuronal damage. Furthermore, the risk of cognitive deficits after surgery is higher in older patients, particularly if the epileptogenic zone involves critical cognitive structures such as the hippocampus (Bouthillier et al., 2015).

Challenges and Controversies in Surgical Candidate Selection

While the predictors discussed above are valuable tools in selecting candidates for surgery, several challenges remain. One of the major challenges is the variability in the presentation of TLE, with some patients presenting with atypical or non-lateralizing seizures that complicate the diagnostic process. Moreover, the risk of cognitive deterioration following surgery, particularly in older patients or those with pre-existing memory deficits, remains a significant concern. Additionally, there is ongoing debate regarding the optimal extent of resection required to achieve seizure freedom without compromising cognitive function.

There is also the issue of selecting patients for invasive monitoring when non-invasive studies have been inconclusive. Some researchers argue that invasive procedures should be reserved for those most likely to benefit, while others emphasize the importance of comprehensive diagnostic evaluation, even in cases where non-invasive tests are ambiguous (Owen et al., 2019). A major area of controversy is the use of non-invasive imaging modalities, such as fMRI and PET, in guiding invasive monitoring. While these techniques have been shown to improve localization accuracy, their cost, availability, and reliability in certain patient populations remain concerns (Zangiabadi et al., 2019).

Resective surgeries and SEEG implantation techniques are evolving rapidly (19, 78). In general, patients that do not undergo resection after SEEG implantation and recording are up to 40%. Particularly in non-lesional TLE, this group had lower outcomes after surgery with or without SEEG implantation. For example, seizure freedom rates in bilateral— SEEG implantation patients were (32%) compared to those unplanned for SEEG and to unilateral SEEG implantations (43%)(79). Some studies have found possible predictors of epilepsy outcomes after SEEG implantation. Negative predictors of seizure freedom after SEEG are more than one

seizure focus, seizure-free periods in their medical history, and a non-localizing ictal scalp EEG. On the other hand, a positive prediction of seizure freedom was observed with identified MRI lesion or PET hypometabolism in concordant with a strong and testable anatomo-functional hypothesis (80, 81). Another outcome series by the Cleveland group aimed to determine the rates and predictors of seizure freedom after resection among bilateral SEEG implanted patients. Observed positive predictors were single seizure type, short epilepsy duration (<10 years), absence of bilateral independent ictal seizure onset, and presence of dominant IEDs, which were among the most significant (76).

For patients that have been treated with failed resection of temporal regions, SEEG can also establish EZ characteristics for further treatment strategies and decision-making. In a study of post-surgical TLE patients in Germany from 2013 to 2017, the investigation of 21 patients that required SEEG led to a change in the initial surgical plan in more than 60% of patients, with resection area ranging in over 81% and an outcome of Engel I in 75% of patients (82). In fact, in a recent retrospective study of 85 patients that underwent anterior temporal lobectomy with bilateral TLE or poor lateralizing data, the SEEG study yielded equivalent outcomes in unilateral TLE (83).

Additionally, one of the reasons for surgery failures in TLE raised attention to the speed of propagation of seizure activity recorded intracranially in both groups of unilateral and bilateral TLE hypotheses. Lieb et al. (84) reported that an interhemispheric propagation time <5s was negatively correlated with seizure outcomes. A mean interhemispheric propagation time of 39s was associated with a favorable outcome. A recent study showed that rapid seizure spread in <10 s was associated with recurrence of seizures, despite 61% of those patients being with lesional TLE (38). Overall, reported outcomes could be controversial given the fact

variations between the centers in patient selection criteria, implantation data processing, and available diagnostic techniques.

Invasive monitoring plays a crucial role in the surgical management of temporal lobe epilepsy by providing precise localization of the epileptogenic zone. However, determining which patients should undergo this procedure remains a complex challenge. A multifaceted approach that considers neuroimaging, electrophysiological data, neuropsychological profiles, seizure semiology, and psychiatric evaluation is essential for optimizing surgical outcomes. While significant progress has been made in understanding the predictors of surgical success, further research is needed to refine selection criteria and improve patient outcomes.

AIMS AND OBJECTIVES:

- To evaluate the effectiveness of invasive EEG monitoring in identifying the epileptogenic zone in TLE
- To identify predictors of surgical outcomes for patients undergoing resective surgery

3 MATERIALS AND METHODS

The Study design is a retrospective cohort study of prospectively maintained records and the data will be collected from electronic medical records. All the patients with TLE who underwent presurgical evaluation along with invasive EEG monitoring from 2002 until 2022 in SCTIMST will be included. The demographic, and electroclinical data including interictal and ictal patterns, imaging will be collected. The clinical semiology, electrophysiological data including number of seizures recorded, location of interictal epileptiform abnormalities, ictal patterns shall be collected. All the patients underwent either 1.5T /3T MRI epilepsy protocol, and in some cases, PET and SPECT have also been done. The imaging data is reviewed by a neuroradiologist.

In cases where the electroclinicoradiological data is discordant or in cases where no lesion was identified, diffuse epileptogenesis, or unidentified epileptogenic region, next phase evaluation with invasive EEG monitoring is done. Thus the candidates in whom the invasive EEG monitoring is required and the reason for invasive monitoring is ascertained. The patients underwent invasive monitoring either with depth electrodes, stereo EEG, subdural grid and strip or a combination. The type and the location of the electrodes will be planned according to the semiology of the seizures, long-term video EEG findings and abnormalities seen on MRI scan. The hypothesis and plan of implantation shall be decided after a patient management conference. The data of patients who have undergone a resective procedure after invasive EEG monitoring will be collected.

The yield of invasive monitoring in TLE shall be calculated by the number of patients in whom a definite epileptogenic zone can be identified, and there by resective

surgery can be planned. The seizure control is assessed at 2-year follow-up. Engels classification is used to assess the post-operative outcome. Class 1 and 2 are considered to have good outcome. The independent predictors of seizure freedom among patients with invasive EEG will also be determined.

INCLUSION CRITERIA

- Patients with refractory temporal lobe epilepsy.
- All patients who underwent invasive EEG monitoring either with subdural grid/ strip or with stereo EEG or with hippocampal depth electrodes will be included.

EXCLUSION CRITERIA:

- Patients with incomplete evaluation
- Patients who were lost to follow-up.

Case ascertainment :

All the patients with refractory temporal lobe epilepsy – defined as those patients with continued seizures inspite of adequate and optimum trial of appropriately chosen 2 antiseizure medications. All the patients should have undergone invasive EEG monitoring.

STATISTICAL ANALYSIS:

Bivariate analysis will be done using Pearson Chi-square and Fisher exact for categorical variables and unpaired T-test for continuous variables. The Shapiro-Wilk test is used to assess the normality. In the case of non-parametric data, Mann-Whitney is used. The potential predictors of favourable resective epilepsy surgery outcomes will be studied in univariate Cox-proportional hazard models and multivariate regression analysis. This study has been conducted with the approval of the institutional ethics committee IEC/2259.

