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Optimized Brain MRI Protocol for Epilepsy Diagnosis in Semarang, Indonesia: A Prospective Study

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A B S T R A C T

Introduction: Epilepsy is a prevalent neurological disorder, and accurate diagnosis is crucial for effective management. Brain MRI plays a pivotal role in identifying epileptogenic foci. This study aimed to develop and evaluate an optimized brain MRI protocol for epilepsy diagnosis in Semarang, Indonesia, where access to advanced imaging may be limited. **Methods:** A prospective study was conducted at a tertiary care hospital in Semarang. Consecutive patients with suspected epilepsy underwent brain MRI using a standardized protocol comprising T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), and susceptibility-weighted imaging (SWI) sequences. Additional sequences like diffusion-weighted imaging (DWI) and post-contrast T1-weighted imaging were acquired when clinically indicated. Two experienced neuroradiologists independently reviewed the images, and their findings were correlated with clinical and electroencephalography (EEG) data. The diagnostic accuracy, sensitivity, specificity, and inter-rater agreement of the optimized protocol were evaluated. **Results:** A total of 150 patients (mean age 32.5 years, range 18-65 years) were enrolled. The optimized protocol identified epileptogenic lesions in 75 patients (50%), with the most common being mesial temporal sclerosis (30%), followed by focal cortical dysplasia (15%), and tumors (5%). The protocol demonstrated a sensitivity of 85%, a specificity of 92%, and an inter-rater agreement of 0.85 (kappa). The addition of DWI and post-contrast imaging improved the detection of subtle lesions and differentiation between tumor and inflammation. **Conclusion:** The optimized brain MRI protocol proved to be a valuable tool for epilepsy diagnosis in Semarang, with high diagnostic accuracy and inter-rater agreement. This protocol can be implemented in resource-constrained settings to improve the detection and characterization of epileptogenic lesions, leading to better patient management and outcomes.

1. Introduction

Epilepsy, a chronic neurological disorder characterized by recurrent unprovoked seizures, poses a significant global health challenge, affecting an estimated 50 million individuals worldwide. Its impact extends beyond the individual, affecting families, communities, and healthcare systems. The burden of epilepsy is particularly pronounced in low- and middle-income countries (LMICs), where access to specialized care and diagnostic facilities may be limited. Accurate and timely diagnosis of epilepsy is crucial for initiating appropriate treatment and management strategies, which can significantly improve the quality of life for people with epilepsy (PWE). Early diagnosis allows for prompt seizure control, reducing the risk of comorbidities, such as cognitive impairment, depression, and injury. Moreover, accurate identification of the underlying cause of epilepsy enables targeted interventions, including surgery or specific anti-seizure medications, leading to better long-term outcomes.[1-3]

Brain magnetic resonance imaging (MRI) has emerged as a cornerstone in the diagnostic workup of epilepsy, offering a non-invasive and highly sensitive

means of visualizing structural abnormalities associated with epileptogenic foci. MRI can detect a wide range of lesions, including mesial temporal sclerosis, focal cortical dysplasia, tumors, vascular malformations, and post-inflammatory changes, which can all contribute to seizure generation. The diagnostic yield of brain MRI in epilepsy varies depending on the underlying etiology, imaging protocol, and expertise of the interpreting radiologist. Studies have reported detection rates ranging from 30% to 80%, with higher yields observed in patients with focal epilepsy and those undergoing dedicated epilepsy protocols. Advanced MRI techniques, such as diffusion-weighted imaging (DWI), susceptibility-weighted imaging (SWI), and magnetization transfer imaging (MTI), can further enhance the detection of subtle lesions and provide valuable information about tissue microstructure and connectivity.[4,5]

Despite the significant advances in neuroimaging, access to MRI remains a challenge in many LMICs, including Indonesia. The high cost of equipment, lack of trained personnel, and limited infrastructure contribute to the disparity in access to diagnostic services. In Semarang, the capital city of Central Java province, the availability of MRI scanners is relatively better compared to rural areas; however, challenges persist in terms of affordability and expertise. Furthermore, even when MRI is available, the optimal protocol for epilepsy diagnosis may not be standardized or readily implemented. Epilepsy protocols typically involve a combination of T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), and SWI sequences, with additional sequences like DWI and post-contrast imaging acquired when clinically indicated. However, the selection of sequences and imaging parameters can vary depending on local practices and available resources.[6-8]

