



Original Article

# Detection of ictal and periictal hyperperfusion with subtraction of ictal-interictal 1.5-Tesla pulsed arterial spin labeling images co-registered to conventional magnetic resonance images (SIACOM)

Keisuke Abe<sup>1</sup>, Takafumi Shimogawa<sup>2</sup>, Nobutaka Mukae<sup>2</sup>, Koumei Ikuta<sup>3</sup>, Tadahisa Shono<sup>1</sup>, Atsuo Tanaka<sup>3</sup>, Ayumi Sakata<sup>4,6</sup>, Hiroshi Shigeto<sup>5,6</sup>, Koji Yoshimoto<sup>2</sup>, Takato Morioka<sup>1,7</sup>

<sup>1</sup>Department of Neurosurgery, Harasanshin Hospital, <sup>2</sup>Department of Neurosurgery, Graduate School of Medical Sciences, Kyushu University, <sup>3</sup>Department of Radiology, Harasanshin Hospital, <sup>4</sup>Department of Clinical Chemistry and Laboratory Medicine, Kyushu University Hospital, <sup>5</sup>Department of Neurology, Graduate School of Medical Sciences, Kyushu University, <sup>6</sup>Division of Medical Technology, Department of Health Sciences, Graduate School of Medical Sciences, Kyushu University, Fukuoka, <sup>7</sup>Department of Neurosurgery, Hachisuga Hospital, Munakata, Japan.

E-mail: Keisuke Abe - keisuke.abe23@gmail.com; \*Takafumi Shimogawa - shimogawa.takafumi.338@m.kyushu-u.ac.jp; Nobutaka Mukae - mukaen0203@gmail.com; Koumei Ikuta - oso.ikuchan@gmail.com; Tadahisa Shono - tadahisashono@gmail.com; Atsuo Tanaka - pxi03234@nifty.com; Ayumi Sakata - sakata.ayumi.791@m.kyushu-u.ac.jp; Hiroshi Shigeto - shigeto.hiroshi.565@m.kyushu-u.ac.jp; Koji Yoshimoto - yoshimoto.koji.315@m.kyushu-u.ac.jp; Takato Morioka - takatons1227@gmail.com



\*Corresponding author:

Takafumi Shimogawa,  
Department of Neurosurgery,  
Graduate School of Medical  
Sciences, Kyushu University,  
Fukuoka, Japan.

shimogawa.takafumi.338@m.kyushu-u.ac.jp

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## ABSTRACT

**Background:** Our recent report showed that 1.5-T pulsed arterial spin labeling (ASL) magnetic resonance (MR) perfusion imaging (1.5-T Pulsed ASL [PASL]), which is widely available in the field of neuroemergency, is useful for detecting ictal hyperperfusion. However, the visualization of intravascular ASL signals, namely, arterial transit artifact (ATA), is more remarkable than that of 3-T pseudocontinuous ASL and is easily confused with focal hyperperfusion. To eliminate ATA and enhance the detectability of (peri) ictal hyperperfusion, we developed the subtraction of ictal-interictal 1.5-T PASL images co-registered to conventional MR images (SIACOM).

**Methods:** We retrospectively analyzed the SIACOM findings in four patients who underwent ASL during both (peri) ictal and interictal states and examined the detectability for (peri) ictal hyperperfusion.

**Results:** In all patients, the ATA of the major arteries was almost eliminated from the subtraction image of the ictal-interictal ASL. In patients 1 and 2 with focal epilepsy, SIACOM revealed a tight anatomical relationship between the epileptogenic lesion and the hyperperfusion area compared with the original ASL image. In patient 3 with situation-related seizures, SIACOM detected minute hyperperfusion at the site coinciding with the abnormal electroencephalogram area. SIACOM of patient 4 with generalized epilepsy diagnosed ATA of the right middle cerebral artery, which was initially thought to be focal hyperperfusion on the original ASL image.

**Conclusion:** Although it is necessary to examine several patients, SIACOM can eliminate most of the depiction of ATA and clearly demonstrate the pathophysiology of each epileptic seizure.

**Keywords:** Arterial spin labeling, Ictal hyperperfusion, SISCOM, Subtraction

## INTRODUCTION

Arterial spin labeling (ASL) is a neuroimaging technique that non-invasively quantifies cerebral blood flow (CBF). Acting as a diffusible tracer, water proton nuclear spins in arterial blood are labeled

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by the application of a radiofrequency (RF) pulse that inverts them at the level of the cervical arteries.<sup>[2,3,21]</sup> A post-labeling delay (PLD) is applied to facilitate the arrival of magnetically labeled blood in the region of interest, where an image was captured through magnetic resonance (MR) imaging.<sup>[2,3,21]</sup>

There are two distinct labeling methods for the clinical use of ASL: Pulsed ASL (PASL) and pseudocontinuous ASL (pCASL).<sup>[2,3,5]</sup> PASL involves the application of a short RF pulse to a thick (15–20 cm) “slab” area of the neck for 10–20 ms to convert the arterial water spins. Despite being a relatively easy technique, this approach has several disadvantages: lower signal-to-noise ratios (SNR), lower delivery of labeled magnetization, visualization of intravascular ASL signals, namely, arterial transit artifact (ATA), and a greater amount of T1 decay. In contrast, pCASL involves rapid application of approximately 1000 RF pulses to the labeling plane at a goal rate of approximately 1/ms. This technique helps to increase the SNR and decrease ATA and T1 decay when compared with PASL. The higher the magnetic field, the longer the T1 value in the blood, that is, the longer the labeling effect. Thus; it is said to be difficult to obtain good images with the 1.5-T MR device compared to the 3-T device.<sup>[2,5,8]</sup>