RESULTS

A total of 70 patients were included after applying the inclusion and exclusion criteria. The mean age of presentation was 27.5 +/- 9.99 yrs . The mean age of onset of epilepsy was 10.4+/- 5.78 yrs.

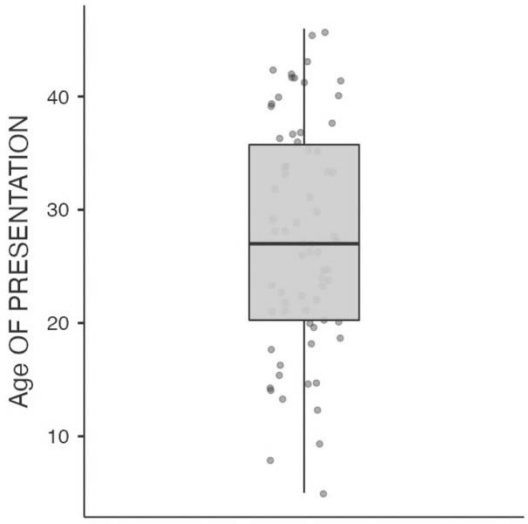


Figure.3: Box plot depicting the distribution of age of presentation

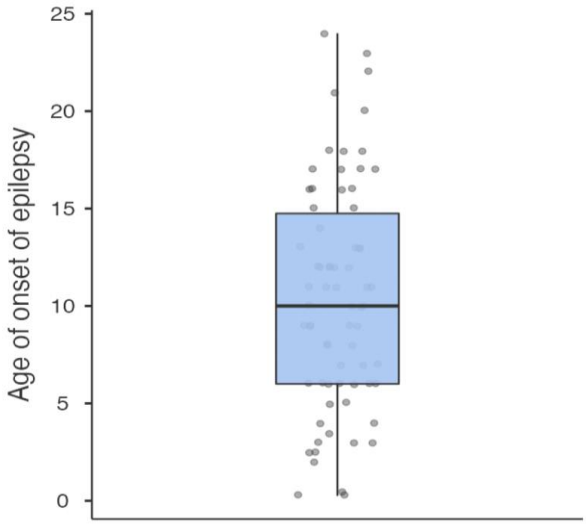


Figure.4: Box plot depicting the distribution of age at onset of epilepsy

Of these 70 patients, 25 were female constituiting 35.7% and 45 were male constituiting 64.3%.

ANTECEDENTS:

Most common antecedent was Febrile seizures noted in 20 patients (28.6%), followed by meningoencephalitis in 6 patients (8.6%); followed by trauma in 3 (4.3%) patients and perinatal insult in 2 (2.9%) patients.

Global developmental delay was noted in 3 (4.3%) patients. Interictal psychosis was noted in 15 patients (21.1%).

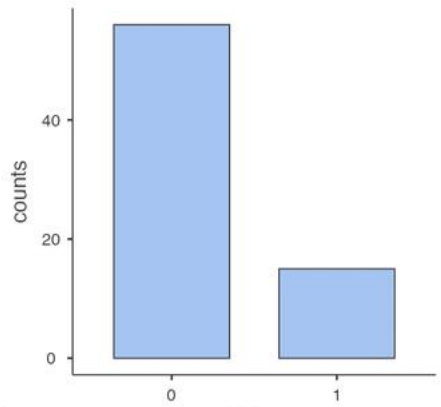


Figure.5: Bar diagram depicting the number of patients with inter-ictal psychosis.

MEMORY

13 patients (41.9%) had impairment of both verbal and visual memory ; 16 patients had impairment in verbal memory(51.6%) and 2 patients (6.5%) had impairment in visual memory.

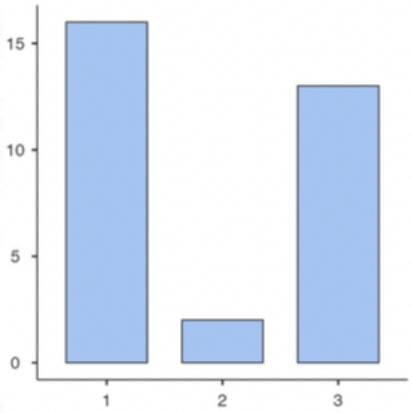


Figure.6. Bar diagram depicting the proportion of patients with impairment of verbal (1), memory (2), and global memory (3)

SEMIOLOGY :

Most common seizure semiology noted was focal seizures with impaired awareness noted in 67 patients (95.7%); focal seizures with intact awareness was noted in 4 patients (5.7%).

Generalised seizures were noted in 42 patients (60%). 4 patients had prior history of status epilepticus (5.6%)

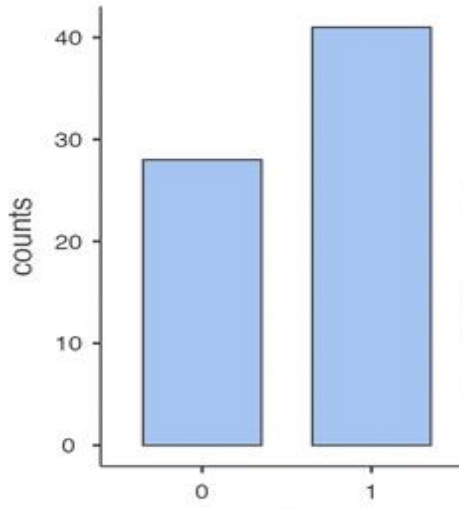


Figure.7: Bar diagram depicting the proportion of patients with generalised seizures

SEMIOLOGICAL DATA:

The most common aura noted was the aura of fear in 22 patients (31%) followed by epigastric aura in 10 patients (14.1%); followed by cephalic aura in 8 patients(11.3%); visual aura in 8 patients (11.3%); somatosensory aura in 6 patients(8.5%) ; and auditory aura in 5 patients(7%). Versive manifestations were seen in 20 patients (33.3%) . Oroalimentary automatisms were seen in 38 patients (57.6%), and gestural automatisms were noted in 14(21.2%) patients. The mean seizure score was 7.77 +/- 0.74.Majority of the patients had high seizure frequency with weekly to daily frequency noted in 38 patients (62.3%); monthly frequency noted in 23 patients (37.7%).

IMAGING :

51 patients had an underlying structural lesion (72.9%), whereas 19 patients had no underlying structural lesion (27.1%). The most common structural lesion identified was Mesial temporal sclerosis in 39 patients (55.7%), followed by gliosis in 8 patients (11.4%), focal cortical dysplasia in 4 (5.7%).

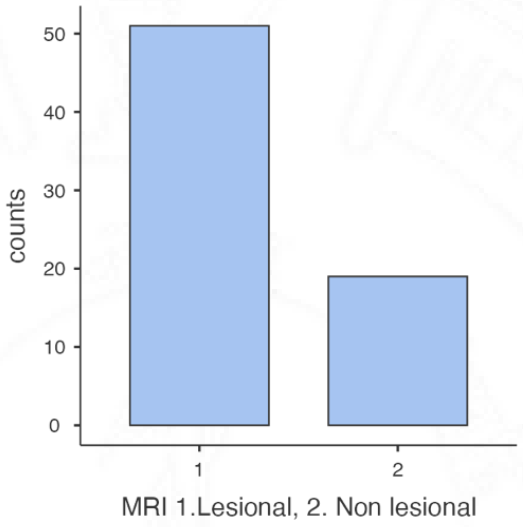


Figure. 8: Bar diagram depicting the proportion of patients with lesional epilepsy.

