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CASE REPORT

Modern advances in epilepsy imaging used on the basis of cost: A review

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ABSTRACT

Epilepsy is a chronic neurologic condition that affects social behavior, health, the economy, and social functioning. Worldwide, an estimated 5 million people are diagnosed with epilepsy each year. More than 50 million people are reportedly affected globally. 49% of epilepsy patients live in low-to middle-income countries; in exceptional situations, this number may reach 139/100,000 people. This review provides imaging therapy used for the diagnoses which are compared according to the cost of individual imaging techniques reliable or affordable for the patient. The main tools used to evaluate patients with epilepsy are electroencephalography (EEG), and the functional imaging modalities for epilepsy are positional emission tomography, single-photon emission computed tomography (CT), tissue ablation using high-intensity focused ultrasound, deep non-invasive neuromodulation, and blood–brain barrier opening using superficial targets, focused ultrasound, magnetoencephalography (MEG), and magnetic resonance imaging (MRI). In the differential diagnosis imaging findings, the treatment of epilepsy is significantly better. By comparing the one-time cost of all imaging techniques, the three techniques mostly used are CT, MRI, and EEG. Patients may easily access and afford these imagining techniques because they are readily available at low cost which lies between 1000 and 10,000 rupees.

KEY WORDS: Blood–brain barrier, Epilepsy, Focused ultrasound, Imaging techniques, Seizure

INTRODUCTION

Worldwide, an estimated 5 million people are diagnosed with epilepsy each year.[1] Over 50 million individuals are thought to be impacted globally. 49% of epilepsy patients live in low-to middle-income countries; in exceptional cases, this number may increase to 139/100,000 people.[2,3] A seizure with a high likelihood of recurrence or a diagnosis of an epilepsy syndrome describes epilepsy, which is a chronic neurological illness.[3,4] It affects people of all ages and has an impact on the patients' and their families' social, behavioral, health, and economic well-being.[3,5] With the right care, the great majority of epilepsy sufferers are able to lead normal lives.[6] However, some people have severe co-morbidities such as mental retardation and psychiatric illnesses.[7] Epilepsy accounts for 0.3% of all fatalities globally, according to the Global Burden of Disease Study, which was carried out by various regulatory bodies such as the World Health Organization, the World Bank, and the Harvard School of Public Health with financing from the Bill and Melinda Gates Foundation.[3,8,9] This review provides imaging therapy used for the diagnoses which are compared according to the cost of individual imaging techniques reliable or affordable for the patient.

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METHODS

Imaging techniques used for detection of epilepsy

The latest advances in structural and functional imaging and post-operative approaches to improve preoperative

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identification of areas of seizure onset in patients with this disease.[3,10] The main tool used to evaluate patients with epilepsy is electroencephalography (EEG), and the functional imaging modalities for epilepsy are positional emission tomography (PET), single-photon emission computed tomography (CT), tissue ablation using high-intensity focused ultrasound, deep non-invasive neuromodulation, and blood–brain barrier (BBB) opening using superficial targets, focused ultrasound, magnetoencephalography (MEG), and magnetic resonance imaging (MRI).[3,11] These are shown in Figure 1 and the estimated cost of particular imagining technique is shown in Table 1.

Targeted ultrasonography for BBB opening

The BBB can be opened selectively to provide novel treatment options for a variety of brain conditions. This procedure combines microbubble IV administration and focused low-energy ultrasound.[11-13] Vibrating microbubbles spread the BBB-endothelial cell junctions in the ultrasonication region, and collapsing microbubbles can cause blood tissue penetration. At present, there are a number of commercial sonication methods including FDA-approved microbubble varieties as well as simulated BBB breach that enables targeted medication delivery. Moreover, the disruption of the BBB causes immunogenic reactions and promotes neurogenesis. In addition, it can alter brain activity in the nearby area, which may improve cognitive abilities.[14] The importance of imaging tools is related to the definition of blood–brain barrier targets, control of brain temperature by magnetic resonance (MR) thermometry, and control of BBB openings by Gd-DTPA-MRI as well as functional outcome can be monitored using functional MRI.[11,15] The cost of a scan is between 15,000 and 25,000 Indian rupees.

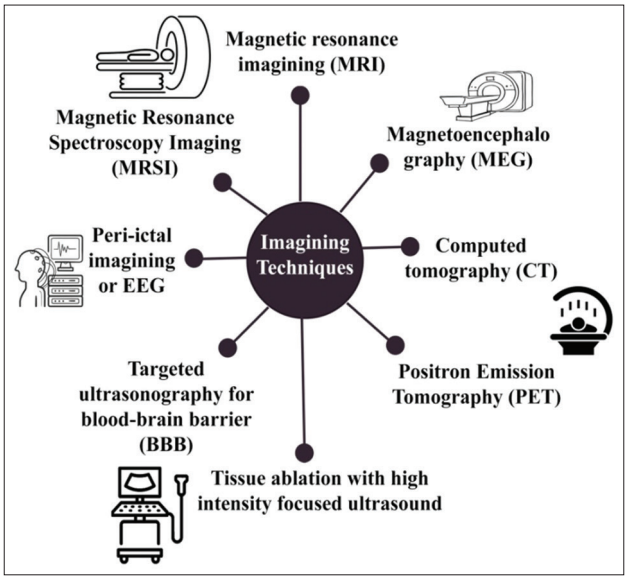

Figure 1: Types of imaging techniques used to detect epilepsy.

