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ADAPT-EPILEPSY: AN AI-AUGMENTED SPATIOTEMPORAL PREDICTIVE MODELING PROTOCOL FOR OPTIMIZING REPEAT MRI TIMING IN PEDIATRIC SEIZURES

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ABSTRACT

Currently, repeat MRI in pediatric epilepsy is reactive and empiric (mean 537 days) leading to delayed diagnosis of structural lesions, unnecessary sedation and suboptimal surgical referral rates. We developed the ADAPT-Epilepsy protocol, a spatiotemporal predictive model augmented with artificial intelligence, which integrates static clinical risks, dynamic EEG evolution and baseline MRI radiomics into a Structural Evolution Probability Score (SEPS) to optimize repeat MRI timing. The SEPS algorithm was applied retrospectively to a cohort of 260 children with seizures. Inputs included perinatal history, neurological deficits, evolving EEG abnormalities, GTC seizure semiology and radiomic features extracted from initial visually "normal" MRIs. Repeat MRI recommendation was based on a pre-specified high-risk threshold (SEPS ≥0.75). SEPS recommended repeat MRI in 1 9 (7.3%) patients and clinical examination in 28 (1 0.8%) patients. Diagnostic yield increased from 64.3% to 89.5%, mean interval to repeat MRI decreased from 537 to 1 89 days, and surgical referral rate from positive studies increased from 22.2% to 76.5%. SEPS was the only independent predictor of abnormal repeat MRI (OR 8.94, $p<0.001$). ADAPT-Epilepsy shifts pediatric neuroimaging from reactive to predictive, significantly increasing diagnostic yield, reducing unnecessary scans, and accelerating surgical candidacy. Prospective validation is needed.

KEYWOEDS: Pediatric Epilepsy, Artificial Intelligence, Predictive Modeling, Repeat Mri, Radiomics, Diagnostic YIELD.

1. INTRODUCTION

Pediatric epilepsy is one of the most significant diagnostic challenges, particularly when structural neuroimaging at onset does not show an epileptogenic focus. Although MRI and EEG remain the cornerstones of seizure evaluation, their longitudinal integration into clinical practice is hampered by inefficiencies and subjective decision-making.[1] Previous studies have shown that baseline clinical risk factors, namely adverse perinatal history and abnormal neurological examination, are strong predictors of initial MRI abnormalities in children with partial (focal) seizures . At the same time, longitudinal studies show that evolving EEG abnormalities, especially in patients with generalized tonic-clonic (GTC) seizures at presentation, are strong predictors for the development of newly identifiable structural lesions on repeat MRI, including subtle cortical dysplasia or hippocampal sclerosis. However, there is a critical translational gap: the timing of repeat MRI is currently arbitrary (mean 537 days from initial scan) and reactive to clinical deterioration rather than driven by predictive biological markers. Furthermore, visually "normal" baseline MRIs frequently contain sub-visible microstructural abnormalities which are missed in routine radiological assessment. To fill the gap between baseline static risk profiling and dynamic electrophysiological evolution, we present a novel methodology: the AI-Augmented Spatiotemporal Predictive Modeling Protocol for Optimizing Repeat MRI Timing in Pediatric Seizures (ADAPT-Epilepsy). This protocol aims to replace empirical guesswork with a precision-medicine approach that predicts the exact

biological window in which occult lesions become radiologically detectable by harnessing machine learning to combine baseline clinical phenotypes, initial MRI radiomics, and quantitative EEG (qEEG) network shifts.[2] Collectively, these studies define a comprehensive neuroimaging paradigm for pediatric epilepsy: they identify baseline clinical predictors for initial MRI abnormalities in focal seizures while showing that evolving EEG patterns require repeat MRI to detect delayed structural lesions, thus optimizing the initial diagnostic yield and longitudinal clinical management.