LESION	No.of patients	% of Total
Focal cortical dysplasia	4	5.7 %
Mesial temporal sclerosis	39	55.7 %
Gliosis	8	11.4 %
Arteriovenous malformation	1	1.4 %
Normal	18	25.7 %

Table. 1: Distribution of the type of structural lesion.

VEEG data:

All the patients underwent prolonged VEEG recording for presurgical evaluation. Interictal epileptiform abnormalities were unilateral in 29 patients (46%) and bilateral in 34 patients (54%). Focal slowing was noted in 39 patients (63.9%). The most common site of ictal noted was temporal onset in 40 patients (66.7%), extratemporal in 5 patients (8.3%), hemispherical in 8 patients (13.3%), and diffuse/uncertain in 6 patients (10%).

ICTAL PATTERNS – VEEG:

The most common ictal pattern observed was rhythmic theta in 47 patients (83.9%); followed by low voltage fast activity in 4 patients (7.1%) ; followed by delta in 3 patients (5.4%)

PATTERNS OF TLE:

Mesial patterns were more commonly seen than lateral ones. Among the temporal plus, orbitofrontal was seen in 3 (5.8%) patients, followed by temporoparietooccipital in 4(7.7%); and insular in 1 patient (1.9%).

TEMPORAL PATTERN -	Counts	% of Total
MESIAL	36	65.5 %
LATERAL	7	12.7 %
TEMPORAL PLUS	8	7.3 %

Table 2 Patterns of TLE

INVASIVE MONITORING:

All the patients underwent invasive monitoring. The most common cause for invasive monitoring was bitemporal epileptogenicity in 24 (40%), followed by non-lesional in 11 patients (18.3%) and temporal plus in 7 (11.7%) patients.

INVASIVE EEG REASON	Number of patients	% of Total
Bitemporal	24	40.0 %
Temporal plus	7	11.7 %
Dual pathology	3	5.0 %
Discordant data	5	8.3 %
Wasted Hippocampal syn	5	8.3 %
Non lesional	11	18.3 %
Better delineation	5	8.3 %

Table. 3. Rationale for invasive EEG

Forty-one patients underwent bilateral hippocampal depth monitoring (68.3%), followed by subdural in 12 patients (20%), combined subdural and depth electrode in 6 patients (10%), and stereo EEG in 1 patient.

IRRITATIVE ZONE:

The most common irritative zone pattern identified was rhythmic spikes in 43 patients (95.6%); followed by low voltage fast activity in 16 patients (36.4%), high amplitude polyspikes in 7 patients (15.9%), High frequency oscillations (HFOs) in 2(4.5%) and fast ripples in 2 patients(4.5%); pathological delta in 2 patients (4.6%).

ICTAL PATTERN

The most common ictal pattern identified was LVFA in 42 patients (82.4%); followed by rhythmic spikes in 21(41.2%) patients, theta pattern in 9 (17.6%) patients, low-frequency periodic spikes in 8 (15.7%) patients followed by bursts of high amplitude spikes in 4(7.8%) patients; delta rhythm in 2(3.9%) and diffuse attenuation in 3 (5.9%).

ICTAL ONSET PATTERNS	Number of patients	% of Total
LVFA	29	55.8 %
LFPS	8	15.4 %
SHARP wave activity	1	1.9 %
Rhythmic spikes	12	23.1 %
High amplitude polyspikes	1	1.9 %
Theta rhythmic	1	1.9 %

Table 4: Patterns of ictal onset

YIELD OF INVASIVE MONITORING:

Definite epileptogenic zone was identified in 51 patients , of which 50 (79.4%) underwent resective surgery ; 1 patient was not offered surgery , as he went into remission with ASM.The final epileptogenic zone was congruent to initial hypothesis in 19 patients (35.2%); non congruent to initial hypothesis in 17(31.5%) ; and novel in 18 patients (33.3%). Thus the yield of invasive EEG monitoring in amounts to about 79.4%.

Resective surgery was done in 50 (79.4%) patients; 39 (86.7%) patients underwent Anterior temporal lobectomy+ amygdalohippocampectomy; lesionectomy in 6 (13.3%) patients.

Electrocorticography:

In 35 patients; a post resection ECoG was obtained ; which showed rare residual spikes in 11(31.4%)patients and frequent spikes in 6 (17.1%) patients.

Histopathology:

Resected specimens were subjected to histopathological analysis. Histopathology was normal in 4 patients (8.9%), non-specific gliosis in 8 (17.8%) patients, hippocampal sclerosis in 31(68.9%)patients and LEATs in 2 patients (4.4%)

OUTCOME:

The outcome was assessed using Engels' outcome at 1 year of age . Class I and II Engels outcomes were considered as good outcomes; class III and IV had poor outcomes. Good surgical outcome was noted in 22 (62.9%) patients.

VARIABLES ASSOCIATED WITH SEIZURE OUTCOME :

Presence of somatosensory aura(p=0.018) , history of generalised seizures(p=0.042) and presence of status epilepticus(p=0.05) were associated with poor surgical outcome.

In addition, the presence of structural lesions was shown to be associated with good surgical outcomes (p=0.036), whereas the type of structural lesion did not show any association with surgical outcomes.

On analysing electrophysiological data on long-term VEEG, the ictal pattern of delta was associated with poor surgical outcome (p = 0.029). In the invasive data, the irritative zone pattern of high amplitude polyspikes was shown to be associated with poor surgical outcomes (p=0.036). The type of ictal pattern did not show any statistical significance with regard to outcome, although LVFA was shown to be associated with good outcome, not statistically significant.

The type of histopathological diagnosis did not affect the surgical outcome. There was no role of ECoG-guided resection in the patients who underwent resective surgery after invasive monitoring in our cohort.