In resource-constrained settings, it's imperative to develop and implement optimized brain MRI protocols that maximize diagnostic yield while remaining feasible and cost-effective. Such protocols should prioritize the detection of common epileptogenic lesions while minimizing the acquisition time and complexity. They should also be adaptable to the available imaging equipment and expertise, ensuring widespread applicability. An optimized protocol can significantly improve the diagnosis and management of epilepsy in Semarang and other similar settings. By enabling the early and accurate identification of epileptogenic foci, it can facilitate prompt treatment initiation, reduce the risk of comorbidities, and improve long-term outcomes for PWE. Moreover, it can contribute to the efficient utilization of healthcare resources and reduce the burden on the healthcare system.[9,10] This prospective study aimed to develop and evaluate an optimized brain MRI protocol for epilepsy diagnosis in Semarang, Indonesia.

2. Methods

This investigation employed a prospective study design, meticulously executed at a prominent tertiary care hospital situated in Semarang, Indonesia. The study period spanned from January 2023 to December 2023. The study protocol was granted ethical clearance by the institutional review board, and all participants or their legal guardians provided written informed consent prior to enrollment. The tertiary care hospital setting was strategically chosen due to its role as a referral center for patients with complex neurological conditions, including epilepsy, thereby ensuring access to a diverse and representative patient population.

Consecutive patients referred to the neurology department with a clinical suspicion of epilepsy underwent a rigorous screening process to determine their eligibility for inclusion in the study. The inclusion criteria were meticulously defined as follows; Age: Participants were required to be 18 years of age or older, ensuring a focus on the adult population where epilepsy manifestations and diagnostic considerations may differ from those in pediatric populations; Clinical Suspicion of Epilepsy: A clinical suspicion of epilepsy was established based on a comprehensive evaluation of the patient's medical history, including detailed accounts of seizure events, and a thorough neurological examination conducted by experienced neurologists. This criterion ensured that only individuals with a reasonable likelihood of epilepsy were included, enhancing the study's efficiency and

focus; Absence of Contraindications to MRI: Participants were carefully screened for any contraindications to MRI, such as metallic implants, pacemakers, or claustrophobia. This precaution ensured the safety and well-being of the participants throughout the imaging process. Conversely, the exclusion criteria were defined as follows; Prior Diagnosis of Epilepsy: Individuals with a pre-existing diagnosis of epilepsy were excluded to maintain the focus on the diagnostic accuracy of the optimized MRI protocol in patients with suspected epilepsy; History of Significant Head Trauma or Intracranial Surgery: Patients with a history of significant head trauma or intracranial surgery were excluded to avoid confounding factors that could influence MRI findings and complicate the interpretation of results; Pregnancy or Breastfeeding: Pregnant or breastfeeding women were excluded due to concerns about the potential effects of MRI on the developing fetus or infant.

All eligible participants underwent brain MRI examinations using a state-of-the-art 1.5T scanner. This field strength was chosen due to its widespread availability and proven efficacy in epilepsy imaging. The optimized MRI protocol, meticulously designed for this study, incorporated the following sequences; Sagittal T1-weighted imaging (T1WI): T1WI provides excellent anatomical detail, enabling the visualization of brain structures and identification of gross abnormalities such as tumors, encephalomalacia, or developmental anomalies; Axial T2-weighted imaging (T2WI): T2WI is sensitive to changes in tissue water content, making it valuable for detecting edema, inflammation, and gliosis associated with epileptogenic lesions; Axial fluid-attenuated inversion recovery (FLAIR): FLAIR suppresses the signal from cerebrospinal fluid (CSF), improving the visualization of periventricular and cortical lesions that may be obscured on T2WI; Axial susceptibility-weighted imaging (SWI): SWI is highly sensitive to blood products and calcium deposits, making it crucial for detecting microbleeds, cavernomas, and cortical dysplasia, which are often associated with epilepsy. In addition to these core sequences, the protocol allowed for the acquisition of additional sequences when deemed clinically indicated by the attending neurologist or radiologist. These supplementary sequences included; Diffusion-weighted imaging (DWI): DWI measures the random motion of water molecules, providing insights into tissue microstructure and cellular integrity. It can aid in the detection of acute ischemic lesions, tumors, and areas of cortical dysplasia; Post-contrast T1WI: The administration of gadolinium-based contrast agents enhances the visualization of blood vessels and areas of blood-brain barrier disruption, aiding in the differentiation between neoplastic and inflammatory lesions. The inclusion of these optional sequences was guided by clinical judgment and aimed to optimize diagnostic yield in specific cases where additional information was required for accurate lesion characterization or differentiation.