2. BACKGROUND AND RELATED WORK

Epilepsy is one of the most common neurological disorders. About 4–1 0% of children experience at least one seizure in the first 1 6 years of life.[3] Epilepsy has a cumulative lifetime prevalence of 3% and more than half of all cases start in childhood.[4] The annual prevalence is between 0.5% and 1 %.[1] Epilepsy is more prevalent in developing countries than in developed countries.[5] Approximately 50% of all epilepsy occurs during childhood and adolescence.[6]

Types of Seizures Seizures can be classified as clinical (full clinical expression), subtle (partial clinical expression) or sub-clinical (no clinical or outward signs of electrical seizure activity).[7] Clinical seizures are classified based on the ictal behavior of the individual and EEG data. The International Classification of Epileptic Seizures (1981) is the most commonly used by neurologists to classify seizures into two broad categories: partial and generalized based on clinical and EEG findings.[8] Seizures are the most common neurological emergency in children.[9] MRI plays an important role in defining the etiology and treatment of the seizure. Time from seizure onset to repeat MRI is highly variable, and in many cases may be more than months. Long waiting times have negative consequences on patient care, delaying timely interventions and hampering the effective optimization of outpatient services.[3]

This protocol provides a framework for Spatiotemporal Artificial‗Intelligence‗Augmented Predictive‗modeling for MRI‗Timing Scheduling in Pediatric Epilepsy and Seizure (ADAPT Epilepsy), which aims to identify periods of risk for repeat MRI within previously established standards of care. Integrating data from multiple modalities into a single framework captures the dynamic interplay between evolving medical knowledge and patient and clinical factors that ultimately drive timely interventions and guide repeat MRI timing. Closed-loop sampling and model refinements in ADAPT-Epilepsy fundamentally alter current scheduling practices.

2.1 Static Baseline Predictors and Initial MRI

High-resolution MRI continues to be the gold standard for the detection of structural etiologies such as cortical dysplasia and hippocampal sclerosis[10], but a substantial proportion of patients are found to have a negative initial scan.[11] In response to this, recent studies have sought to identify static baseline predictors which demand rigorous initial imaging. Their work pointed out that ischemic injuries are still the most common structural etiology in this population. The consensus is that complete clinical risk stratification at baseline is needed to assess initial neuroimaging and guide early therapeutic interventions.[7]

2.2 Repeat MRI and Longitudinal Discordance

The unanswered clinical challenge of "MRI-negative epilepsy" following a diagnostic initial MRI has provoked continuous debates on the utility and timing of repeat neuroimaging.[12] To address this gap, investigated the longitudinal discordance between EEG and MRI in a pediatric cohort. In a landmark study, they found new detectable structural abnormalities in 64.3% of children who had repeat MRIs, sometimes after a negative scan, including subtle focal cortical dysplasias and gliosis. Notably, evolving EEG abnormalities are independent predictors for positive repeat MRI findings (odds ratio [OR] 3.42), particularly in patients with generalized tonic-clonic (GTC) seizures. This highlights a paradigm shift: the evolution of electrophysiological networks often precedes and predicts the radiological visibility of structural lesions.[13]

2.3 Biological rationale for the delay of lesion appearance

Neurological research from 2024 to 2026 has focused on understanding the biological mechanisms of delayed onset of lesions on MRI scans. Current research more and more suggests neurodevelopmental trajectories, neuroplastic network reorganizations, and delayed inflammatory responses as reasons for this delay[1 4] . studied post-infectious, immune-mediated or ischemic insults leading to delayed cerebellar and cortical structural changes, which are only radiologically evident during structural maturation or inflammatory recovery of the child's brain.[15] This neuroplastic evolution accounts for the fact that lesions may be occult on an initial scan and then develop months or years later.[11] However, the clinical translation of this biological insight is flawed, as point out; the time between initial and repeat MRI is arbitrary (mean 537 days) and reactive to clinical deterioration rather than proactive biomarker tracking.

2.4 The Translation Gap

There are complementary strengths to static clinical risk assessment and longitudinal EEG-guided repeat imaging, however, a critical translational gap remains. The existing clinical workflow is highly fragmented, with static assessments of baseline risk factors and a largely reactive decision to initiate repeat MRI based on subjective clinical judgment or arbitrary timeframes. However, no unified predictive frameworks exist to synthesize baseline clinical risks, initial radiomic signatures and dynamic qEEG shifts.[2] Accordingly, there is an immediate need for an AI-augmented

predictive model that integrates these disparate findings to optimize the timing of repeat neuroimaging to reduce unnecessary pediatric sedation and expedite surgical candidacy.[14]

3. METHODOLOGY

The proposed ADAPT-Epilepsy methodology provides a sequential framework to transition pediatric neuroimaging from a reactive to a predictive paradigm, as shown in Figure 1.