Therefore, to date, the use of 3-T pCASL is recommended for the evaluation of CBF in a clinical setting.<sup>[2,21]</sup> We also reported that 3-T pCASL is extremely useful in assessing ictal hyperperfusion during non-convulsive status epilepticus (NCSE) and periictal hyperperfusion after convulsive status epilepticus (SE) or prolonged seizures.<sup>[12,13,15,18,20,22,24]</sup> However, pCASL can only be implemented in a limited number of MR machines and 3-T MR devices are not widespread in all facilities. Therefore, we demonstrated the ability to visualize ictal hyperperfusion during NCSE with 1.5-T PASL, which can be widely applied in the field of neuroemergency, although it depends on the electrophysiological intensity of the epileptic ictus.<sup>[8]</sup> However, the visualization of ATA of the main arteries was more remarkable than that of tissue CBF.<sup>[8]</sup> For example, regarding the middle cerebral artery (MCA), the ATA of the horizontal (M1) and insular (M2) portions could be judged from its shape; however, the ATA of the opercular (M3) and cortical (M4) portions were sometimes mistaken for tissue CBF.<sup>[8]</sup>

Single-photon emission computed tomography (SPECT), a preoperative examination for epilepsy surgery, is often used to identify the hypoperfusion area during the interictal period and hyperperfusion area during the ictal period in patients with drug-resistant epilepsy. In these cases, it is evident that the subtraction of ictal-interictal SPECT co-registered to magnetic resonance imaging (MRI) (SISCOM), which subtracts the interictal SPECT image from the ictal SPECT image and superimposes it on the anatomical MR image, is useful for localizing the epileptogenic zone.<sup>[14,16,25]</sup> Analogous to SISCOM, we have developed the subtraction

of ictal-interictal 1.5-T PASL images co-registered to conventional and morphological MR images (SIACOM), to eliminate the ATA of major arteries and increase the detectability of ictal or periictal hyperperfusion, and examined its usefulness in the daily clinical setting.

## MATERIALS AND METHODS

### Patients

From June 2021 to June 2022, 51 patients underwent control of epileptic ictus either as neuroemergency cases or postoperatively at our hospital. Most patients underwent neuroradiological examinations, such as computed tomography or conventional MRI combined with routine electroencephalogram (EEG), within 2 days of onset. In 10 (17.3%) of the 51 patients, PASL sequences were added to the conventional MRI examination for clinical purposes depending on the patient's condition and at the discretion of the attending physicians. Of these ten patients, we retrospectively selected four patients (three women and one man; mean age, 70 years; range, 57–85 years) who underwent both ASL and EEG during both ictal and interictal states [Table 1]. Regarding the order of EEG and ictal MRI, EEG was first performed in three patients (Patients 1, 2, and 4), and ASL was performed first in patient 3. The interval between these examinations varied from 2 h to 1 day (mean, 9.3 h). The interval between these tests during the ictal and interictal periods was 2–6 months (mean, 3.5 months). Ethical approval was obtained from the Institutional Review Board of Harasanshin Hospital (No. 2021-10). The need for patient consent was waived owing to the retrospective study design.

### ASL imaging

MRI was performed using a 1.5-T scanner (MAGNETOM Aera; Siemens, Erlangen, Germany) equipped with a 20-channel head/neck coil as previously described.<sup>[8]</sup> A 3-D turbo gradient spin echo and PASL protocol were used in this study. Other acquisition parameters were as follows: phase encoding in the z-direction = 24, time to repeat (TR) = 3000 ms, TE = 17.18 ms, field of view = 220 mm, matrix = 64 × 52, slice thickness = 3 mm, reconstructed voxel size = 3.4 × 3.4 × 3.0 mm, and number of slices = 48. Two PLDs (inversion times) of 1500 ms (1.5 s) and 1990 ms (2.0 s) were used routinely. The ASL acquisition times for each PLD were 2 min and 30 s.

To obtain SIACOM, the data from each voxel of the ictal ASL were automatically subtracted from the data from the corresponding voxel of the interictal ASL using a clinically used volume analyzer SYNAPSE VINCENT (Fujifilm, Tokyo, Japan) as previously described.<sup>[10,22]</sup> In addition, the subtracted ASL images were automatically superimposed on the conventional anatomical MR images, including

**Table 1:** Clinical profiles, EEG, and subtraction of ictal-interictal 1.5-tesla pulsed ASL co-registered with conventional magnetic resonance imaging (SIACOM) findings of four patients.