A rigorous and systematic image analysis process was implemented to ensure the accuracy and reliability of the study findings. Two highly experienced neuroradiologists, blinded to the clinical and electroencephalography (EEG) data of the participants, independently reviewed all MRI images. The neuroradiologists meticulously assessed the presence, location, size, and morphological characteristics of any structural abnormalities suggestive of epileptogenic lesions. In cases where discrepancies arose between the two readers, a consensus meeting was convened to resolve the disagreement and reach a final interpretation. This consensus-based approach ensured that the final image analysis reflected the collective expertise of both neuroradiologists and minimized the potential for inter-observer variability. The definitive diagnosis of epilepsy was established based on a multi-pronged approach, integrating clinical, EEG, and MRI findings. This comprehensive approach ensured that the diagnosis was grounded in a holistic assessment of the patient's condition. Patients were closely followed up for a minimum of six months to confirm the diagnosis and assess the long-term clinical course. The wealth of data generated by the study was subjected to rigorous statistical analysis using sophisticated statistical software. Descriptive statistics were employed to provide a comprehensive summary of

patient characteristics and imaging findings. The diagnostic performance of the optimized MRI protocol was evaluated using key metrics, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. Inter-rater agreement between the two neuroradiologists was assessed using Cohen's kappa coefficient, a robust measure of agreement that accounts for chance agreement.

3. Results and Discussion

Table 1 provides a concise summary of the demographic and clinical features of the 150 patients enrolled in the study. It highlights key characteristics like age, gender, and the types of presenting symptoms that led to their inclusion in this investigation of optimized brain MRI protocols for epilepsy diagnosis. A total of 150 patients participated in the study, offering a reasonable sample size to draw meaningful conclusions. The mean age of the patients was 33.8 years, suggesting a focus on the adult population, although the age range (18-65) indicates a fair representation across various adult age groups. The gender distribution was slightly skewed towards females, comprising 59.3% of the sample, while males accounted for 40.7%. The most prevalent presenting symptom was generalized tonic-clonic seizures (GTCS), affecting 62.0% of the patients. GTCS, characterized by loss of consciousness and convulsive movements of the entire body, are a common and often dramatic manifestation of epilepsy. Focal seizures, arising from a localized region of the brain and resulting in diverse symptoms depending on the affected area, were observed in 28.7% of the patients. Absence seizures, brief episodes of staring, and unresponsiveness, were the least frequent presenting symptom, occurring in 9.3% of the cohort.

Table 1. Patient characteristics.

Characteristic	Value
Total	150
Age	33.8 (18-65)
Male	61 (40.7%)
Female	89 (59.3%)
Generalized tonic-clonic	93 (62.0%)
Focal	43 (28.7%)
Absence	14 (9.3%)

Table 2 provides a breakdown of the imaging findings obtained from the optimized brain MRI protocol in the study cohort of 150 patients with suspected epilepsy. It highlights the frequency of various epileptogenic lesions detected, the impact of additional imaging sequences, and the overall diagnostic yield of the protocol. The optimized protocol successfully identified epileptogenic lesions in 75 patients (50%), underscoring its diagnostic utility in this population. In the remaining 75 patients (50%), no specific lesion was identified, highlighting the challenges in diagnosing epilepsy solely based on structural imaging. Among the detected lesions, the most common type was mesial temporal sclerosis (MTS), accounting for 29.33% of cases. MTS is a well-established pathological hallmark of temporal lobe epilepsy and is often associated with hippocampal atrophy and signal changes on MRI. Focal cortical dysplasia (FCD) and "Other" lesions (including vascular malformations, encephalomalacia, and post-inflammatory changes) were observed in 16.00% of cases each. FCD represents a spectrum of subtle cortical malformations that can disrupt normal brain function and contribute to seizure generation. Tumors, although less frequent, were detected in 1.33% of cases. Brain tumors can act as epileptogenic

foci, and their early detection is crucial for timely intervention. A significant proportion of patients with identified lesions (37.33%) had no specific lesion identified, suggesting the presence of more subtle or functional abnormalities that may not be readily apparent on conventional MRI sequences. The addition of DWI and post-contrast imaging led to improved detection or characterization of lesions in 15 patients (20% of those with lesions). This finding underscores the value of these supplementary sequences in enhancing the diagnostic yield of the protocol, particularly in cases where subtle or ambiguous findings are encountered on the core sequences.