Table.5: variables associated with surgical outcome				
VARIABLE		**GOOD OUTCOME**	**POOR OUTCOME**	**P Value**
Gender	**Males**	14 (63.6%)	8 (36.4%)	0.412
	Females	8 (66.7%)	4(33.3%)	
Age at presentation		27.9+/-9.59	13+/-10.5	0.421
Age of onset		8.49+/- 5.31	9.59+/-5.66	0.473
Aura	**Epigastric**	6(75%)	2(25%)	0.418
	Fear	9 (42.9%)	4(28.6%)	0.392
	Somatosensory	0	3(100%)	**0.018**
	Auditory	1(25%)	3(75%)	0.096
	Visual aura	2(50%)	2(50%)	0.572
Semiology	**Oroalimentary**	12(66.7%)	6(33.3%)	0.435
	Gestural	5(62.5%)	3(37.5%)	0.900
	Versive	5(45.5%)	6(54.5%)	0.216
Memory	**Verbal**	6(54.5%)	5(45.5%)	
	Visual	1(100%)	0	0.662
	Both	5(62.5%)	3(37.5%)	
Generalised seizures		12(52.2%)	11(47.8%)	**0.042**
Status epilepticus		0	2(100%)	**0.05**
MRI	**1.Lesional**	20(71.4%)	8(28.6%)	
	2.Non lesional	2(28.6%)	5(71.4%)	**0.036**
IEDS-VEEG	**TEMPORAL ONLY**	18(62.1%)	11(37.9%)	
	EXTRATEMPORAL	3(60%)	2(40%)	0.930

Ictal pattern - VEEG	**Theta -Rhythmic**	16(64%)	9(36%)	0.141
	LVFA	1(50%)	1(50%)	0.798
	DELTA	0	3(100%)	**0.029**
IRRITATIVE	**Rhythmic spikes**	13(54.2%)	11(45.8%)	0.141
	High amp polyspikes	0	4(100%)	**0.036**
	LVFA	5(50%)	5(50%)	0.87
	HFOs	1(50%)	1(50%)	0.95
	Fast ripples	0	1(100%)	0.327
ICTAL Pattern	**LVFA**	15(65.2%)	8(34.8%)	0.064
	LFPS	2(50%)	2(50%)	0.755
	Rhythmic spikes	5(45.5%)	6(54.5%)	0.315
	Burst of high amplitude polyspikes	1(50%)	1(50%)	0.832
	Theta	3(75%)	1(25%)	0.436
	Delta	1(100%)	0	0.378
Residual spikes	**Rare**	5(62.5%)	3(37.5%)	
	Frequent	3(75%)	1(25%)	0.486
HPR	**Normal**	1(50%)	1(50%)	0.901
	Non-specific gliosis	2(50%)	2(50%)	
	Hippocampal sclerosis	15(65.2%)	8(34.8%)	
	LEATs	1(50%)	1(50%)	

PREDICTORS OF SEIZURE OUTCOME:

Multivariate analysis however showed that only non-lesional MRI (P=0.036); presence of generalized seizures (0.05) were independent predictors of seizure outcome ; rest of the variables which were statististically significant in univariate analysis lost their significance on applying the logistic regression model.

DISCUSSION

Demographic and Clinical Characteristics:

This study evaluated 70 patients with temporal lobe epilepsy (TLE) who underwent invasive monitoring. The mean age at presentation was 27.5 years, with an average epilepsy onset at 10.4 years. This is consistent with prior studies reporting early seizure onset in TLE, which is common and associated with a more severe course of epilepsy (Engel et al., 2003; Lyu et al., 2018). Our cohort also showed a male predominance (64.3%), which aligns with the findings of other studies indicating a slightly higher prevalence of TLE in males (Sander et al., 1996; Lyu et al., 2018).

Antecedents identified in our cohort included febrile seizures (28.6%), meningoencephalitis (8.6%), and trauma (4.3%). These are commonly reported risk factors for TLE (Muller et al., 2001), with febrile seizures being particularly strongly linked to temporal lobe epilepsy (Annegers et al., 1995). The presence of psychiatric comorbidities, such as interictal psychosis (21.1%) and global developmental delay (4.3%), is notable. These psychiatric conditions complicate the management and prognosis of TLE patients and have been linked to poorer post-surgical outcomes (Murray et al., 2011).

Seizure Semiology and Localization

The semiology of seizures in our cohort was predominantly focal with impaired awareness (95.7%), followed by generalized seizures (60%). These findings align with other studies that report focal seizures as the most common semiological manifestation of TLE (Moran et al., 2001). The high prevalence of generalized

seizures observed here suggests multifocal or bilateral epileptogenic activity, which can complicate surgical management (Engel, 1996).

Auras, particularly fear (31%) and epigastric sensations (14%), were also frequently reported. These are typical of temporal lobe seizures, with fear often linked to seizures originating from the amygdala and epigastric sensations associated with hippocampal or mesial temporal involvement (Duncan, 1997). The presence of somatosensory auras, which can indicate a more widespread epileptogenic network, may suggest poorer surgical outcomes (Haneef et al., 2012). This highlights the importance of considering seizure semiology as a diagnostic tool in surgical planning (Mohanraj et al., 2006).

Imaging Findings:

Structural imaging in our cohort revealed identifiable lesions in 72.9% of patients, with mesial temporal sclerosis (MTS) being the most common finding (55.7%). This is consistent with existing literature, which identifies MTS as the most common structural abnormality in TLE and a key predictor of favorable surgical outcomes (Thom et al., 2005). MTS is often associated with higher rates of post-surgical seizure freedom, particularly when confined to one temporal lobe (Engel, 2001).

In contrast, 27.1% of patients in our study had no visible structural lesions on conventional MRI, which is a common challenge in TLE. Non-lesional epilepsy is frequent in TLE patients, and such cases often require advanced imaging techniques, such as functional MRI and PET, to identify areas of functional abnormality that might not be visible on structural scans (Keller et al., 2009). For these patients, invasive monitoring becomes essential to accurately localize the epileptogenic zone.

VEEG Findings

Prolonged video-EEG (VEEG) monitoring plays a central role in the pre-surgical evaluation of TLE patients. In our cohort, VEEG revealed unilateral interictal abnormalities in 46% of patients and bilateral abnormalities in 54%, reflecting the complexity of TLE. Bilateral abnormalities are common in TLE and can complicate the surgical decision-making process (Stefan et al., 2000). The ictal patterns observed in our cohort were predominantly temporal in origin (66.7%), which is typical for TLE and underscores the role of mesial temporal structures in seizure onset and propagation (Lhatoo et al., 1999).

The most common ictal pattern observed was rhythmic theta activity (83.9%), which is consistent with findings from other studies (Iwasaki et al., 2013). However, low-voltage fast activity (LVFA) was found in 7.1% of patients. LVFA is often associated with more refractory epilepsy and poorer surgical outcomes (Thom et al., 2010). However, no such association was noted in our cohort, suggesting that factors such as the location of the epileptogenic zone or structural abnormalities may play a more significant role in surgical success.

Our study also found an association between delta ictal patterns and poorer surgical outcomes ($p = 0.029$), which is consistent with the literature suggesting that delta activity may reflect more widespread or multifocal epileptiform networks that are harder to resect effectively (Tassi et al., 2012).

Invasive Monitoring and Diagnostic Yield

Invasive monitoring was performed in 79.4% of our cohort, yielding a definitive epileptogenic zone in the majority of patients. This finding is consistent with previous studies that report high diagnostic yields with invasive monitoring, especially in patients with bitemporal or non-lesional epilepsy (Ochi et al., 2002). The most common reason for invasive monitoring in our cohort was suspected bitemporal epileptogenicity (40%), a common challenge in TLE that requires advanced techniques to differentiate between unilateral and bilateral temporal lobe seizures.