Patient No.	Age/Gender	Clinical diagnosis	Epileptogenic lesion	Interval between ictal EEG and MRI	Ictal EEG findings	Interval between ictal and interictal ASL/EEG (month)	Interictal EEG findings	SIACOM	
								PLD (sec)	Elimination of ATA
1	57/F	Focal NCSE	Contusional lesion, Rt fronto-parietal	EEG 1 <sup>st</sup> 5 H	Ictal discharges from PDs+F at C4, P4 and O2	3	Focal slow waves, Rt posterior quadrant	1.5	+ Tight anatomical relationship with the lesion Ipsilateral thalamic involvement
2	63/F	Focal NCSE	Resected osteosarcoma, Lt temporal	EEG 1 <sup>st</sup> 1 D	Ictal discharges from PDs+F at T3 and T5	2	Focal slow waves with rare paroxysms, Lt temporal	1.5 1.8 2.0	+ Tight anatomical relationship with the lesion Gradual increase in ASL signals Minute increased signal at Rt frontal convexity
3	85/F	Situation related seizure	-	MRI 1 <sup>st</sup> 2 H	PDs at F4	3	No abnormality	1.5	+ No focally increased signal
4	75/M	Generalized epilepsy	-	EEG 1 <sup>st</sup> 6 H	Frequent generalized epileptiform bursts	6	Sporadic generalized epileptiform discharges	1.5	+ No focally increased signal

EEG: Electroencephalography, ASL: Arterial spin labeling, MRI: Magnetic resonance imaging, PLD: Post-labeling delay, ATA: Arterial transient artifact, F: Female, M: Male, Rt: Right, Lt: Left, NCSE: Non-convulsive status epilepticus, H: Hours, D: Day, PD: Periodic discharge, +F: With fast activities

T1-weighted images (T1WI), T2-weighted images (T2WI), and images with fluid-attenuated inversion recovery sequence (FLAIR). The evaluation of ASL findings was based on visual inspection by a board-certified radiologist (A.T.) and a neurosurgeon (T.S.) who were familiar with ASL evaluation, as described in our previous report<sup>[8]</sup> and blinded to the clinical data. No differences in their interpretations were observed in the independent assessments.

## EEG

Routine EEG recordings were obtained using a digital EEG machine (Neurofax 1200; Nihon-Kohden, Tokyo, Japan), with electrode placement according to the International EEG 10-20 system. EEG recordings were performed for at least 30 min. The evaluation of EEG findings was performed on visual inspection by two board-certified electroencephalographers (T.M. and H.S.) who were blinded to the clinical data based on the critical care EEG terminology proposed by the American Clinical Neurophysiological Society in 2021.<sup>[11]</sup> No differences in electroencephalography interpretations were recorded in the independent assessments.

## RESULTS

The clinical profiles and the EEG, and SIACOM findings of the four patients are summarized in Table 1, and the detailed findings are described below.

### Patient 1

A 57-year-old woman had a head injury due to a fall 4 years prior and underwent craniotomy for a right acute subdural hematoma at our hospital. MRI revealed three contusional lesions in the convexity of the right frontoparietal lobe, right frontal base, and right frontal pole [Figure 1a]. She was transported to our hospital by ambulance with focal-to-bilateral tonic-clonic seizures. Her seizures were controlled by intravenous administration of diazepam (DZP); however, impaired consciousness persisted. EEG demonstrated lateralized periodic discharges (LPDs) with fast wave activities (+F) in the right parieto-centro-occipital lesion (at P4, C4, and O2), which became ictal discharges with evolution in frequency [Figures 1b and c]. She was diagnosed with focal NCSE and intravenous fosphenytoin (fPHT) administration was initiated. Ictal ASL, which was performed 5 h after EEG examination, showed increased ASL signals in the right posterior cortex, in addition to the ATA of the MCAs and posterior cerebral arteries (PCAs) on both sides at PLD of 1.5 s [Figure 1d]. Increased signals were observed in the ipsilateral thalamus. The increased ASL signals in the right posterior cortex decreased at PLD of 2.0 s.

Interictal ASL, which was performed at the outpatient service 3 months after her epileptic ictus, showed no site of increased