Table 1: Estimated cost of particular imagining technique

S. No.	Imaging technique	Estimated cost (RS)
1.	Targeted ultrasonography for blood–brain barrier opening	15,000–25,000
2.	Tissue ablation with high-intensity focused ultrasound	18,000
3.	Positron emission tomography (PET)	10,000–35,000
4.	Magnetoencephalography	12,000–18,000
5.	Magnetic resonance imagining	5000–10,000
6.	Computed tomography	2500–6000
7.	Electroencephalography	1000–3500
8.	Magnetic resonance spectroscopy imaging	13,000–14,000

Tissue ablation with high-intensity focused ultrasound (HIFUS)

The current state-of-the-art for HIFUS ablation is FDA-approved in which mechanical disruption can be seen by vibrating bubbles inherent in the target tissue.[11] The FDA has granted clinical approval for refractory essential tremor, but current investigations span a range of disorders.[16-19] A typical ablation session for essential tremor therapy is ventral internuclei of the thalamus. Imaging is an important part of new therapeutic modalities in which diffusion tensor imaging helps to define the precise neuroanatomical location of the ablation target. Functional MR imagining can be used to monitor ablation efficacy through online or longitudinal post-ablation functional monitoring. The importance of HIFUS for epileptic disorders is related to its potential to ablate the epileptogenic zone or disrupt the epileptic form network in a minimally invasive manner.[11,18,20,21] The typical cost of HIFUS treatment in India starts at Rs. 18,000 and can reach several lakhs depending on the frequency and intensity of the therapy.

Positron emission tomography (PET)

PET is a functional imaging method that tracks glucose metabolism and absorption in multiple tissues. 2-deoxy-2[18F]-fluoro-D-glucose (FDG), which is made in a cyclotron, emits gamma rays, and may pass the BBB, is the most widely used tracer.[11] A PET analyzer must identify tissue uptake, storage, and activation after intravenous administration of FDG.[22] To help epilepsy surgeons avoid having bad major and postoperative outcomes, PET gives lateralization and localization information.[22,23] PET outperforms traditional MRI in spotting modest cortical developmental abnormalities that were overlooked by MRI. Furthermore, higher seizure-free outcomes are linked to surgical excision of PET-MRI-positive regions.[24] Hybrid PET-MRI has the same sensitivity as PET-CT but has the

advantage of lower radiation exposure and absorbed dose to the brain and eyes as the images are acquired in a single session.[11] PET typically costs between Rs. 10,000 and 35,000 in India.

MEG

MEG assesses magnetic field changes resulting from bioelectrical signatures generated by excitatory and inhibitory postsynaptic potentials with greater accuracy than EEG and better temporal resolution than functional-MRI (fMRI).[11,25] High frequency compared to MEG, which must be housed in a comprehensive magnetic shield. MEG serves as an excellent electrophysiological imaging modality, extending the measurement of postsynaptic potentials and providing a broader and spatially more precise assessment of the whole brain.[26] Therefore, MEG, when available, can serve as an important clinical tool in the pre-operative assessment of epilepsy by recognizing the unique magnetic signature of epileptic form spikes to help identify epileptogenic zones.[27,28] The strength of the dipole signal is inversely proportional to the distance from the detector, the orientation to the skull, and interference from multiple sources in the brain discharges of epileptiform.[11,29] MEG is a valuable tool in high temporal resolution whole-brain neuroimaging approaches for abnormal network function in epilepsy as well as it results in using short temporal resolution that shows increased oscillatory connectivity between brain regions in the focal cortical, subcortical, and cerebellar regions during absence seizures and interictal periods.[30,31] The typical price of MEG in India is between Rs. 12,000 and Rs. 18,000.