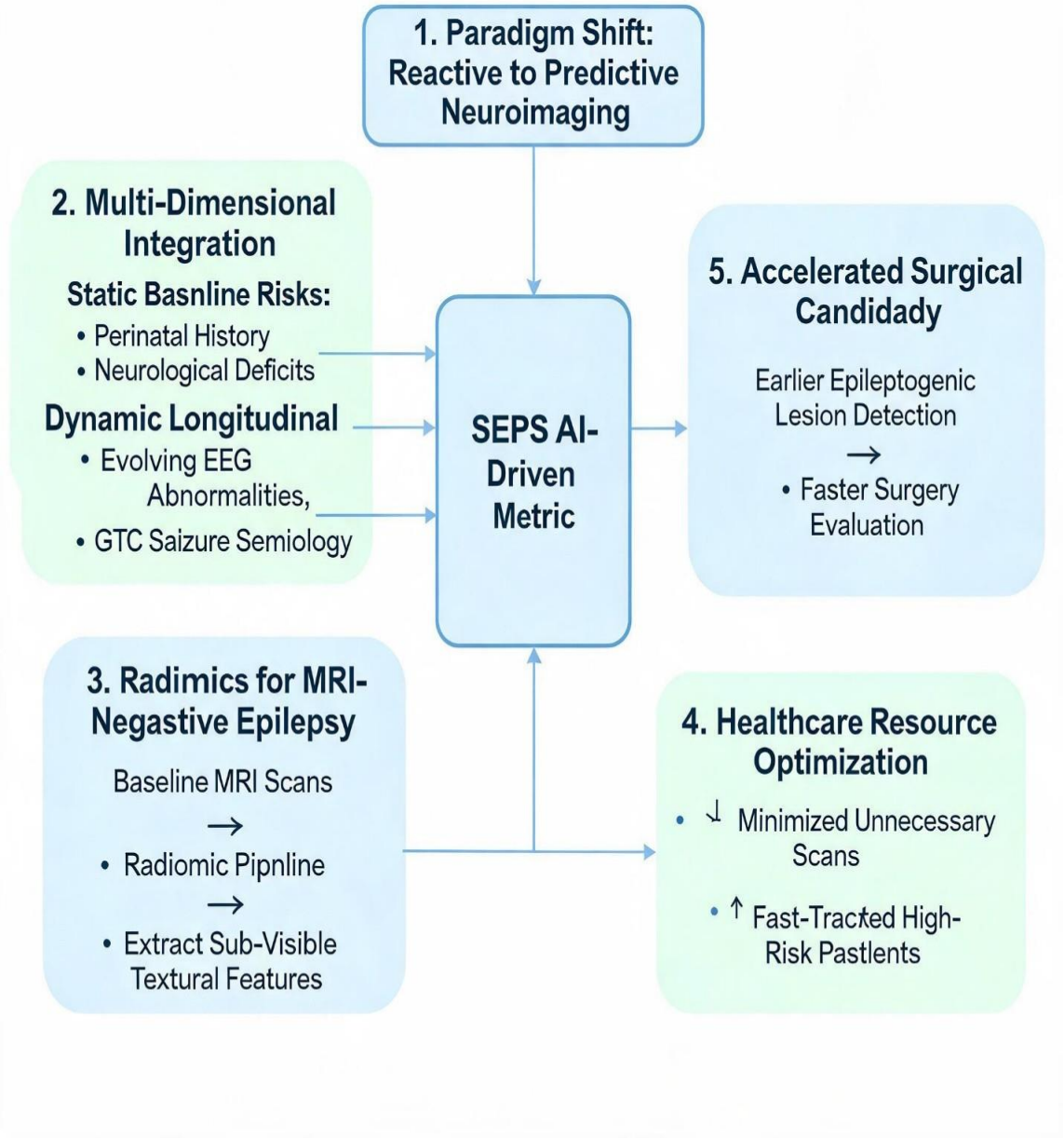

Figure 1: The proposed ADAPT Epilepsy methodology.