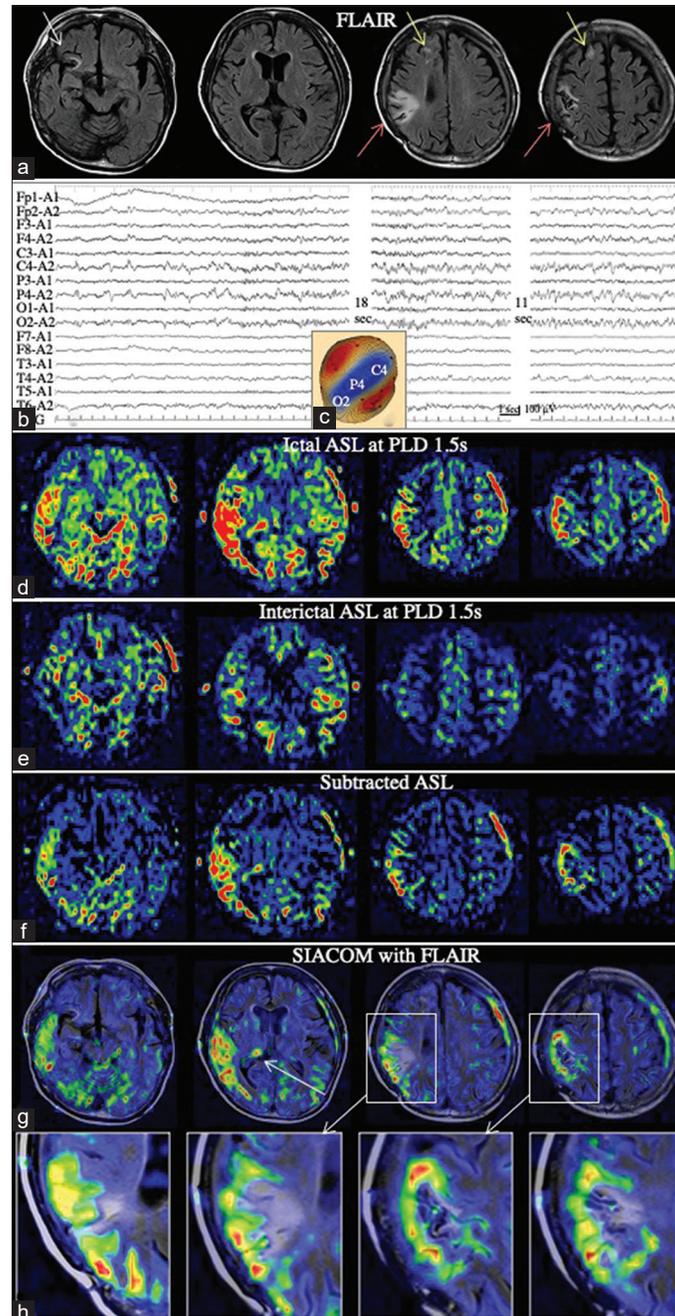
signal, while the ATA of the bilateral MCAs and PCAs were observed [Figure 1e]. Subtraction of the ictal ASL at a PLD of 1.5 s from the interictal ASL at a PLD of 1.5 s demonstrated that the ATA of the bilateral MCAs and PCAs was almost eliminated, and the increase in ASL signals in the right posterior quadrant became prominent [Figure 1f]. When the subtracted ASL was superimposed on the FLAIR, it was revealed that an increase in ASL signals occurred from the cortical convex on and the cortex in the sulcus around the contusional lesion of the right frontoparietal lobe and extended to the ipsilateral temporal lobe [Figures 1g and h]. An increased ASL signal was also observed in the ipsilateral thalamus. The ATA remained partially in the contralateral ambient cistern.

### Patient 2

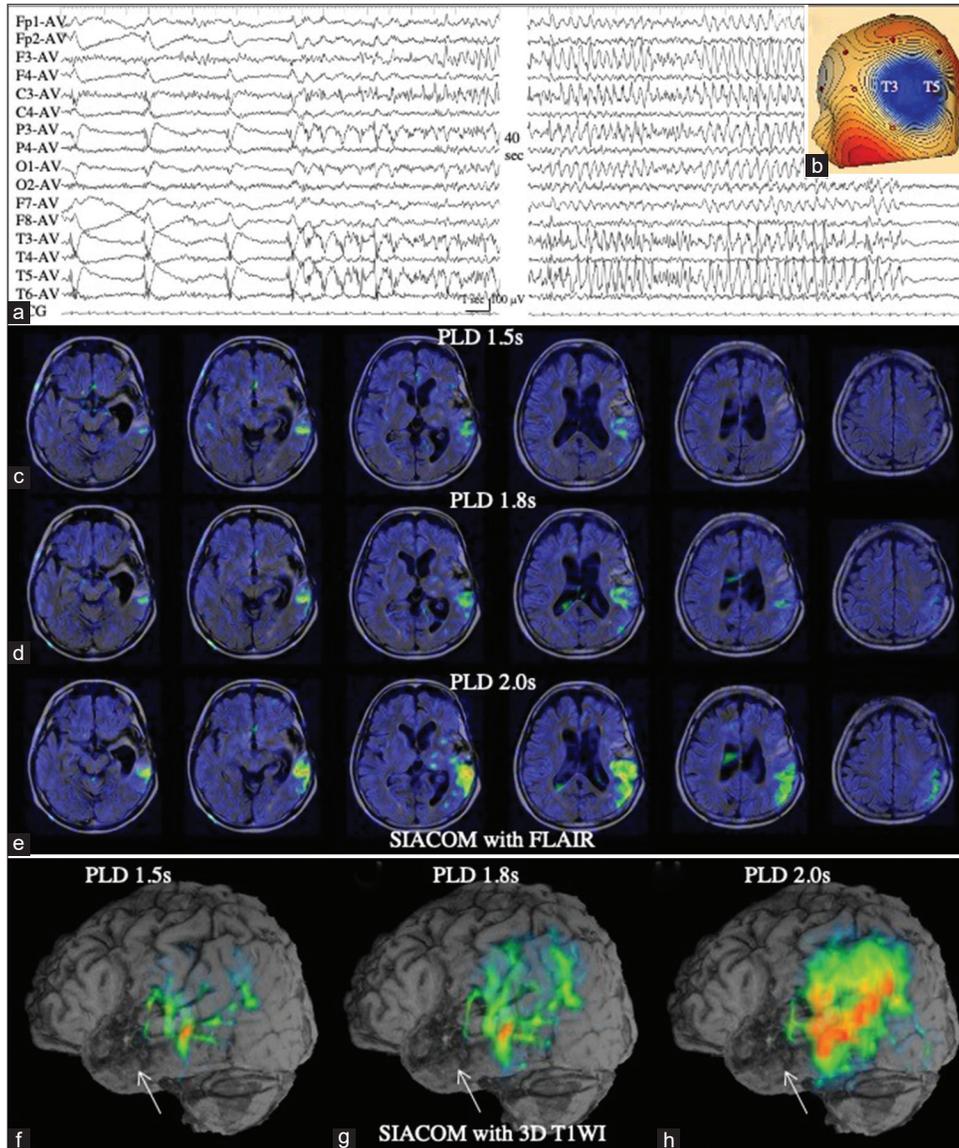
The 63-year-old woman, as previously reported,<sup>[7,8]</sup> developed repeated attacks of aphasia due to focal NCSE following surgical removal of radiation-induced osteosarcoma of the left temporal region. Despite taking multiple anti-seizure medications (ASM), she developed a similar aphasic seizure. On the EEG, LPDs + F persisted in the left temporal region (T3 and T5), spread to the left frontoparietal region, and became ictal discharges with evolution to the left hemisphere [Figures 2a and b]. With the diagnosis of focal NCSE, she underwent intravenous administration of fPHT and 1 day later, aphasia slightly improved, the periictal ASL with PLD of 1.5 s, 1.8 s, and 2.0 s was obtained. She also underwent interictal ASL 2 months later, and the subtracted ASL image was superimposed on the FLAIR image to create SIACOM. ASL signals posterior to the surgical scar on the left temporal lobe were focally increased at the PLD of 1.5 s [Figure 2c]. At a PLD of 1.8 s, the site extended to the posterior temporal and parietal lobes [Figure 2d]. The signals were further increased at a PLD of 2.0 s [Figure 2e]. No residual ATA were observed. SIACOMs, which were created by superimposing the subtracted ASL of each PLD on the lateral view of the three-dimensional (3D)-T1WI images, clearly demonstrated that a gradual extension and increase of the ASL signals occurred in the posterior temporal and parietal cortices posterior to the surgical scar of the left temporal lobe [Figures 2f-h]. The site of increased CBF shown by SIACOM at a PLD of 2.0 s with 3D-T1WI [Figure 2h] almost exactly matched the potential distribution shown by the voltage topography of LPDs [Figure 2b].