Bilateral hippocampal depth electrodes (68.3%) were the most commonly used technique for invasive monitoring, which is consistent with practices in other centers (Hassan et al., 2011). Importantly, 33.3% of patients in our cohort had novel epileptogenic zones identified after invasive monitoring, highlighting the value of this technique in refining surgical planning and confirming the location of the epileptogenic focus (Engel, 1996).

Surgical Outcomes

Seventy-nine percent of our cohort underwent resective surgery, with 62.9% achieving good outcomes (Engel class I or II). This is consistent with the findings of other studies on temporal lobectomy, where approximately 60-80% of patients achieve favorable outcomes (Wiebe et al., 2001). The high success rate of anterior temporal lobectomy (86.7% of surgeries) in our cohort further emphasizes the importance of this procedure as the gold standard for surgical treatment of TLE, particularly in patients with MTS (Rosenow & Lüders, 2001).

Several variables were identified as significant predictors of poorer surgical outcomes. The presence of somatosensory aura ($p = 0.018$), generalized seizures ($p = 0.042$), and status epilepticus ($p = 0.05$) were all associated with poor outcomes, supporting the notion that more complex seizure semiology, which may indicate a more diffuse epileptogenic network, is linked to less favorable surgical results (Tellez-Zenteno et al., 2005). Conversely, the presence of structural lesions, especially MTS, was associated with better surgical outcomes ($p = 0.036$), consistent with prior studies that emphasize the role of identifiable structural abnormalities in predicting surgical success (Thom et al., 2005).

Interestingly, the type of histopathological diagnosis did not significantly affect surgical outcomes in our cohort. This contrasts with other studies, where the presence of hippocampal sclerosis is consistently linked to better outcomes (Tassi et al., 2012). This discrepancy may be due to the relatively small sample size or the multifactorial nature of surgical outcomes in TLE.

Electrophysiological Data and Histopathology

Invasive EEG revealed rhythmic spikes as the most common irritative zone pattern (95.6%), and LVFA was the most common ictal pattern (82.4%). High-amplitude polyspikes were associated with poorer surgical outcomes ($p = 0.036$), supporting the idea that more complex and widespread epileptiform activity is less likely to be amenable to resection (Morrell, 2006). The lack of a significant relationship between histopathological diagnosis and surgical outcome suggests that electrophysiological data may be a more reliable predictor of surgical success in TLE (Tellez-Zenteno et al., 2005).

SUMMARY AND CONCLUSIONS

1. Invasive monitoring plays a critical role in the surgical treatment of temporal lobe epilepsy, particularly in patients with non-lesional or bitemporal epilepsy.
2. This study suggests that seizure semiology, imaging results, and electrophysiological patterns contribute to surgical decision-making.
3. We have demonstrated a high yield of invasive monitoring in temporal lobe epilepsy, constituting about 80%
4. The study also demonstrated good surgical outcomes in patients who underwent resective surgery.
5. Invasive data showed that irritative zone patterns, such as high-amplitude polyspikes, were associated with worse surgical outcomes, whereas ictal patterns, like LVFA, were associated with good surgical outcomes.
6. The presence of structural lesions remains a key predictor of favourable surgical outcomes.
7. Ultimately, invasive monitoring remains indispensable for refining surgical planning and improving outcomes in TLE patients.

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ANNEXURES

Curriculum Vitae

Proforma

Ethics committee approval

CV OF PRINCIPAL INVESTIGATOR

Last Name K YALAPALLI	First Name MANISHA	Middle Name
Date of Birth (dd/mm/yy) 09/12/1990		Sex FEMALE
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Academic Qualifications (Most recent qualification first)

Degree/Certificate	Year	Institution, Country
DM NEUROLOGY	2023	SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, KERALA, INDIA
MD GENERAL MEDICINE	2020	KURNOOL MEDICAL COLLEGE, Dr.NTR UNIVERSITY OF HEALTH SCIENCES,ANDHRA PRADESH INDIA
MBBS	2013	KURNOOL MEDICAL COLLEGE, Dr.NTR UNIVERSITY OF HEALTH SCIENCES,ANDHRA PRADESH INDIA

Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration

ANDHRA PRADESH MEDICAL COUNCIL
REGISTRATION NUMBER: APMC/FMR/88336
YEAR OF REGISTRATION: 2014
TRAVANCORE MEDICAL COUNCIL REGISTRATION : 83506

Current and previous positions (most recent position first)

Month and Year	Title	Institution/Company, Country
JANUARY 2024	POST DOCTORAL FELLOW IN EPILEPSY	SCTIMST, INDIA
JANUARY, 2021-DECEMBER 2023	SENIOR RESIDENT, NEUROLOGY	SCTIMST, INDIA
MARCH 2017 –	SENIOR RESIDENT, GENERAL MEDICINE	KURNOOL MEDICAL COLLEGE ,KURNOOL,ANDHRA PRADESH

AUGUST 2020		

Brief summary of relevant research experience:

CONFERENCE PRESENTATIONS

- "Genotype -Phenotype correlates of monogenic focal epilepsies in an Indian Cohort " at IANCON 2024 – Received the Deepak Arjundas- AV Srinivasan award for Best paper in Neurogenetics
- "Best award paper in General Neurology at IANCON 2023 for the study titled "Prevalence and patterns of cognitive impairment in Amyotrophic Lateral Sclerosis and Correlation with the Outcome."
- "Thrombus Histology – Correlation with stroke aetiology and recanalization" at KAN monsoon summit, International Neurology update, 2023 – BEST PAPER AWARD
- World stroke congress 2023, TORONTO, CANADA for the study titled "Thrombus Histology – Correlation with stroke aetiology and recanalization" – YOUNG INVESTIGATOR AWARD
- WORLD STROKE CONGRESS 2022 , SINGAPORE for the study titled "Prevalence, Predictors and Outcome of Stuttering Lacunar Strokes" – YOUNG INVESTIGATOR AWARD
- "Gelastic seizures beyond hypothalamic hamartomas- Predictors of outcome" – ECON 2023
- Study titled "Prevalence, Predictors and Outcome of Stuttering Lacunar Strokes" at Travancore Neurocon 2022- BEST AWARD PAPER
- Award paper presentation under neurogenetics in AOCN- IANCON 2022 for the study titled "Diagnostic Utility of Next generation Sequencing in Leukodystrophies and genetic leukoencephalopathies"
- International bursary award for international child neurology conference 2024 to be held in Capetown -2024 for project titled "Gelastic seizures beyond hypothalamic hamartomas- Predictors of outcome
- Paper presentation : etiology and clinical profile of pregnancy related acute Kidney injury ;APICON guntur 2019
- Poster presentation: an unusual cause of gross hematuria ;APICON guntur 2019

PUBLICATIONS IN JOURNALS

1. Manisha KY, Varma R, Sylaja PN, Sreedharan SE. Progressive lacunar strokes behave differently from stable ones even at one year—An observational study. Journal of Stroke and Cerebrovascular Diseases. 2023;32(12):107434. doi: 10.1016/j.jstrokecerebrovasdis.2023.107434

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3. Manisha KY, Fasaludeen A, Poulose P, Menon R, Thomas B, Nair SS, Cherian A, Divya KP, Sundaram S. Spectrum of Leukodystrophy and Genetic Leukoencephalopathy in Indian Population Diagnosed by Clinical Exome Sequencing and Clinical Utility. Neurol Genet. 2024 Aug 22;10(5):e200190. doi: 10.1212/NXG.0000000000200190. PMID: 39184309; PMCID: PMC11343561.