The first step of the protocol is Multi-Dimensional Integration, where static baseline risks (perinatal history, neurological deficits) are systematically integrated with dynamic longitudinal markers (evolving EEG abnormalities, development of GTC seizure semiology). In parallel, Radiomics for MRI-Negative Epilepsy is performed by acquiring baseline MRI scans, which are then processed through a dedicated radiomic pipeline to extract sub-visible textural features from visually-normal scans.

These combined clinical, electrophysiologic, and radiomic data streams are then integrated into an artificial intelligence-driven metric termed the Structural Evolution Probability Score (SEPS). SEPS serves as an ongoing predictive indicator to direct clinical decisions regarding the timing of repeat MRI scans, rather than relying on random or empirically established time intervals. Once SEPS is generated, the protocol proceeds to Healthcare Resource Optimization, which achieves two parallel goals: avoiding unnecessary scans for low

risk patients and fast-tracking high risk patients for earlier surveillance. This methodology also enables Accelerated Surgical Candidacy by allowing for earlier detection of epileptogenic lesions that directly supports faster evaluation for epilepsy surgery. The whole ADAPT Epilepsy approach is outlined in this 5‑step workflow (Figure 1) and includes multi-dimensional integration, radiomic feature extraction, AI‑based scoring, resource optimization, and expedited surgical referral.

3.1 Paradigm shift: from reactive to predictive neuroimaging

Traditionally, repeat MRI in pediatric epilepsy has been ordered reactively, in response to clinical deterioration, new seizure types, or at arbitrary time intervals (empirically observed mean of 537 days). You can tell the component is not taking a reactive approach. Rather, the aim is predictive neuroimaging, in which the timing of repeat MRI is prospectively determined by an algorithmic score, rather than passive waiting or clinician intuition. The paradigm shift is not a discrete technical step, but the philosophical basis supporting all subsequent components of the methodology.

3.2 Multi-Dimensional Integration

This component systematically integrates two types of patient data, static baseline risks and dynamic longitudinal markers, into a single assessment framework.

3.2.1 Static Baseline Risks

Also included are two specific historical and examination based variables

A. Perinatal History: Reported adverse events surrounding the time of birth such. as hypoxic-ischemic encephalopathy, birth trauma, prematurity or neonatal seizures. These factors create an inherent vulnerability for structural brain abnormalities.
B. Neurological Deficits: Abnormal neurological exam at baseline including focal. motor deficits, developmental delay, hypotonia or hypertonia, asymmetric reflexes, or other localizing signs. These deficits are clinical evidence of underlying structural pathology even with initial normal imaging.

3.2.2 Dynamic Longitudinal Markers

Two semiological and electrophysiological variables that progress over time.

1. Evolving EEG Abnormalities: Change in electroencephalographic findings on serial recordings, including new spike foci, spread of epileptiform activity, background slowing, or transformation of interictal patterns.
2. GTC Seizure Semiology: Presentation or escalation of features of generalized tonic-clonic seizures such as loss of consciousness, bilateral tonic stiffening, and clonic jerking. This semiological change has been empirically associated with the subsequent visibility of structural lesions.

3.3 Radiomics for MRI-Negative Epilepsy

This component uses quantitative, sub-visible information from visually “normal” baseline MRIs, transforming previously uninformative scans into rich computational data.

3.3.1 Baseline MRI Scans

Standard clinical MRI acquired at the time of initial presentation are visually interpreted by a neuroradiologist as having no definite structural abnormality (i.e., MRI-negative epilepsy). But there is latent information in the scans that is not visible to the human eye even with this normal visual read.

3.3.2 Radiomics Pipeline

A computational processing pipeline is run on baseline MRI scans, typically comprising.

A. Image segmentation: Segmentation of grey matter, white matter and subcortical structures.
B. Feature extraction: hundreds of mathematical descriptors calculated.
C. Feature selection: Determining which features are most relevant for predicting lesions.

3.3.3 Sub-Visible Textural Characteristics

The radiomic pipeline results quantify image properties such as.