### Patient 3

An 85-year-old woman had been taking hypnotics and neuroleptics, including zopiclone, brotizolam, suvorexant, and etizolam, for insomnia for a long time. However, the patient suddenly stopped taking these medications when she underwent bladder hydrodilatation for interstitial cystitis under general anesthesia. Although she had no problems



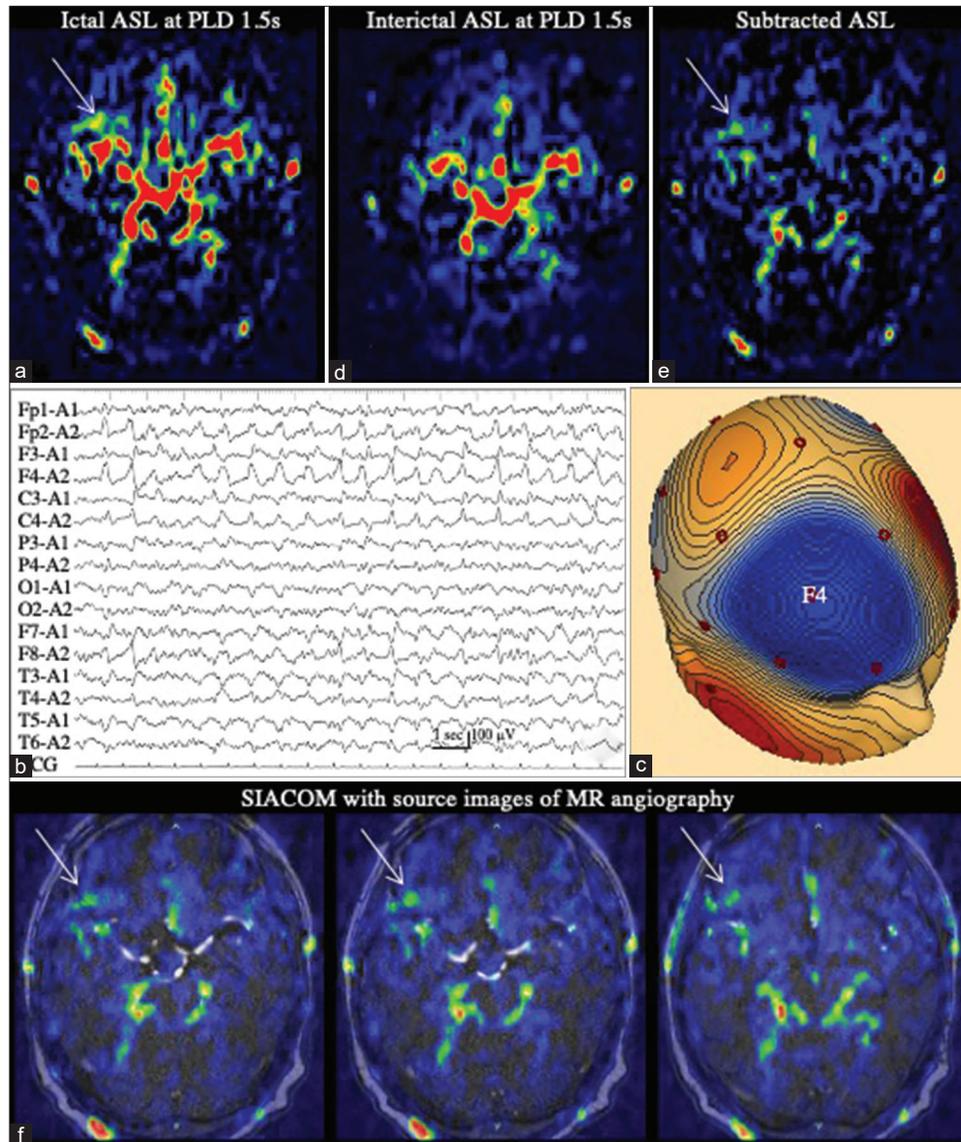
**Figure 1:** Patient 1 (a) Magnetic resonance (MR) images with fluid attenuated inversion recovery sequences (FLAIR) shows three contusional lesions in the right fronto-parietal lobe (red arrows), right frontal base (white arrow), and right frontal pole (yellow arrow). (b) Electroencephalogram (EEG) demonstrates lateralized periodic discharges (LPDs) with fast wave activities (+F) in the right parieto-centro-occipital lesion, which becomes ictal discharges. (c) Voltage topography depicts that the maximal amplitude of negativity (indicates blue) of LPD is located at P4, C4, and O2 of International EEG 10-20 system. (d) MR perfusion image with arterial spin labeling (ASL) at post-labeling delay (PLD) of 1.5 s during ictal periods shows increased ASL signals in the right posterior cortex, in addition to the arterial transit artifact (ATA) of the middle cerebral arteries (MCAs) and posterior cerebral arteries (PCAs) on both sides. (e) Interictal ASL at a PLD of 1.5 s fails to reveal the site of increased ASL signal, while the ATA of the bilateral MCAs and PCAs are observed. (f) Subtraction of the ictal ASL from the interictal ASL (subtracted ASL) demonstrates that the ATA of the bilateral MCAs and PCAs is mostly eliminated, and the increase in cerebral blood flow in the right posterior quadrant becomes prominent. (g and h) Subtraction of ictal-interictal ASL images co-registered to FLAIR images (SIACOM) reveals that an increase in ASL signals occurs from the cortical convexity and the cortex in the sulcus around the contusional lesion of the right fronto-parietal lobe, and extends to the ipsilateral temporal lobe. Increased ASL signal in the ipsilateral thalamus is also revealed (white arrow). (h) Shows enlarged views around the contusional lesion on (g).