4. Vysakha KV, Jain K, Nandana J, Manisha KY, Menon RN, Vilanilam G, Abraham M, Thomas B, Kesavadas C, Radhakrishnan A. Do we have to continue antiseizure medications post-surgery in long-term epilepsy associated tumors (LEATs)? Clin Neurol Neurosurg. 2024 Sep;244:108433. doi: 10.1016/j.clineuro.2024.108433. Epub 2024 Jul 5. PMID: 38991393.

5. Diagnostic Utility Of Magnetic resonance Imaging In Autoimmune Encephalitis – Prognostic Implications Narayanan Nambiar, Poornima* ; Manisha, K Y*; Nandana, Jayakumari; Ramshekhar N Menon; Vinayagamani, S.; Thomas, Bejoy; Radhakrishnan, Ashalatha*Both authors contributed equally for the work- Accepted in Acta radiologica

6. Developmental and epileptic encephalopathy due to CDKL5 deficiency - a single centre experience across the gender spectrum- Alfiya Fasaludeen PhD scholar1*, Ramshekhar N Menon DM1*, Manna Jose PhD1, Adarsh Anil Kumar MD2, KY Manisha DM1, Ashalatha Radhakrishnan MD, DM1, Soumya Sundaram DM3- Journal of paediatric neurology – review

7. Mapping of Heschl's gyrus aids in planning successful surgery in "TLE with auditory aura- Ashalatha Radhakrishnan¥, Anuvitha Chandran, Manisha KY,Nandana J,Ramshekhar N Menon,Bejoy Thomas, Chandrashekharan Kesavadas, George Vilanilam, Mathew Abraham -Under review -JOurnal of clinical neuroscience

8. Manisha KY, Nair SS, Kumar AA, Sundaram S. Brown's syndrome: a rare cause of vertical diplopia. Pract Neurol. 2024 Apr 8:pn-2023-004028. doi: 10.1136/pn-2023-004028. Epub ahead of print. PMID: 38589214.

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10. Paramasivan NK, Yallapalli MK, Sundaram S, Vijayaraghavan A, Sukumaran S. Hypomagnesemia induced encephalopathy with transient torsional nystagmus evolving into downbeat nystagmus: a rare complication of ileostomy. Acta Neurol Belg. 2023;123(4):1545-1547. doi:10.1007/s13760-022-01997-y

11. Nandana J, Manisha KY, Surabhi P, Veena S, Koshy KG, Menon RN, Radhakrishnan A. Teaching Video NeuroImage: Noogenic Epilepsy With Orofacial Reflex Myoclonus: A Rare Distinct Electroclinical Syndrome. Neurology. 2024 Dec 10;103(11):e210045. doi: 10.1212/WNL.0000000000210045. Epub 2024 Nov 4. PMID: 39496103.

12. Prasannakumar Surabhi, Lakshmi J Nair, Jayakumari Nandana, Karamala Yalapalli Manisha, Ramshekhar N. Menon, Ashalatha Radhakrishnan. A rare genetic association of one silent (ADGRV1) and other unquiet (MED13L) mutation: A case report. Advanced Neurology 3602. https://doi.org/10.36922/an.3602

13. ROWELL'S SYNDROME-A RARE CLINICAL ENTITY,INDIAN JOURNAL OF APPLIED RESEARCH, VOLUME 10, ISSUE 2, FEBRUARY, 2020

DM DISSERTATION

Prevalence and patterns of cognitive impairment in Amyotrophic lateral sclerosis and correlation with outcome

MD DISSERTATION

A STUDY OF CLINICAL PROFILE OF HYPERTENSIVE EMERGENCIES IN A TERTIARY CARE INSTITUTE

Current project/s at hand:

- Phenotypic-Genotypic Spectrum of epilepsy with myoclonic atonic seizures in an Indian cohort
- Genotype- Phenotype Correlates of Drug Resistant Epilepsy related sodium channelopathies in an Indian Cohort
- Gelastic seizures beyond hypothalamic hamartomas – prevalence, predictors of outcome .

Signature: 	Date: 30.12.2024 Place: Thiruvananthapuram, Kerala

CV of Guide

Last Name: **Radhakrishnan**	First Name: **Dr Ashalatha**	Middle Name
Date of Birth (dd/mm/yy): 13/05/1970		Sex: Female
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator) Co- Investigator		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
Professor of Neurology, Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Medical College P.O, Thiruvananthapuram - 695011		SCTIMST, Medical College P.O, Thiruvananthapuram
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Academic Qualifications (Most recent qualification first)

Degree/Certificate	Year	Institution, Country
Fellow of American Neurological Association (FANA) Fellow of Royal College of Physicians (Glasgow) MBA(Hospital Administration & HRD)	2017 -18	The Royal College of Physicians and Surgeons of Glasgow, Scotland
Training in Stereo EEG for utilization in surgical evaluation of refractory Epilepsy	2016	Montreal, Canada
Training in EEG co-registered MRI for application in refractory epilepsy	2012	Queen Square Hospital, University College, London
Fellowship in Epilepsy & Sleep Medicine	2007- 2008	Austin Health, Melbourne, Victoria, Melbourne University, Australia (under supervision of Prof. Samuel F Berkovic and Rob J Pearce, University of Melbourne)
M.D General Medicine	1999	Govt. Medical College, Alappuzha, University of Kerala
MBBS	1994	Govt. Medical College, Alappuzha, University of Kerala

Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration: TCMC-21956/1994

Current and previous positions (most recent position first)		
Month and Year	Title	Institution/Company, Country
January 2016-continuing	Professor	SCTIMST, Trivandrum
2015-2017	Additional Professor	SCTIMST, Trivandrum
January 2009 - 2015	Associate Professor	SCTIMST, Trivandrum
June 2008 – December 2008	Consultant in Neurology(Sleep Project)	SCTIMST, Trivandrum
January 2007-May 2008	Fellowship Training in Epilepsy and Sleep Medicine	SCTIMST, Trivandrum
August 2006 – February 2007	Assistant Professor	SCTIMST, Trivandrum
June 2003 – July 2006	Ad Hoc Consultant in Neurology and Epilepsy Program	SCTIMST, Trivandrum

Brief summary of relevant research experience:

The applicant has been working as a faculty member in the Department of Neurology, Sree Chitra Tirunal Institute and Medical Sciences (an institute of national importance under the Department of Science and Technology, Govt. of India) since 2003 after completing the graduation in Neurology in the same institute. She is devoting 70% of her time in the R. Madhavan Nayar Center for Comprehensive Epilepsy Care which is the largest of its kind in the country with state of the art facilities catering to patients with epilepsy headed by Dr. Sanjeev Thomas, Professor of Neurology and a renowned epileptologist. During this period she has focused in the evaluation and management of medically refractory epilepsy and its surgical management by developing new neuroimaging techniques like functional MRI-coregistered EEG, diffusion tensor imaging and fiber tracking, voxel based morphometry etc related to epilepsy.

