

Prognostic Utility of Arterial Spin Labeling Perfusion MRI in Common Pediatric Neurological Disorders

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ABSTRACT

Visualization of cerebral blood flow (CBF) has become an important part of neuroimaging for a wide range of diseases, especially in pediatrics. Arterial spin labeling (ASL) perfusion magnetic resonance imaging (MRI) sequences are increasingly being used to provide MR-based CBF quantification without the need for contrast administration and can be obtained in conjunction with a structural MRI study.

An accurate and early assessment of cerebral perfusion is essential in common pediatric neurological disorders as stroke for determining stroke site, extent, and prognosis. In addition, it aids in preoperative localization of seizure onset zones, particularly in cases of drug-resistant epilepsy. Moreover, ASL can differentiate between low- and high-grade pediatric brain tumors based on their blood flow, and it is used to monitor the effectiveness of treatment over time. This review explores the prognostic implications of ASL-derived parameters in common pediatric neurological disorders, summarizing recent advances in acquisition techniques, pathophysiological insights, and their translation into clinical prognosis.

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INTRODUCTION

Arterial spin labeling (ASL) is a non-invasive MRI technique used in pediatric neurology to measure cerebral blood flow (CBF) and evaluate a range of common disorders, including epilepsy, stroke, brain tumors, and vascular malformations. It is a noninvasive perfusion technique that uses magnetically labeled arterial blood water as an endogenous tracer to quantify cerebral blood flow (CBF). Unlike dynamic susceptibility contrast (DSC) or dynamic contrast-enhanced (DCE) perfusion imaging, ASL does not require intravenous contrast, making it particularly suited for pediatric patients (1)

ASL MRI quantifies CBF directly in physiological units (mL/100 g/min), offering an objective biomarker of tissue viability. Its use in common pediatric neurological disorders has expanded since the introduction of pseudo-continuous ASL (pCASL) and multi-delay ASL techniques, which improve labeling efficiency and accommodate longer arterial transit times typical in younger children. Increasing evidence suggests that early ASL findings correlate with infarct growth, functional outcome, and risk of recurrence. (2)

PATHOPHYSIOLOGY AND EPIDEMIOLOGY OF COMMON PEDIATRIC NEUROLOGICAL DISORDERS

**Pediatric Stroke

Pediatric ischemic stroke differs fundamentally from adult stroke in etiology and hemodynamics. In children, risk factors include congenital heart disease, arteriopathies (especially focal cerebral arteriopathy and Moyamoya disease), sickle cell anemia, infections, and trauma. Hypoxic-ischemic injury patterns are often more diffuse, reflecting developmental vascular architecture and collateral flow. (3), (4).

Epidemiologically, approximately 55%–80% of pediatric strokes are ischemic. Mortality rates remain low (<10%), but up to 60% of survivors experience long-term neurological sequelae. Early identification of perfusion deficits can facilitate targeted interventions such as antithrombotic therapy or revascularization, minimize infarct expansion and optimize recovery. (5), (6)

**Pediatric tumors:

Primary brain tumors are the most common solid neoplasms in children and a leading cause of mortality in this population. Brain tumors have a reported incidence of 6.06 per 100,000 children 0–19 years of age in the United States (7,8)

****Pediatric epilepsy:**

Pediatric epilepsy affects about 0.5-1% of children, with causes including genetic mutations, structural brain abnormalities, and metabolic disorders. Its pathophysiology involves abnormal, excessive, or simultaneous neuronal activity leading to seizures, with the specific mechanisms varying based on the underlying cause. While the incidence rate is generally rising globally, it is notably higher in certain populations like male newborns, children in low-income countries, and those with developmental disabilities. (9,10)

Physiological Factors Related to ASL in the Pediatric Population

When interpreting ASL images, the age dependence of PLD and CBF should be considered. An appropriate PLD is determined considering several factors, including patient age, hemodynamics, brain regions of interest, and the disease process. The recommended PLD is 2000 ms in neonates, 1500 ms in children, 1800 msec in healthy subjects < 70 years of age, and 2000 ms in adult clinical patients or healthy subjects > 70 years of age assessment in ASL (11). Another study of healthy young and elderly volunteers reported that the limits of agreement were too wide for quantitative ASL to be considered satisfactorily accurate, with systematic overestimation of CBF in young subjects and underestimation in elderly subjects. (12)