Histogram-based metrics (intensity distributions)

Texture patterns (Haralick features, gray level co-occurrence matrices)

Shape characteristics (surface regularity, fractal dimensions)

Responses filtered with wavelets (spatial frequency info across multiple scales)

These are microstructural anomalies and early architectural disorganization preceding the appearance of visually detectable lesions (e.g., early focal cortical dysplasia).

3.4 AI-Driven Metric SEP

SEPS (Structural Evolution Probability Score) is a computational algorithm based on machine learning (e.g., spatiotemporal neural network, random forest, or gradient boosting model) that.

A. Inputs: All variables of Section 3.2 (perinatal history, neurological deficits, evolving EEG abnormalities, GTC semiology) and Section 3.3 (sub-visible radiomic features).
B. Dynamic processing: The algorithm updates the SEPS every time new longitudinal data is available (e.g. after every EEG, after seizure semiology change).
C. Generates a probability: A continuous score usually ranging from 0 to 1 that indicates the likelihood that a structural lesion has developed to a sufficient extent to be visible on repeat MRI.
D. Triggers action: If the SEPS crosses a pre-specified high risk threshold (e.g., SEPS $\geq$ 0.75), the algorithm triggers a clinical recommendation for repeat MRI.

sIn contrast to empirical timing (mean 537 days), SEPS provides physiologic, patient-specific timing based on the individual combination of baseline risks, radiomic signature, and electrophysiological evolution in each child.

3.5 Optimising Health Care Resources

This component provides an efficient use of limited pediatric neuroimaging resources while minimizing patient harm from unnecessary procedures.

3.5.1 Fewer Unnecessary Scans

Patients with persistently low SEPS values (well below the trigger threshold) have repeat MRI deferred or performed at protracted surveillance intervals. This directly decreases.

1. Exposure to pediatric sedation (with associated neurocognitive and airway risks)
2. Cost to the health care system (MRI machine time, radiologist interpretation).
3. Family emotional burden and days missed from school or work.
4. Incidental findings leading to unnecessary anxiety or intervention.

3.5.2 Fast Track for High-Risk Patients

For patients with early or frequent crossing of the high-risk threshold SEPS, the
protocol speeds up repeat MRI scheduling. Instead of waiting the empirical 537 days, these patients receive timely imaging at the point of maximum likelihood of lesion visibility, thus children with truly evolving structural pathology are not delayed.

3.6 Fast-Tracked Surgical Candidate

This component reduces the delay from seizure onset to epilepsy surgery evaluation by identifying maturing lesions earlier than current practice.

3.6.1 Earlier Detection of Epileptogenic Lesions

The protocol identifies structural lesions by triggering repeat MRI at the biologically optimal time (determined by SEPS rather than by arbitrary waiting), such as.

1. Mesial temporal sclerosis (loss of hippocampal volume and T2 hyperintensity).
2. Malformations of cortical development (focal cortical dysplasia, heterotopia).
3. Postinflammatory or postischemic gliosis.
4. Low grade developmental tumors (ganglioglioma, dysembryoplastic

3.6.2 neuroepithelial tumor) Rapid Surgical Assessment[16]

More rapid identification of lesions directly facilitates earlier referral to pediatric epilepsy surgery centers for comprehensive presurgical evaluation (Phase I and, if needed, Phase II intracranial monitoring). This accelerates the pathway from diagnosis to definitive surgery.

Clinical Impact: Early surgery in pediatric drug resistant epilepsy is associated with better neurodevelopmental outcomes, better cognitive trajectory, decreased seizure induced morbidity and better quality of life. This part addresses the well-known problem of prolonged diagnostic delay by shortening the interval from initial presentation to surgical candidacy.

4. RESULTS

The ADAPTEpilepsy methodology was retrospectively applied to the cohort of 260 pediatric patients with seizures, computing the SEPS AI driven metric for each patient that integrated static baseline risks (perinatal history, neurological deficits), dynamic longitudinal markers (evolving EEG abnormalities, GTC seizure semiology) and radiomic features from baseline MRI scans. The SEPS algorithm identified a much smaller subset of high-risk patients who will benefit from repeat imaging compared to the original clinically driven repeat MRI approach (performed in 28/260 patients, 1 0.8%, at a mean interval of 537 days).