Functional MRI-EEG coregistration technique aids in the pre-surgical workup of epilepsy patients when other investigation tools fail to localize the area of epileptogenic focus. Dr Ashalatha along with her colleagues in Neuroradiology and Biomedical technology wing standardized the procedure of EEG-fMRI for the first time in the country which is now in the process of being utilized in the field of pre-surgical evaluation of refractory cases of epilepsy.

In conventional MRI negative epilepsy patients, she along with computer scientists has developed newer computational software for detection of subtle cortical dysplasia by a method called voxel based morphometry (VBM) which was presented for the first time from India in the International Conference on Epilepsy at Melbourne, Australia in October,2010. Newer sequences have been applied for the clinical problem. These methods are now going to be utilized for the detection of such subtle lesions like focal cortical dysplasias which may aid the epileptologist to proceed with better treatment for epilepsy.

The applicant has also applied advanced neuroimaging protocols such as diffusion tensor imaging with fiber tracking of white matter tracts aiding in the mapping of white matter tracts in the pre-surgical evaluation of patients with epilepsy. This will aid the surgeon to plan out his surgery at or close to eloquent areas in order to avoid untoward complications like hemiparesis, speech difficulty etc which are the major hindrances in selection of candidates for brain surgery. This work is not being done in any other parts of the country and author won the Young Investigator award for this pioneering work at the 100th International Congress of Epilepsy at Budapest, Hungary in

2009.

Current project/s at hand:

1. Multimodal imaging in pre surgical evaluation of extra temporal lobe epilepsy-(PI)
2. Utility of 3D pseudo continuous ASL perfusion in pre- surgical evaluation of focal temporal and Extratemporal epilepsy -(Co- PI)
3. Prevalence of sleep disordered breathing (SDB) in children with attention deficit hyperactivity disorder (ADHD) and its response to treatment in school going children in Thiruvanathapuram district-(PI)
4. A genetic association for severe hyponatremia and central pontinemyelinolysis-(PI)
5. Genome-Wide Association and Blood Marker study in Narcolepsy and Hypersomania-(PI)
6. Association of Pulmonary arterial hypertension (PAH) and cardiac arrhythmias in patients of Obstructive sleep apnea (OSA) and possible therapeutic benefit with CPAP treatment-(PI)
7. Clinical profile and outcome in patients with autoimmune encephalitis-(PI)
8. Global audit of treatment of refractory Status Epilepticus-(PI)
9. Development of intracranial electrodes for use in acute and chronic electrocorticography-(Co-PI)
10. Indigenous Intracranial electrode manufacture (TRC) – (DST Funded) - (Co–PI)
11. Model the effect of Mutations of HCN Channels in Neuronal Excitability and impact of GABABR on GIRK and HCN mutations using NEURON - (DBT Funded) – (Co-PI)
12. Validation of memory fMRI paradigms and its utility in pre-surgical evaluation of patients with refractory TLE – (Co-PI)
13. A resting state fMRI and task based fMRI study: Optimization, language lateralization, memory lateralization and connectivity in normal subjects versus patients with epilepsy - (DBT Funded) – (Co_PI)

Signature:	Date: 03/08/2019 Place: Thiruvananthapuram

CV of Co-Guide

Last Name: Menon	First Name: Ramshekhar	Middle Name: N
Date of Birth (dd/mm/yy) 25/09/1978		Sex M
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator) Co Investigator		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
Epilepsy Office, 4th floor , Block 2, SCTIMST, Trivandrum-11		Department of Neurology, SCTIMST, Trivandrum 11
Telephone (Office): 0471- 2524481		Mobile Number: 9946916769
Telephone (Residence):0471- 2734040		Email: rsnmenon@sctimst.ac.in

Academic Qualifications (Most recent qualification first) Epilepsy Fellowship, DM, DNB, MD, MBBS

Degree/Certificate	Year	Institution, Country
MBBS	2002	University of Pune, India
MD, DNB Medicine	2006	University of Mumbai, India
DM Neurology	2009	Maharashtra University of Health Sciences, India
Epilepsy Fellowship	2010	SCTIMST

Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration- TCMC- 30958/2002

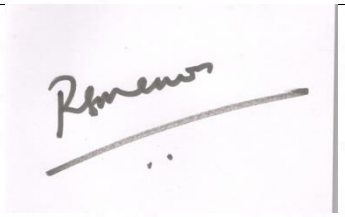
Current and previous positions (most recent position first) Professor, Department of Neurology

Month and Year	Title	Institution/Company, Country
2022- Till Now	Professor	SCTIMST
2017-2022	Additional Professor	SCTIMST
2015-2017	Associate Professsor	SCTIMST
2011-2015	Assistant Professor	SCTIMST

Brief summary of relevant research experience:
Research and clinical experience in epilepsy, cognitive neurology, autoimmune disorders, status epilepticus and general neurology
No. of publications and book chapters: 61
No. of extramural funded projects: 15

Current project/s at hand:

1) PI: Effect of yoga on neuropsychological functions and brain connectivity networks in mild cognitive impairment and cognitively normal subjects.3 years. Commenced on 30/07/2016; Status ongoing.
2) Project PI: The influence of sleep architecture on the severity of memory disruption in amnestic MCI- Funded by Kerala State Council for Science, Technology and Environment. INR 8,41,500. Status completed in November 2016.
3) Project PI: Validation of memory fMRI paradigms and its utility in pre-surgical evaluation of patients with refractory TLE. Funded by Department of Science & Technology. INR 14,85,000. Status- completed on 31/03/2017
4) Site Project PI: Development and validation of a comprehensive clinical and neuropsychological test battery for use in the Indian context for patients with Vascular Cognitive Impairment. Funded by ICMR. INR 14,00,000. Status completed on 31/12/2015
5) Project PI: The human brain mapping project- a resting state fMRI study of healthy controls and patients with MCI & AD. Funded by cognitive science initiative of DST. INR 18, 77,600. Status ongoing.
6) Technology development- Site Project PI: Biomedical signal analyzer for seizure prediction, in collaboration with Centre for development of Advanced Computing, Trivandrum. Funded by Department of Electronics & Information Technology. INR 4,62,000 out of INR 30,38,000. Commenced on 30/06/2014. Pilot phase completed on 30/06/2015
7) Collaboration with BMT wing projects- Development of intracranial electrodes for use in acute and chronic electrocorticography for periods up to 15 days.- Clinical PI
8) Co-PI: Non-linear analysis of EEG signals in Alzheimer's Disease through DST funding provided to collaborating centre, NIT Kozhikode. Commenced on 04/07/14. Status completed on 30/06/2015
9) Co-PI: Biochemical and functional investigation of dorsolateral prefrontal cortex in mild cognitive impairment using functional magnetic resonance spectroscopy and functional magnetic resonance imaging. Commenced on 2/7/2016;INR 14,40,000 (DST-SERB); status completed on 01/07/2018.
10) Co-PI: A resting state fMRI and task based fMRI study: Optimization, language lateralization, memory lateralization and connectivity in normal subjects versus patients with epilepsy. Commenced on 1/7/2014; Status Ongoing; DBT
11) Co-investigator: In vitro beta-amyloid uptake by peripheral blood macrophages: predictor for progression of mild cognitive impairment to Alzheimer's disease. Commenced on 1/3/2015; ICMR- Rs. 40,99,400; Status Ongoing.
12) Co-investigator: Study of genetic risk factors associated with inflammation, autophagy and oxidative stress in Alzheimer's Disease and Frontotemporal Dementia; DST-SERB Postdoc fellowship- INR 19,20,000