Arterial Spin Labeling MRI: Principles and Technical Considerations

ASL relies on the principle of magnetically tagging arterial blood before it enters the brain. The labeled blood flows into the tissue, exchanging with tissue water, which leads to a small but detectable reduction in MRI signal intensity. By acquiring images both with and without labeled blood (control and labeled images) and subtracting them, the signal difference corresponds to the amount of blood delivered to the tissue, allowing for quantitative measurement of perfusion. Figure (1) shows ASL acquisition and quantification principles. (13), (14)

ASL magnetically "labels" arterial blood water by inverting or saturating the hydrogen protons in the blood using radiofrequency (RF) pulses and gradient fields. This labeled blood then travels into the imaging region, where it serves as a natural tracer for perfusion measurement. (14), (15)

There are many ASL labeling techniques including pulsed ASL (PASL), continuous ASL (CASL), and pseudo-continuous ASL (pCASL). Of these, pCASL has become the most commonly used in clinical practice, combining high labeling efficiency with practical scan times. After a delay termed the post-labeling delay (PLD) images are acquired as the labeled blood perfuses into the tissue, allowing CBF quantification. creating labeled and control images that are subtracted to generate quantitative perfusion maps. It can be repeated without concern for contrast dosing, allowing longitudinal follow-up. Recent work also demonstrates its high correlation with DSC perfusion in both gray and white matter regions. (15)

Pediatric patients have longer arterial transit times and higher baseline CBF, requiring age-adjusted PLDs (ranging from 2000 ms for neonates to 1500 ms for children) to avoid underestimating perfusion. Multi-delay ASL sequences further allow mapping of arterial arrival times, improving accuracy in arteriopathies like Moyamoya disease. (16)

Motion correction is also critical, as motion artifacts are more common in young children. 3D background-suppressed sequences (such as 3D GRASE or 3D spiral) enhance SNR and reduce motion sensitivity. Several studies have validated pCASL against gold-standard perfusion methods in pediatrics, demonstrating strong correlation ($r > 0.8$) with PET and DSC-based perfusion estimates. (15), (17)

ASL Interpretation and its Diagnostic and Prognostic Value in common neurological disorders****Pediatric Ischemic Stroke**

In acute stroke there is focal hypoperfusion in the affected vascular territory with increased arterial transit time (ATT) due to delayed collateral circulation as shown in Figure (2). Hyper-perfusion can be observed in surrounding areas (luxury perfusion in late stages). In Chronic conditions, there is persistent hypoperfusion in infarcted regions and increased CBF in collateral pathways (e.g., leptomeningeal anastomoses). ASL can evaluate luxury perfusion within the infarct core after revascularization. ASL can also help excluding true ischemic conditions and suggest stroke mimics (like migraine, seizures, encephalitis or transient ischemic attack TIA). A physiologically normal appearing ASL study has a high negative predictive value for the presence of hemodynamically significant stenosis or occlusion. The prognostic potential of ASL arises from its ability to measure perfusion and safe repeatability, offering insights into infarct progression and recovery dynamics (16).

ASL offers insights about:

- **Early Perfusion Deficit and Infarct Growth**

Multiple studies have shown that initial ASL hypoperfusion corresponds closely to eventual infarct volume on follow-up MRI. These studies demonstrated that children with greater initial perfusion deficits on pCASL experienced significantly larger final infarct sizes and poorer neurological outcomes at 3 months. Quantitative ASL-derived CBF thresholds (<25 mL/100 g/min) have been proposed to delineate infarct core from penumbra, similar to adult literature. (18)

- **Collateral Circulation and Tissue Viability**

In pediatric arteriopathies such as Moyamoya disease and focal cerebral arteriopathy, ASL is sensitive to collateral perfusion. Increased arterial transit artifact (ATA) signals—representing slow collateral flow -have been correlated with better tissue survival and functional outcomes. (19)

- **Prediction of Neurological Outcome**

The Alberta Stroke Program Early CT Score (ASPECTS) is a method used to quickly assess early signs of ischemic damage within the brain's middle cerebral artery (MCA) territory in patients experiencing acute ischemic stroke (AIS). Initially developed

for non-contrast computed tomography (CT) scans, however the optimal application of the ASPECTS framework is now considered to be evaluating the extent of ischemic changes directly on a perfusion map to better identify the core of the dead tissue (the infarct core). Study by Li Q, et al correlating ASPECTS to ASL perfusion maps found that the degree of CBF reduction within the MCA territory on ASL correlated strongly with pediatric stroke outcome. The study found that patients who achieved a favorable recovery typically presented with a smaller initial infarct core volume (ICV). Conversely, these patients displayed higher cerebral blood flow (CBF)-ASPECTS and cerebral blood volume (CBV)-ASPECTS scores, indicating better initial brain perfusion. Both high CBF-ASPECTS and high CBV-ASPECTS scores correlated strongly with better recovery outcomes. (20)