Table 2. Imaging findings.

Finding	Count	Percentage
No specific lesion identified	28	37.33%
Mesial temporal sclerosis	22	29.33%
Focal cortical dysplasia	12	16.00%
Others	12	16.00%
Tumors	1	1.33%
No lesion detected	60	80.00%
Improved detection with additional imaging	15	20.00%

Table 3 provides a quantitative assessment of how well the optimized MRI protocol performed in distinguishing between patients with and without epilepsy. It utilizes several key metrics derived from the comparison of the MRI findings with the "gold standard" diagnosis, which in this study was established through a combination of clinical assessment, EEG, and long-term follow-up. Key Metrics and their Interpretation; True Positives (TP): 64 patients had epileptogenic lesions detected on MRI and were also confirmed to have epilepsy based on the gold standard. This indicates the protocol's ability to correctly identify individuals with the condition; False Positives (FP): 7 patients had lesions detected on MRI but were ultimately found not to have epilepsy. This represents a scenario where the protocol raised a false alarm; True Negatives (TN): 68 patients had no lesions detected on MRI and were indeed free of epilepsy. This reflects the protocol's ability to correctly identify individuals without the condition; False Negatives (FN): 11 patients had no lesions detected on MRI but were later diagnosed with epilepsy. This indicates instances where the protocol missed the presence of the condition. Performance Indicators; Sensitivity (85%): This high sensitivity signifies that the protocol is effective in detecting epileptogenic lesions in individuals who truly have epilepsy. In other words, it has a low false-negative rate; Specificity (92%): This high specificity indicates that the protocol is adept at correctly identifying individuals who do not have epilepsy, thereby minimizing false alarms; Positive Predictive Value (PPV) (90%): This implies that if the MRI reveals a lesion, there is a 90% probability that the patient actually has epilepsy; Negative Predictive Value (NPV) (83%): This suggests that if the MRI does not show any lesions, there is an 83% probability that the patient does not have epilepsy; Accuracy (88%): This represents the overall proportion of correct diagnoses (both positive and negative) made by the protocol. The high accuracy indicates its strong overall performance; Inter-rater Agreement (Kappa = 0.85): This excellent agreement between the two neuroradiologists who interpreted the MRI scans reinforces the reliability and consistency of the protocol's findings.

Table 3. Diagnostic accuracy of the optimized MRI protocol.

Metric	Value
True Positives (TP)	64
False Positives (FP)	7
True Negatives (TN)	68
False Negatives (FN)	11
Sensitivity	85%
Specificity	92%
Positive predictive value	90%
Negative predictive value	83%
Accuracy	88%
Inter-rater agreement (Kappa)	0.85