**Figure 2:** Patient 2 (a) Electroencephalography (EEG) shows lateralized periodic discharges (LPDs)+F persist on the left temporal region, spread to the left fronto-parietal region, and become ictal discharges on the left hemisphere. (b) Voltage topography indicates that the maximal amplitude of the negativity of LPD is located at T3 and T5. (c-e) SIACOM, which was superimposed on the fluid attenuated inversion recovery sequences, show arterial spin labeling (ASL) signals posterior to the surgical scar at the left temporal lobe is focally increased at a post-labeling delay (PLD) of 1.5 s (c). At a PLD of 1.8 s, the site is extended to the posterior temporal and parietal lobes (d). The signals are further increased at a PLD of 2.0 s (e). (f-h) When the subtracted ASL of each PLD is superimposed on the lateral view of the three-dimensional image created from 3-dimensional T1-weighted images, a gradual extension and increase of the ASL signals occurs in the posterior temporal and parietal cortices posterior to the surgical scar (white arrow) is demonstrated.

with surgery and anesthesia, she developed convulsive SE at night after surgery. Her seizures were controlled with the intravenous administration of DZP and fPHT. She underwent MRI 6 h later, which failed to reveal any epileptogenic lesions. As ASL with a PLD of 1.5 s showed a marked ATA depiction of the major arteries at the bottom of her brain, it was difficult to determine a minute increase in ASL signals in the right frontal lobe [Figure 3a]. Two hours later, EEG

demonstrated LPDs with 1 Hz or higher in the right frontal region (F4) [Figures 3b and c], indicating the ictal-interictal continuum, and she was diagnosed with a situation-related seizure associated with the sudden discontinuation of hypnotics and neuroleptics. Three months later, without ASM, the patient underwent interictal ASL [Figure 3d]. On subtracting ASL at a PLD of 1.5 s, ATA was eliminated, and a minute increase in ASL signal at the right frontal lobe became