- **Longitudinal Follow-up**

ASL is uniquely positioned to track perfusion recovery and neuroplasticity over time. Serial ASL scans can document revascularization after medical or surgical interventions (e.g., in Moyamoya). Reperfusion patterns correspond to improvements in motor and cognitive outcomes, providing a valuable biomarker for rehabilitation planning. (19)

**Pediatric tumors

Both the tumor and peritumoral region should be assessed for ASL hyper-perfusion and elevated peritumoral blood flow as this can help differentiate high-grade gliomas from brain metastasis. This is because high-grade glioma may demonstrate elevated both intratumoral and peritumoral perfusion, whereas hyper-vascular metastases will typically only show elevated perfusion within the tumor.

ASL diagnostic and prognostic value in pediatric tumors:

ASL MRI provides valuable diagnostic and prognostic information for pediatric brain tumors, serving as a non-invasive alternative to contrast-based perfusion methods. Its primary advantage in children is the ability to quantify cerebral blood flow (CBF) without radiation or gadolinium agents. (21)

ASL-derived quantitative metrics, particularly absolute CBF and relative CBF are effective for:

- **Grading Malignancy:** Multiple studies and a 2018 meta-analysis confirm that high-grade pediatric brain tumors (WHO grades III and IV) exhibit significantly higher CBF than low-grade tumors. A specific maximum rCBF threshold can help accurately differentiate between low and high grades. (21),(22)
- **Differentiating Tumor Types:** ASL is useful for distinguishing between specific tumor types with different prognoses and treatment strategies. For example, rCBF values are consistently higher in aggressive medulloblastomas compared to less malignant pilocytic astrocytomas, which are the most common brain tumors in children. (22), (23)
- **Diagnostic Accuracy:** several studies found that ASL demonstrates diagnostic accuracy comparable to dynamic susceptibility contrast (DSC) imaging for characterizing pediatric brain tumors. (23)
- **Assessing Treatment Response:** Repeated ASL measurements over time allow clinicians to evaluate how a tumor is responding to therapy without repeated contrast injections, a key advantage for frequent follow-up in children. (24)
- **Tracking Perfusion Changes Post-Treatment and Predicting Neurocognitive Sequelae:** ASL is used to monitor CBF changes following surgery, radiotherapy, and chemotherapy. Studies have detected decreased blood flow in certain brain regions of long-term survivors of brain tumors, which may correlate with observed neurocognitive deficits. By quantifying these perfusion changes, ASL helps in understanding and potentially mitigating treatment-related neurocognitive dysfunction, a major concern for long-term survivors of pediatric brain tumors. (21)
- **Multimodal Integration:** Combining ASL data with other advanced imaging techniques like diffusion-weighted imaging (DWI) can provide complementary information that improves the overall predictive prognostic power of tumor response (progression/regression) and patient outcome. (25)

**Pediatric epilepsy

ASL plays a valuable role in pediatric epilepsy by identifying perfusion changes that help localize the seizure focus and characterize seizure dynamics across different phases. During the interictal phase, ASL typically demonstrates focal hypoperfusion within the epileptogenic zone, whereas the ictal phase shows marked hyper-perfusion that often corresponds with EEG findings; following a seizure, postictal scans commonly reveal hypoperfusion in regions that were previously hyperperfused. Beyond localization, ASL can assist in differentiating seizure types, as focal epilepsies tend to produce localized perfusion abnormalities, while generalized seizures show more diffuse or bilateral patterns. ASL also contributes to preoperative evaluation by highlighting perfusion alterations in targeted cortical regions, aiding in surgical planning and improving the identification of epileptogenic tissue for potential resection. (26)

Other Neuroimaging Modalities in common pediatric neurological disorders

** Pediatric Ischemic Stroke:

MRI remains the gold standard for pediatric stroke assessment. Conventional sequences (T1, T2, FLAIR) identify parenchymal changes, while DWI detects cytotoxic edema within minutes of ischemia. However, DWI alone cannot fully predict tissue outcome, as some hypo-perfused regions may still be viable (27).