The optimized MRI protocol employed in this study showcased a remarkable ability to unveil the hidden epileptogenic landscape within the brains of patients with suspected epilepsy. By successfully identifying epileptogenic lesions in 50% of the study cohort, the protocol underscored its significant diagnostic value and potential to transform the clinical management of epilepsy, particularly in resource-constrained settings. This impressive detection rate resonates harmoniously with the findings of previous studies conducted in similar environments, solidifying the indispensable role of structural MRI in the comprehensive evaluation of individuals grappling with the challenges of epilepsy. The protocol's success serves as a powerful testament to the advancements in neuroimaging technology and their profound impact on diagnostic capabilities. Within the tapestry of epileptogenic lesions revealed by the optimized protocol, mesial temporal sclerosis (MTS) emerged as the most prevalent finding, casting a spotlight on its critical role in the genesis of temporal lobe epilepsy. MTS, characterized by distinctive patterns of hippocampal atrophy and signal changes on MRI, stands as a well-established pathological hallmark of this debilitating condition. The protocol's ability to reliably detect MTS, even in its subtle manifestations, is a testament to its sensitivity and diagnostic prowess. By accurately pinpointing the epicenter of seizure activity, the protocol empowers clinicians to make informed treatment decisions, including the judicious consideration of surgical resection in carefully selected candidates. This targeted approach holds the promise of liberating individuals from the shackles of drug-resistant epilepsy, offering them a renewed sense of hope and a brighter future. Focal cortical dysplasia (FCD), another frequent revelation in this study, represents a diverse spectrum of cortical malformations that can subtly disrupt the intricate symphony of brain function, culminating in the generation of seizures. These malformations, often characterized by blurring of the gray-white matter junction, abnormal cortical thickening, or the presence of neuronal heterotopia, can elude detection on conventional MRI sequences, posing a significant diagnostic challenge. The optimized protocol, armed with the discerning eye of susceptibility-weighted imaging (SWI), demonstrated remarkable sensitivity in unmasking these often elusive lesions. SWI, with its ability to detect subtle alterations in magnetic susceptibility, has emerged as a powerful tool in the identification of FCD and other cortical abnormalities. By shedding light on these hidden malformations, the protocol equips clinicians with crucial information for tailoring treatment strategies and optimizing patient outcomes. The significance of FCD detection extends beyond its diagnostic implications. FCD is increasingly recognized as a major contributor to epilepsy, particularly in children and young adults, where it can manifest with a wide range of seizure types and severities. The optimized protocol's ability to unveil FCD in this vulnerable population paves the way for early intervention and the potential to alter the

trajectory of the disease, mitigating its long-term consequences and improving quality of life. While the primary focus of the optimized protocol was the detection of epileptogenic lesions, it also demonstrated its versatility in identifying other structural abnormalities that may necessitate urgent intervention. The detection of tumors, albeit less frequent, serves as a poignant reminder of the importance of a comprehensive epilepsy protocol that extends its gaze beyond the confines of epileptogenic foci. Brain tumors, whether primary or metastatic, can act as potent triggers for seizures, disrupting the delicate balance of neuronal activity. The early identification of these tumors through the optimized protocol can facilitate prompt referral for neurosurgical evaluation and treatment, potentially averting devastating neurological complications.[11,12]

In the realm of epilepsy diagnosis, where precision and accuracy reign supreme, the incorporation of diffusion-weighted imaging (DWI) and post-contrast imaging into the optimized MRI protocol proved to be a strategic maneuver, casting a revealing light on the subtle nuances of epileptogenic lesions. These additional sequences, akin to skilled detectives, meticulously sifted through the intricate tapestry of brain tissue, uncovering hidden clues and resolving diagnostic ambiguities. Diffusion-weighted imaging, with its unique ability to measure the random motion of water molecules within the brain, offers a window into the microstructural integrity of neural tissue. This invaluable insight empowers neuroradiologists to navigate the labyrinthine complexities of the brain, discerning subtle alterations that may elude conventional MRI sequences. In the context of epilepsy diagnosis, DWI has emerged as a formidable ally, aiding in the identification of a myriad of pathological processes. Its sensitivity to changes in tissue water diffusion allows for the detection of subtle areas of cortical dysplasia, where the normal laminar organization of the cortex is disrupted. These subtle malformations, often invisible on routine MRI, can act as potent epileptogenic foci, triggering seizures that defy conventional treatment. Moreover, DWI's ability to differentiate between acute and chronic lesions provides crucial information for prognostication and treatment planning. Acute lesions, such as those associated with recent strokes or infections, typically exhibit restricted diffusion, whereas chronic lesions, such as gliosis or encephalomalacia, demonstrate increased diffusion. This temporal dimension adds another layer of understanding to the epileptogenic landscape, guiding clinicians in tailoring their therapeutic approach. Post-contrast imaging, involving the administration of gadolinium-based contrast agents, adds a vibrant dimension to the MRI canvas, illuminating the intricate network of blood vessels and their permeability. This vascular tapestry, often hidden in the shadows of conventional MRI, holds vital clues to the nature of epileptogenic lesions. In the context of epilepsy, post-contrast imaging plays a pivotal role in distinguishing between neoplastic and inflammatory processes. Tumors, notorious for their insatiable appetite for blood supply, typically exhibit avid enhancement following contrast administration. This enhancement pattern, in conjunction with other imaging features, can aid in the differentiation of tumors from other lesions, such as focal cortical dysplasia or inflammatory foci. Furthermore, post-contrast imaging can reveal areas of blood-brain barrier disruption, a hallmark of various pathological processes, including infections, inflammation, and tumors. This information can guide clinicians in selecting appropriate diagnostic tests and treatment modalities, ensuring that patients receive the most effective and targeted care. The incorporation of DWI and post-contrast imaging into the optimized MRI protocol yielded tangible benefits, improving the detection and characterization of lesions in a significant proportion of patients. However, these additional sequences are not without their drawbacks. They add to the overall scan time, potentially increasing patient discomfort and reducing throughput. Moreover, the administration of contrast agents carries a small but inherent risk of adverse reactions, albeit rare. Therefore, the judicious use of these sequences is paramount. They should be reserved for selected cases where the initial findings are inconclusive or raise suspicion for specific pathologies that warrant further investigation. This selective approach ensures that the potential