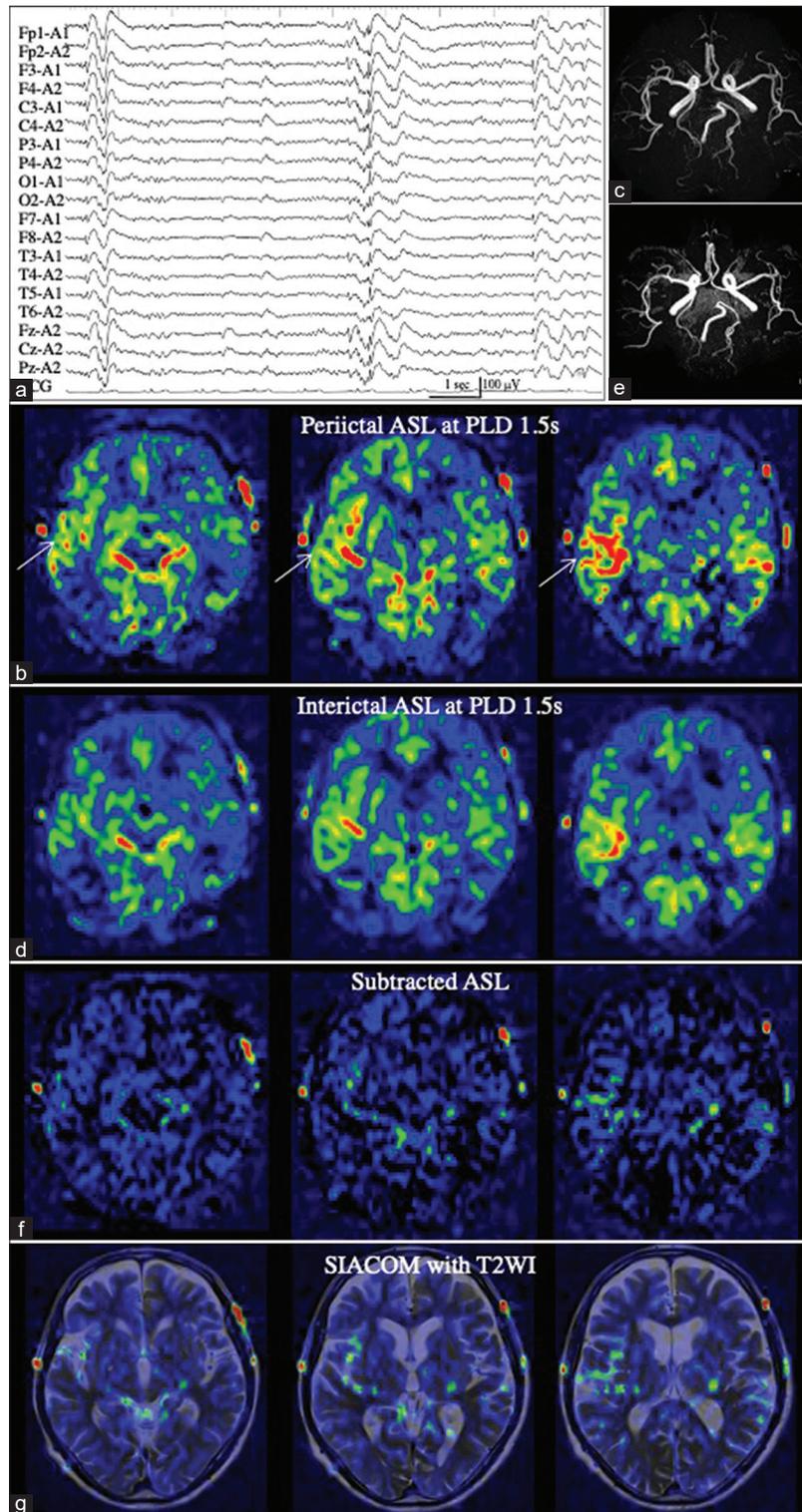


**Figure 3:** Patient 3 (a) Ictal arterial spin labeling (ASL) at a post-labeling delay (PLD) of 1.5 s shows a marked arterial transit artifact (ATA) depiction of the major arteries, while it is difficult to determine a minute increase in ASL signals in the right frontal lobe (white arrow). (b) Electroencephalography demonstrates lateralized periodic discharges (LPDs) in the right frontal region. (c) Voltage topography shows that the maximal amplitude of the negativity of LPD is located at F4. (d) Interictal ASL at a PLD of 1.5 s again shows a marked ATA depiction. (e) On the subtracted ASL, ATA is mostly eliminated and minute increase of ASL signal at the right frontal lobe becomes prominent (white arrow). (f) SIACOM, which is created with source images of magnetic resonance angiography, shows the increased ASL signal site is at the convexity of the right frontal base (white arrows). On serial SIACOM with a slice width of 0.6 mm, this increase in ASL signal was observed over 20 slices, that is, with a width of 1.2 cm, and the figures show, from the left, the most ventral part, the central part, and the most dorsal part of the increased ASL signal areas of right frontal base. Other remaining signals are identified as ATA, because they correspond to the subarachnoid space, including the bilateral ambient cisterns and frontal interhemispheric cistern, or arteries therein.

prominent [Figure 3e]. When SIACOM was created with the source images of MR angiography, the increased ASL signal site was at the convexity of the right frontal base [Figure 3f], which coincided with the site where the LPDs were recorded on EEG. Since other increased signals were located in the bilateral ambient cisterns and frontal interhemispheric cistern on SIACOM, they were judged as residual ATA.

#### Patient 4

A 75-year-old man initially developed generalized tonic-clonic seizures and was admitted to the emergency department. On arrival, he had no convulsions and his consciousness was almost clear. EEG examination revealed frequent generalized epileptiform bursts [Figure 4a]. MRI



**Figure 4:** Patient 4 (a) Electroencephalography showing frequent generalized epileptiform bursts. (b) Periictal arterial spin labeling (ASL) at a post-labeling delay (PLD) of 1.5 s shows increased ASL signals in the right frontal lobe (white arrow). Even when compared with magnetic resonance (MR) angiography (c), it is not possible to determine whether it is the arterial transit artifact (ATA) of the middle cerebral arteries or increased tissue cerebral blood flow. (d and e) Interictal ASL at a PLD of 1.5 s (d) and MR angiography (e) demonstrate findings similar to those of periictal ASL. (f) On the subtracted ASL, the increased ASL signal in the right frontal lobe is almost eliminated (f). (g) SIACOM, superimposed on T2-weighted images, shows that slightly increased residual signals are present within the subarachnoid space.