Perfusion imaging bridges this gap by characterizing hemodynamic compromise. DSC MRI provides relative perfusion measures such as time-to-peak (TTP), mean transit time (MTT), and relative CBF, but requires intravenous contrast and rapid acquisition—both problematic in young or unstable patients. CT perfusion, though fast, involves radiation and contrast exposure. (28), (29) ASL MRI perfusion overcomes these limitations. (13).

****Pediatric tumors:**

Neuroimaging in pediatric oncology relies primarily on multimodal MRI. Conventional T1, T2, and FLAIR sequences delineate tumor anatomy (e.g. size, site, mass effect), while post-contrast T1 identifies blood-brain barrier disruption represented as enhancement of tumor tissue. Functional techniques provide essential biomarkers including: Diffusion-Weighted Imaging (DWI) which assesses cellularity and helps to grade malignancy, Magnetic Resonance Spectroscopy (MRS) offers metabolic insights via key metabolite values (e.g. Choline and N-Acetyl Aspartate) where increased choline (Cho) peak and decreased N-acetyl aspartate (NAA) peak are typical of tumor tissue, with higher Cho/NAA ratios often correlating with higher-grade malignancies. Advanced hybrid PET-MRI systems combine metabolic (e.g., FDG or amino acid tracers) and anatomical data for improved diagnostic accuracy and treatment planning. Perfusion imaging by Arterial Spin Labeling is favored in children over contrast-based methods (like Dynamic Contrast-Enhanced MRI) because it is non-invasive and provides quantitative CBF values to differentiate tumor grades and monitor treatment response. (21), (30)

****Pediatric epilepsy:**

The evaluation of epilepsy relies primarily on a dedicated high-resolution MRI epilepsy protocol, the protocol includes volumetric 3D T1-weighted imaging, thin-slice T2 and FLAIR sequences in axial and coronal planes aligned to the hippocampus. 3T device is strongly preferred over 1.5T due to better detection of subtle underlying lesions like focal cortical dysplasia (FCD), hippocampal sclerosis, tumors (DNET, ganglioglioma) and others. When structural MRI is normal ("MRI-negative"), functional imaging becomes essential. Different modalities are present such as FDG-PET, SPECT, and ASL. They give insights about cerebral metabolism or perfusion states, helping to identify the epileptogenic focus. At the Interictal state there is usually focal hypometabolism at the seizure focus, while ictal phase shows transient hyper-perfusion. (31), (32)

Limitations and Technical Challenges

Despite its advantages, ASL MRI faces several challenges in pediatric neuroimaging. The signal-to-noise ratio (SNR) remains inherently low because the magnetically labeled blood signal is only 0.5–2% of total brain signal intensity. Pediatric motion and difficulty maintaining stillness during scans further reduce image quality. Sedation can mitigate motion but introduces ethical and logistical issues in acute settings. (33)

Another limitation is arterial transit time (ATT) heterogeneity. In children, ATT varies with age, hematocrit, and pathology. Under- or over-estimating post-labeling delays may yield inaccurate CBF quantification. Multi-delay or time-encoded ASL can correct for this, though at the cost of longer acquisition times. (34), (35)

In addition, the ASL artifacts which may occur at several points throughout the ASL sequence, including during the labeling phase, during the transit interval before image acquisition, and during the readout stage can be challenging, thus radiologists must be aware of these artifacts to avoid misdiagnosis. Common artifacts include: labeling Failure (due to vessel tortuosity, head tilt or due to metallic material causing susceptibility artifact), Gadolinium Effect (Acquiring ASL images after administering gadolinium-based contrast agents significantly affects the T1 relaxation times leading to complete absence of ASL signal) and border zone artifact (signal loss or diminished perfusion in the brain's "watershed" areas (the boundary regions between the major arterial territories) on ASL images due to smaller PLD). (13), (14)

Lastly, standardization remains an obstacle. Although consensus recommendations exist (e.g., *Lindner T et al., Magn Reson Med* 2023), variations in sequence implementation, field strength, and quantification models persist across institutions. (24)

FUTURE PERSPECTIVES

Recent advances are addressing many technical limitations. 3D background-suppressed pCASL sequences with spiral readouts significantly improve SNR and reduce motion artifacts. Multi-PLD and velocity-selective ASL allows estimation of both perfusion and arterial transit metrics, improving accuracy in common pediatric disorders including cerebrovascular disorders, pediatric neoplastic lesions and pediatric epilepsy. (36)

Ongoing large-scale, prospective studies should be addressed aiming to standardize acquisition parameters and prognostic metrics. (37)