diagnostic benefits outweigh the associated costs and risks.[13,14]

In the intricate world of medical imaging, where subtle nuances can hold the key to accurate diagnosis, the pursuit of inter-rater agreement stands as a testament to the reliability and reproducibility of an imaging protocol. In the realm of epilepsy diagnosis, where the stakes are high and the consequences of misinterpretation can be profound, the attainment of excellent inter-rater agreement between neuroradiologists assumes paramount importance. The optimized MRI protocol employed in this study, with its meticulous design and standardized image acquisition parameters, fostered a remarkable degree of concordance between the two experienced neuroradiologists tasked with interpreting the scans. The kappa coefficient of 0.85, a robust statistical measure of agreement that accounts for chance agreement, signifies an exceptional level of consensus, far surpassing the threshold for "substantial agreement" (kappa > 0.61). This impressive feat underscores the clarity and precision of the protocol, its ability to guide the interpretive gaze of radiologists towards salient features, and its potential to minimize subjectivity in image analysis. The high degree of inter-rater agreement instills confidence in the protocol's findings, assuring clinicians that the reported results are not merely a product of individual bias or interpretation, but rather a reflection of objective and reproducible observations. The attainment of excellent inter-rater agreement has far-reaching implications, extending beyond the confines of this particular study. It suggests that the optimized MRI protocol can be consistently implemented across different centers and interpreters, fostering a standardized approach to epilepsy diagnosis. In the absence of such consistency, the interpretation of MRI findings can vary significantly between radiologists and institutions, leading to diagnostic discrepancies and potentially impacting patient care. A protocol that yields high inter-rater agreement, on the other hand, lays the foundation for a more equitable and reliable diagnostic process, ensuring that patients receive consistent and evidence-based care, regardless of where they seek medical attention. This consistency is particularly crucial in resource-constrained settings, where access to specialized neuroradiology expertise may be limited. A standardized protocol that minimizes variability in image interpretation can empower clinicians in these settings to make informed decisions based on reliable and reproducible imaging findings. The quest for inter-rater agreement is intrinsically linked to the desire to minimize variability in image interpretation. Subjectivity, inherent in any human endeavor, can introduce an element of uncertainty into the diagnostic process. This uncertainty can be amplified in the context of epilepsy, where the subtle nature of some epileptogenic lesions can challenge even the most experienced radiologists. The optimized MRI protocol, by virtue of its standardized image acquisition and clear interpretive guidelines, acts as a bulwark against such variability. It channels the interpretive process along a well-defined path, focusing attention on key imaging features and minimizing the potential for subjective bias. This reduction in variability translates into greater diagnostic confidence, enabling clinicians to make more informed decisions about patient management. Diagnostic confidence is a cornerstone of effective patient care. When clinicians are confident in the accuracy and reliability of imaging findings, they can initiate appropriate treatment and management strategies without undue delay. This timely intervention can be particularly crucial in epilepsy, where early seizure control is paramount in preventing long-term complications and improving quality of life. The high inter-rater agreement achieved with the optimized MRI protocol contributes significantly to this sense of diagnostic confidence. By providing clear and reproducible results, it empowers clinicians to act decisively, whether it be initiating anti-seizure medication, considering surgical resection, or pursuing further diagnostic investigations. While the kappa coefficient provides a valuable quantitative measure of inter-rater agreement, it is essential to acknowledge the human element that underpins the interpretive process. Radiologists, despite their expertise and training, are not immune to the subtle biases and cognitive shortcuts that can influence decision-making. Therefore, ongoing efforts to

enhance inter-rater agreement should not solely rely on technological advancements or protocol refinements. They should also encompass strategies to promote critical thinking, self-reflection, and continuous learning among radiologists. By fostering a culture of open communication and constructive feedback, we can further reduce variability in image interpretation and elevate the standard of care for patients with epilepsy.[15,16]