Signature:
Ramshekhar N Menon

Date: 10/5/2020
Place: Trivandrum

PROFORMA

- Subject ID No:
- Age: Sex: Age of presentation: Age at diagnosis:
  Mobile no:
- Weight: Handedness
- Family History:
- **Clinical data:**
- Antecedents-
- Aura – Epigastric/ Fear/ auditory /Gustatory hallucinations/ Vertigo/ visual/somatosensory
- Seizures – Aura only, Focal sz with intact awareness, impaired awareness, generalization
- Versive manifestations/ gestural automatisms/ Hypermotor
- Localisation/ Lateralisation
- Seizure score
- ASM- Current / previous/ Best response
- Red flags

- Clinical diagnosis- Temporal. – MTLE Vs non MTLE
  Temporal / Temporal Plus / Extratemporal
- Neuropsychology- Verbal vs visual memory / inconclusive
- **VEEG**
- Duration of monitoring -
- Interictal data-
- IEDS- Temporal / ratio / unilateral / bilateral/ Frontal/ Parietooccpital/ precentral
- Ictal data – Rhythm type – temporal/ Extratemporal/ hemispherical/ diffuse / uncertain
- Localisation and lateralization –

IMAGING - MRI

- MTS
- Temporal neocortex
- FCD
- AV malformations
- Dual pathology

- Unilateral vs Bilateral
- ASL-
- PETCT –
- Concordance of data

INVASIVE EEG

- Reason – Bitemporal epileptogenesis, Dual pathology, Non lesional, Discordant data,wasted hippocampal syndrome, better delineation
- Type – subdural/ Depth/ Stereo/combined
- Number of electrodes -
- Ictal onset zone – Temporal – Hippocampus/ Neocortex/ Insula/ Orbitofrontal/ cingulate ; Extratemporal
- Ictal onset Patterns-
- Type 1- LVFA
- Type 2 - low frequency periodic spikes
- Type 3- Sharp waves
- Type 4 – Rhythmic spikes
- Type 5 – High amplitude burst of polyspikes
- Type 6 -Theta
- Type 7- Delta
- Type 8 – Diffuse attenuation
- Interhemispheric propagation time-
- Irritative Zone - Spikes/ Sharps/ LVFA/ HFOs/ Fast ripples
- Second irritative xone
- HFOs-
- Localisation-
- Lateralisation

Congruency to initial hypothesis-

Type –TEMPORAL - Mesial / Mesiolateral/ Lateral/ temporopolar

TEMPORAL PLUS- Orbito-frontal cortex/ the insula/ the frontal and parietal operculum / temporo-parieto-occipital junction

Extra temporal-

SURGICAL DATA

- Surgery –

- Date-
- Type of surgery –
- If deferred – Reason for surgery defferal. – Bilateral ictal onset; epileptogenic zone away from lesion, multifocal ictal onset
- Histopathology-
- Surgery outcome at 2 yrs –
- Postoperative MRI -

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee

CDSCO Registration No: ECR/189/Inst/KL/2013/RR-21
DHR Registration No:EC/NEW/INST/2022/2775

SCT/IEC/2259/JULY/2024 14.08.2024

Dr. Manisha K Yalapalli
Post Doctoral Fellow
Department of Neurology
SCTIMST, Thiruvananthapuram

Dear Dr. Manisha K Yalapalli,

The Institutional Ethics Committee held on 20th July, 2024, reviewed and discussed your application to conduct the study titled **"INVASIVE EEG MONITORING IN REFRACTORY EPILEPSY AND PREDICTORS OF SURGICAL OUTCOME (IEC /2259)"**.

Principal Investigator	Dr. Manisha K Yalapalli, Post-doctoral fellow in Epilepsy, Department of Neurology, SCTIMST
Co-Principal Investigator(s)	Dr. Ashalatha Radhakrishnan, Professor, Department of Neurology, SCTIMST Dr. Nandana J, Post-doctoral fellow in Electrophysiology, Department of Neurology, SCTIMST Dr. Ramshekhar N Menon, Professor, Department of Neurology, SCTIMST Dr. George C Vilanilam, Professor, Department of Neurosurgery, SCTIMST Dr. Bejoy Thomas, Professor, Department of IS & IR, SCTIMST Dr. C Kesavadas, Professor and head, Department of IS & IR, SCTIMST
Duration of the study	6 months

The following members of the Ethics Committee were present at the meeting held on 20th July, 2024

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. Kusuma Kumary P	M D in Paediatrics	Female	Clinician (Chairperson)	No
2.	Dr. Pradeep S	MBBS, MD	Male	Basic Medical Scientist	No
3.	Dr. Annapurna.Y	MD	Female	Basic Medical Scientist	No
4.	Dr. Indu PV	MBBS, DPM, MPhil, PhD	Female	Clinician	No
5.	Dr. Rejnish Kumar	MBBS,MD ,DNB	Male	Clinician	No
6.	Smt. Rekha Radhakrishnan	M.A (Eng.); B.Ed	Female	Lay person	No
7.	Dr. Manoj Murhekar	MD (Preventive & Social Medicine)	Male	Social Scientist	No
8.	Adv. Priya Kaimal	LLM, MBL	Female	Legal Expert	No
9.	Dr. Biju Soman	MBBS,MD, DPH, MSc, DLSHTM	Male	Basic Medical Scientist	Yes
10.	Dr. Syam K	MBBS, MD, DM	Male	Clinician	Yes
11.	Dr. Srinivas G	PhD	Male	Basic Medical Scientist (Member Secretary)	Yes

The following documents were reviewed:

1. *Responses /Amendments made based on the Reviewer's comments*
2. *Checklist Form*
3. *Covering letter addressed to the Chairman, IEC, SCTIMST dated 22.04.2024 forwarded by HOD*
4. *IEC Application Form*
5. *Research Proposal*
6. *CV of Principal Investigator and Co-PIs*
7. *Proforma*
8. *Declaration Form*
9. *SRC Recommendation Letter*

IEC Decision
The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Dr. Syam. K
Alternative Member Secretary, IEC

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST
THIRUVANANTHAPURAM