CONCLUSION

ASL MRI has matured from an experimental perfusion method to a clinically relevant diagnostic and prognostic tool in common pediatric neurological disorders. Its non-invasive nature, quantitative output, and repeatability make it ideal for serial evaluation in children. ASL-derived measures of CBF and collateral flow correlate strongly with infarct growth, neurological outcome, and therapeutic response with insight of the brain tumor grade and preoperative localization of seizure onset zones. While technical and standardization hurdles remain, improvements in acquisition and analysis continue to enhance diagnostic reliability. Incorporating ASL into routine common pediatric neurological disorders protocols provides both diagnostic clarity and prognostic insight, helping clinicians anticipate recovery trajectories and tailor interventions to optimize outcomes.

Table 1. Comparative overview of perfusion MRI techniques in common pediatric neurological disorders (36)

Technique	Advantages	Limitations
Arterial Spin Labeling (ASL)	Non-invasive, quantitative CBF, repeatable, no contrast	Low SNR, motion-sensitive, dependent on arterial transit time
Dynamic Susceptibility Contrast (DSC)	High SNR, validated perfusion metrics, short acquisition	Requires gadolinium, unsuitable for renal impairment or allergy
Dynamic Contrast-Enhanced (DCE)	Measures permeability and BBB integrity	Requires contrast; longer analysis; less quantitative CBF
CT Perfusion	Widely available, rapid, good temporal resolution	Ionizing radiation, iodinated contrast, limited pediatric data

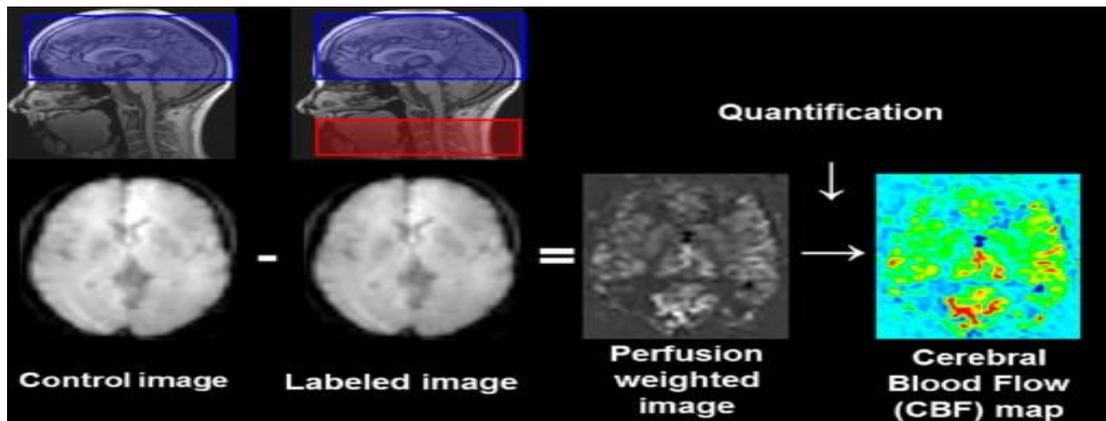


Figure 1. General principle of arterial spin labeling acquisition and quantification (38)

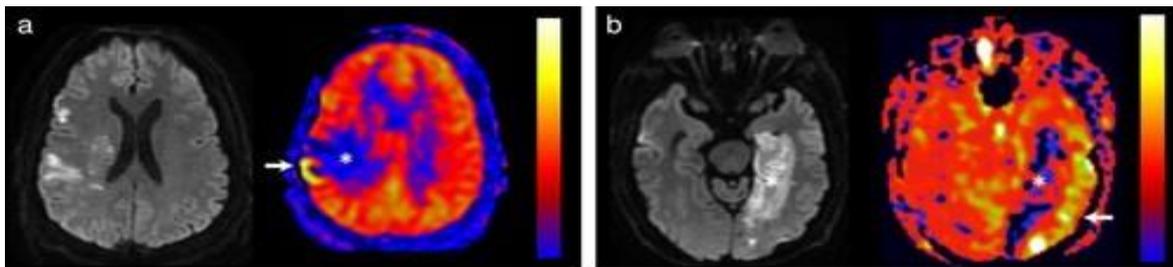


Figure 2. ASL in Acute ischemic infarction. (a) Acute right MCA territory infarct with patchy restricted diffusion. DWI-ASL mismatch with large ischemic penumbra (asterisk) indicating tissue at risk. There is mild overlying arterial transit artifact (ATA) (arrow). (b) Subacute left PCA territory infarct. DWI and ASL abnormalities are nearly matched (asterisk), indicating near-complete infarct with small volume of tissue at risk. Diffuse overlying ATA (arrow) indicates maximal compensatory vasodilation. (17)