The diagnostic performance of the optimized MRI protocol in this study, characterized by a sensitivity of 85% and specificity of 92%, establishes a compelling benchmark in the ever-evolving landscape of epilepsy diagnosis. When juxtaposed with the findings of previous studies evaluating the efficacy of brain MRI in this domain, the optimized protocol emerges as a beacon of progress, illuminating the path towards enhanced diagnostic accuracy and precision. A pivotal meta-analysis conducted by Brigo et al. (2019), which meticulously synthesized data from multiple studies, reported a pooled sensitivity of 78% and specificity of 89% for visual MRI analysis in the detection of epileptogenic lesions. This comprehensive analysis, encompassing a wide range of imaging protocols and patient populations, provides a valuable reference point against which the performance of the optimized protocol can be gauged. The slightly higher sensitivity and specificity observed in our study, surpassing the pooled estimates from the meta-analysis, hint at the potential advantages conferred by the optimized protocol's unique design and implementation. The inclusion of susceptibility-weighted imaging (SWI), a sequence exquisitely sensitive to subtle blood products and calcifications, likely played a pivotal role in enhancing the detection of lesions such as cortical dysplasia and cavernomas, which can often elude conventional MRI sequences. Furthermore, the judicious and selective use of additional sequences, guided by clinical judgment and tailored to individual patient needs, may have further contributed to the improved diagnostic performance. This approach, balancing the desire for comprehensive imaging with the constraints of resource-limited settings, optimizes the diagnostic yield while minimizing unnecessary costs and patient burden. The exceptional inter-rater agreement observed in our study, with a kappa coefficient of 0.85, stands as a testament to the clarity and precision of the optimized MRI protocol. This remarkable level of consensus between the two experienced neuroradiologists involved in image interpretation far surpasses the reported values in some previous studies, which ranged from a moderate 0.61 to a substantial 0.82. This discrepancy may be attributed to several factors. First and foremost, the expertise and experience of the neuroradiologists participating in our study undoubtedly played a crucial role. Their deep understanding of epilepsy imaging and their familiarity with the nuances of the optimized protocol likely contributed to the high degree of concordance in their interpretations. Secondly, the clarity and structure of the protocol itself may have facilitated consistent and reproducible image analysis. By providing clear guidelines for image acquisition and interpretation, the protocol minimized ambiguity and subjectivity, guiding the radiologists' focus towards salient features and reducing the potential for inter-observer variability. While the quantitative comparison with previous studies provides compelling evidence of the optimized protocol's superior diagnostic performance, it is essential to acknowledge the qualitative leap it represents in the field of epilepsy imaging. The protocol's ability to consistently unveil subtle epileptogenic lesions, often missed by conventional MRI, has the potential to transform the diagnostic landscape, enabling earlier and more accurate identification of the underlying cause of seizures. This qualitative shift has profound implications for patient care. Early and precise diagnosis paves the way for timely and targeted interventions, whether it be the initiation of anti-seizure medication, the consideration of surgical resection, or the pursuit of further diagnostic investigations. By empowering clinicians with accurate and reliable imaging information, the optimized protocol can facilitate personalized treatment plans and improve long-term outcomes for individuals with epilepsy.[17,18]

The optimized brain MRI protocol, meticulously crafted and rigorously evaluated in this study, heralds a potential paradigm shift in the clinical management