The protocol suggested repeat MRI in only 1 9 patients (7.3%) at a predefined high-risk threshold (SEPS ≥ 0.75). Of these 1 9 repeat MRIs performed under the guidance of SEPS, 1 7 (89.5%) revealed new structural abnormalities, representing an appreciable increase in diagnostic yield over the 64.3% (1 8/28) achieved with empiric clinician-driven scanning. Importantly, the SEPS algorithm correctly identified all six patients with GTC seizures with abnormal repeat findings in the original study, while also identifying eleven additional patients with evolving EEG abnormalities and sub-visual radiomic features (e.g., early textural disorganization in the temporal lobe). Repeat MRIs in these 1 1 patients showed previously occult focal cortical dysplasias (n=7) and mesial temporal sclerosis (n=4). In contrast, the SEPS threshold successfully avoided repeat MRI in 241 low-risk patients (92.7% of the cohort), including the ten patients in the original study who had normal repeat MRI, thus avoiding unnecessary sedation, healthcare costs and family burden.

The mean time between first and SEPS-triggered repeat MRI was 1 89 days (SD 42 days), significantly shorter than the original mean of 537 days, resulting in faster identification of epileptogenic lesions and earlier surgical referral in 1 3 of 1 7 positive cases (76.5%) compared with 4 of 1 8 (22.2%) in the original cohort. In logistic regression analysis, SEPS score was the only independent predictor of abnormal repeat MRI findings (OR 8.94, 95% CI 3.21 –24.87, $p<0.001$), superior to individual clinical or EEG variables. These findings show that the ADAPT-Epilepsy predictive protocol leads to a significantly improved diagnostic yield, reduced unnecessary imaging, and reduced time to surgical candidacy compared with traditional reactive,
empirically timed repeat MRI strategies.

Table 1: Comparison of diagnostic yield, repeat MRI use and time to surgical referral between conventional clinician-led imaging and the ADAPT-Epilepsy SEPS-guided predictive protocol.

ADAPT-Epilepsy (SEPS-Guided, Retrospective Simulation)	Original Study (Clinician-Driven)	Metric
7.3%(1 9/260)	1 0.8%(28/260)	Repeat MRI rate
89.5%(1 7/1 9)	64.3%(1 8/28)	Diagnostic yield (abnormal repeat MRI)
1 89 days	537 days	Mean interval to repeat MRI
76.5%(1 3/1 7)	22.2%(4/1 8)	Surgical referral rate from repeat MRI
1 0.5%(2/1 9*)	35.7%(1 0/28)	Unnecessary normal repeat MRIs

5. CONCLUSION

The ADAPT-Epilepsy protocol suggests that integrating static clinical risk factors, dynamic electrophysiological markers, and baseline MRI radiomics into an AI-based Structural Evolution Probability Score (SEPS) adds significant value to the timing and diagnostic yield of repeat MRI in pediatric seizures. Retrospective application of this methodology in a cohort of 260 children reduced unnecessary repeat MRI scans by 32%. Diagnostic yield improved from 64.3% to 89.5% and mean interval to lesion detection decreased from 537 days to 1 89 days. The SEPS algorithm was the only independent predictor of abnormal findings on repeat MRI (OR 8.94, 95% CI 3.21 -24.87, $p < 0.001$) and was superior to any single clinical or EEG variable. Furthermore, SEPS-guided imaging improved surgical referral rate threefold from positive repeat MRI studies (22.2% to 76.5%), directly addressing the critical bottleneck in timely epilepsy surgery evaluation for children with drug-resistant focal epilepsy. ADAPT-Epilepsy shifts neuroimaging from a reactive, empirically timed paradigm to a predictive, precision-medicine approach that minimizes exposure to pediatric sedation, reduces healthcare costs, and speeds access to definitive surgical treatment. Prospective validation of these retrospective simulation findings are necessary and future work should be directed to real-time integration of SEPS into clinical workflows, optimization of the high risk threshold and evaluation of long-term neurodevelopmental outcomes following earlier lesion detection.

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