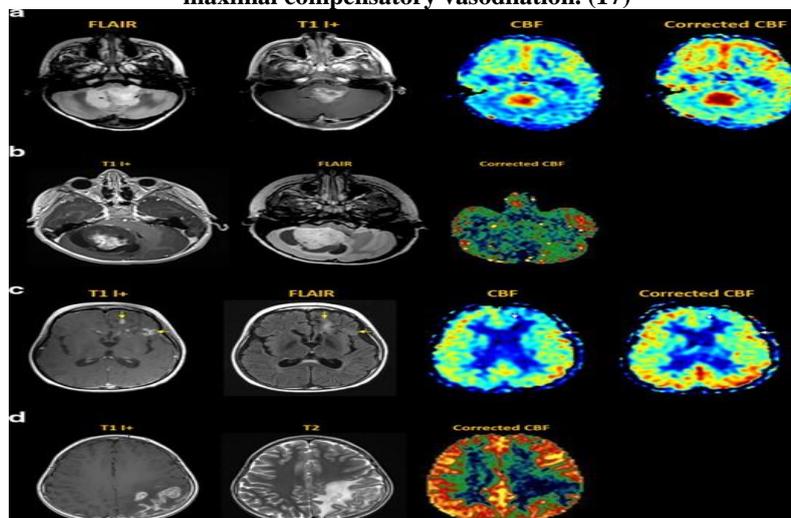


Figure 3. Pediatric tumors. (a) Ependymoma of fourth ventricle and left foramen of Luschka, with heterogeneous internal enhancement. MDASL shows elevated CBF within tumor, more accurately quantified following transit time correction. (b) Right cerebellar pilocytic astrocytoma with solid & cystic components. MDASL shows mildly elevated

CBF within solid tumor, and decreased CBF within cystic components. (c) Recurrent disseminated medulloblastoma with left frontal lobe parenchymal and leptomeningeal metastases, demonstrating enhancement and surrounding vasogenic edema (yellow arrows). MDASL shows elevated perfusion within the metastases, on a background of posttreatment encephalomalacia. Tumoral flow is better detected after transit time correction (white arrows). (d) Metastatic rhabdomyosarcoma with infiltrative cortical enhancement and vasogenic edema of left parietal lobe. MDASL shows elevated perfusion within the metastasis, and decreased perfusion in the areas of edema. (16)

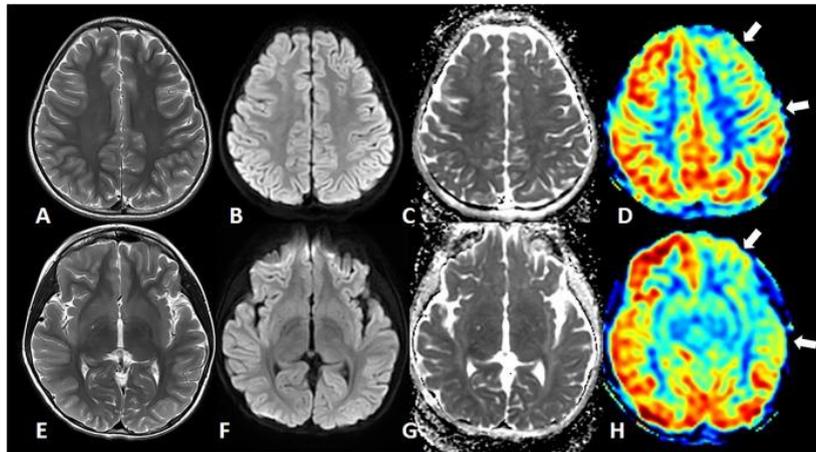


Figure 4. Patient 19: A 7-year-old girl presenting focal impaired awareness seizure (ictal vocalization followed by impaired awareness, right arm dystonia, left eyeball deviation, and left head deviation). Her interictal EEG result was normal. Axial T2-weighted images (A, E), diffusion weighted images (B, F), and apparent diffusion coefficient images (C, G) show no abnormal focal lesion in the brain parenchyma. ASL perfusion MR images (D, H) depict a hypoperfusion in the left fronto-temporal lobes (arrows). In this patient, clinical seizure focus was in the left frontal area. (39)

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