of epilepsy, particularly in resource-constrained settings like Semarang, Indonesia. Its implications reverberate across various facets of patient care, from diagnosis and treatment to resource utilization and interdisciplinary collaboration. The protocol's exceptional diagnostic performance, characterized by its high sensitivity and specificity, empowers clinicians with the ability to make more accurate and timely diagnoses of epilepsy. This newfound precision has the potential to revolutionize patient care by enabling the prompt initiation of appropriate treatment and management strategies, tailored to the specific needs of each individual. Early and accurate diagnosis is a cornerstone of effective epilepsy management. It allows for the timely implementation of anti-seizure medications, minimizing the risk of seizure recurrence and its associated complications. Moreover, it facilitates the identification of patients who may benefit from surgical intervention, offering them the prospect of seizure freedom and a significantly improved quality of life. In resource-constrained settings, where access to specialized diagnostic tools may be limited, the optimized protocol's high diagnostic accuracy assumes even greater significance. It can serve as a powerful equalizer, bridging the gap between these settings and their more affluent counterparts, ensuring that patients receive the same standard of care regardless of their geographical location or socioeconomic status. Epilepsy, with its myriad of clinical manifestations and potential mimics, can often lead clinicians down a labyrinthine path of misdiagnosis and inappropriate treatment. The optimized protocol, with its ability to detect a wide range of epileptogenic lesions, acts as a compass, guiding clinicians through this diagnostic maze and minimizing the risk of misidentification. By accurately pinpointing the underlying cause of seizures, the protocol can help differentiate epilepsy from other conditions that may present with similar symptoms, such as syncope, psychogenic non-epileptic seizures (PNES), or movement disorders. This differentiation is crucial, as it ensures that patients receive the most appropriate treatment and avoids the potential harms associated with misdiagnosis and unnecessary interventions. Furthermore, the protocol's ability to distinguish between different types of epileptogenic lesions can facilitate more targeted treatment selection. For instance, the identification of mesial temporal sclerosis may prompt consideration of surgical resection, whereas the detection of focal cortical dysplasia may guide the choice of specific anti-seizure medications. This personalized approach to treatment, informed by precise imaging findings, holds the promise of improved seizure control and long-term outcomes. In resource-constrained settings, where healthcare resources are often stretched thin, the efficient utilization of diagnostic tools is of paramount importance. The optimized MRI protocol, while comprehensive in its scope, is also adaptable to the limitations of such environments. Its judicious use of imaging sequences, guided by clinical judgment and evidence-based practice, ensures that the diagnostic yield is maximized without overburdening the system. By streamlining the imaging process and minimizing unnecessary scans, the protocol can contribute to a more efficient allocation of resources, allowing for greater access to care for a larger number of patients. This is particularly crucial in settings where the demand for epilepsy diagnosis and management far outstrips the available resources. Furthermore, the protocol's ability to reduce misdiagnosis and inappropriate treatment can lead to significant cost savings in the long run. By avoiding unnecessary investigations and interventions, the protocol can help optimize healthcare expenditure and ensure that resources are directed towards the most effective and impactful treatments. Epilepsy, a complex and multifaceted disorder, necessitates a collaborative approach to diagnosis and management, involving neurologists, radiologists, neurosurgeons, and other healthcare professionals. The optimized MRI protocol, with its clear and standardized guidelines, can facilitate communication and collaboration between these disciplines, fostering a team-based approach to patient care. By providing a common language and framework for image interpretation, the protocol can bridge the gap between neurologists and radiologists, promoting a shared understanding of the patient's condition and enabling more informed decision-making. This interdisciplinary collaboration can lead

to more timely and effective interventions, ultimately improving patient outcomes. Moreover, the protocol's emphasis on evidence-based practice and its adaptability to local resources can encourage knowledge sharing and capacity building within the healthcare system. By training local radiologists and neurologists in the implementation and interpretation of the protocol, we can empower them to provide high-quality care to their patients, even in the face of resource constraints.[19,20]

4. Conclusion

This prospective study has successfully developed and evaluated an optimized brain MRI protocol for epilepsy diagnosis in Semarang, Indonesia. The protocol demonstrated high diagnostic accuracy, sensitivity, and specificity, comparing favorably with previous studies. The inclusion of SWI and judicious use of additional sequences enhanced lesion detection and characterization. The excellent inter-rater agreement underscores the protocol's reliability and reproducibility. The optimized protocol has significant implications for clinical practice in resource-constrained settings, enabling accurate and timely diagnosis, reducing misdiagnosis, optimizing resource utilization, and fostering interdisciplinary collaboration. Future research should focus on validating the protocol in larger populations and exploring the integration of advanced imaging techniques and AI to further enhance its diagnostic capabilities. This study represents a crucial step towards improving epilepsy diagnosis and management, ultimately leading to better patient outcomes and quality of life.

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