MRI

Modern imaging based on MR has been employed largely for conditions related to high metabolic demand and conditions related to cerebral hyperperfusion during the seizure cycle. MRI examinations and demonstrated within and between subject differences associated with changes in epilepsy-induced status and baseline differences in regional cerebral blood flow have potential utility for comparison.[11,32] Perfusion MRI and diffusion-weighted imaging are indirect methods focused on imaging the correlation between supersynchronous discharges and postictal fatigue, whereas alternative attempts have focused on fMRI methods that can directly detect neuronal magnetic fields.[33] A new MRI technique using spin-lock pulses has attracted attention for its potential to detect small oscillating magnetic fields. Spin-lock experiments allow the study of contrasts in unstable proton ensembles with Larmor frequencies different from water. When synchronous magnetic fields are generated by neuronal signals during epileptic discharge, they interact with externally applied oscillating magnetic fields and attenuate the local MR signal strength. Detection of MR signal attenuation by neuronal currents requires temporal synchronization between synchronous magnetic field and image acquisition. Detection of neuronal activity can be achieved by lowering the Larmor frequency to frequencies in the high and ultrahigh range through interaction with spin-lock mechanisms.[34] Transient peri-ictal MRI abnormalities (TPMA) include signal abnormalities, vasogenic and cytotoxic edema, altered diamagnetic and paramagnetic susceptibility as well as it includes a variety of reversible brain lesions, such as abnormalities. Abnormalities in TPMA can also be visualized without gadolinium injection. Pseudo-narrowing of cortical veins has been demonstrated in association with increased regional perfusion in patients with non-convulsive status epilepticus and shows an association between decreased cortical vein deoxyhemoglobin levels and increased regional cerebral perfusion.[11,35] Typically, an MRI in India costs between Rs. 5000 and Rs. 10,000.

CT

Perfusion CT (PCT) is used to identify perfusion abnormalities in patients with persistent neurological deficits that are moderate and dependent on the time between seizure onset and scan.[11] Although diagnostic sensitivity is low due to normal perfusion or cortico-subcortical hypoperfusion and cortical hypoperfusion should be considered specific, findings of low sensitivity provide diagnostic utility.[36] PCT is used when transient ischemic attack or acute ischemic stroke is suspected.[33] Hyperperfusion with stroke-like symptoms and hypoperfusion were assessed by PCT, predominantly with persistent neurologic deficits.[34] In India, CT scanning probably costs between Rs 2500 and Rs 6000 on average.

EEG

One of the primary diagnostic procedures for epilepsy is the EEG. A test known as an electroencephalogram (EEG) uses tiny metal discs (called electrodes) connected to the scalp to measure the brain's electrical activity.[37] Electrical impulses are the primary means of communication among brain cells, which are always active – even while you are asleep. Wavy lines can be seen during this activity on an EEG recording.[38] This method is crucial for identifying further brain problems. When someone is placed in a medically induced coma, a continuous EEG is utilized to determine the appropriate amount of anesthetic. India costs from Rs. 1000 to Rs. 3500 for EEG examinations.

MR spectroscopy imaging (MRSI)

H-MRSI is an established method for studying many major metabolites in the brain. Such metabolites include the inhibitory neurotransmitters gamma-aminobutyric acid or glutamic acid, glutamine, N-acetylaspartic acid, choline, and creatinine act as an indicator of neural or cellular state as well as metabolic function.[11,39,40] The metabolites are conventionally isolated within a single region of the brain, especially medial temporal or medial

frontal regions using a relatively large single voxel MRSI in epilepsy. The application of whole-brain MRSI is to characterize metabolite changes distributed throughout the brain in epilepsy rather than specific regions. The technique, known as MRSI thermometry, can provide additional assessment of local and generalized changes in neuron inflammatory biomarkers associated with seizure initiation and maintenance in epilepsy.[41] In particular, neuroinflammation has recently emerged as an important phenomenon potentially related to neuronal hyperexcitability in epilepsy. However, in epilepsy, this technique works without tissue damage or infection, disrupting the BBB and lowering seizure thresholds by increasing hyperexcitability throughout the brain.[11,42,43] The average cost of MRSI ranges between INR 13,000 and INR 14,000 in India.

DISCUSSION AND CONCLUSION

In the differential diagnosis imaging findings, the treatment of epilepsy is significantly better. By comparing the one-time cost of all imaging techniques, the three techniques mostly used are CT, MRI, and EEG which range from 1,000 to 10,000 rupees. Patients may easily access and afford these imagining techniques because they are readily available at low cost. Targeted ultrasonography for BBB opening, tissue ablation with HIFUS, PET, MEG, and MRSI is too expensive and not within the reach of the patients. A more accurate diagnosis can be made to cure epileptic individuals if other imaging techniques lower the cost of a single scan.

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AUTHORS CONTRIBUTIONS

Dr. Amit Sharma and Mr. Hardik Kumar collected literature for this review article and writing the manuscript. Dr. Amit Sharma, Mr. Hardik Kumar, Mr. Kamaljeet, and Ms. Shilpa Debnath are major contributor in writing, analyzing, drafting, and referencing the manuscript. Dr. Amit Sharma, Mr. Hardik Kumar, and Mr. Kamaljeet are major contributor in writing and drafting the manuscript as well as all authors read and approved the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors have declared that no competing interests exist.

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