after 6 h did not reveal an epileptogenic lesion. On periictal ASL, the signal in the right frontal lobe seemed to be increased [Figure 4b]; however, even when compared with MR angiography [Figure 4c], it was not possible to determine whether it was ATA of the MCA or increased tissue CBF in the same area. The signal at the site was also elevated in the interictal ASL 6 months later [Figure 4d]. In addition, the ATA of the MCA could not be excluded by referring to the MR angiography [Figure 4e]. In the subtracted ASL, the increased ASL signal in the right frontal lobe was mostly eliminated [Figure 4f]. This can be diagnosed as ATA of the MCA, as even the slightly increased residual signals were all present within the right Sylvian fissure when SIACOM was created with T2WI [Figure 4g]. Since follow-up interictal EEG findings showed sporadic appearance of generalized paroxysmal discharges, a diagnosis of generalized epilepsy was made, and his seizures were controlled with 200 mg of lacosamide.

## DISCUSSION

This study revealed the possibility of subtraction of ictal-interictal 1.5-T PASL images to considerably eliminate the depiction of ATA in all four patients. In addition, by creating SIACOM from the subtracted ASL, the pathophysiology of the seizure in each patient was more clearly demonstrated than that in the original ictal ASL image.

In patients 1 and 2 with focal epilepsy, a tight topographical relationship between the epileptogenic lesions and site of increased CBF was clearly depicted. We previously investigated the hemodynamics of periictal hyperperfusion using 3-T pCASL with the dual PLD method and reported that the flow velocity of periictal hyperperfusion was high in patients with structural focal epilepsy.<sup>[22]</sup> That is, the increase in ASL signals at a PLD of 1.5 s was washed out to some extent at a PLD of 2.5 s.<sup>[22]</sup> In Patient 1, SIACOM at a PLD of 1.5 s clearly demonstrated that the increase in CBF with high velocity occurred from the cortex surrounding the contusional lesion in the right frontoparietal lobe, and extended to the ipsilateral temporal lobe. In this case, SIACOM also revealed an increase in CBF in the ipsilateral thalamus in addition to the right posterior cortex. Ohtomo *et al.*<sup>[17]</sup> demonstrated that thalamocortical hyperperfusion on ASL could be a new biomarker of NCSE and that specific thalamic hyperexcitability might modulate the LPDs and rhythmic delta activity associated with NCSE, as seen in Patient 1.

Conversely, in Patient 2, SIACOM clearly revealed that the slight increase in CBF at a PLD of 1.5 s, which was visualized posterior to the lesion, gradually increased in intensity and extent at a PLD of 1.8 s and 2.0 s. These hemodynamic changes, which could be visualized by taking advantage of the characteristic that ASL is susceptible to arterial transit

time (ATT),<sup>[1,8-10,19,22,23]</sup> indicate a slower blood flow velocity, despite being with structural focal epilepsy. In this case, it is possible that the NCSE was already in the improvement process, since ictal ASL was obtained 1 day after intensive treatment for the epileptic ictus. It was considered that the blood flow velocity, which increased due to NCSE, decreased with the improvement of NCSE as CBF decreased.

In Patient 3 with situation-related seizures, SIACOM revealed a minute increase in CBF in the area consistent with the abnormal EEG region. In general, the development of ictal hyperperfusion on 3-T pCASL depends on the electrophysiological intensity or power of the epileptic ictus,<sup>[12,13,15,18,20,22]</sup> and this is more pronounced with 1.5-T PASL than with 3T pCASL.<sup>[8]</sup> In our experience so far, situation-related seizures are weak in this power,<sup>[18,22]</sup> and we have experienced a case in which ictal hyperperfusion could not be visualized with 1.5-T PASL.<sup>[8]</sup> Also in Patient 3, we speculated that this power was weak, and the present study also demonstrated that SIACOM is useful in detecting minute changes associated with situation-related seizures.

In Patient 4 with generalized epilepsy, increased CBF focally in the right frontal lobe was suspected with periictal ASL; however, SIACOM revealed that the increased ASL signals were the ATA of the right M2, M3, and M4 portions of the MCA. Few reports have captured periictal hyperperfusion with ASL in patients with generalized epilepsy. Chen *et al.*,<sup>[4]</sup> using 3-T pCASL, reported that the ATT in the left superior temporal gyrus during the periictal state of absence seizures was prolonged, and it is not straightforward compared to periictal hyperperfusion in focal epilepsy. As the current evaluation method for ASL, especially 1.5-T PASL, is to detect local hyperperfusion on visual inspection, it is considered that there is a limitation to its detection, even with SIACOM.

Fukuma *et al.*<sup>[6]</sup> reported that SISCOM is useful for diagnosing prolonged hyperperfusion in post-stroke epilepsy in the field of neuroemergency. As our study did not directly compare SIACOM with SISCOM in the same patient, it is not possible to state the superiority or inferiority of the diagnostic ability of both for periictal hyperperfusion. However, the advantages of SIACOM over SISCOM are, first, that SPECT requires intravenous injection of radioisotopes (RI), whereas ASL uses an endogenous tracer; thus, it is completely non-invasive. Second, for the same reason, it takes approximately a day to obtain a diagnostic RI; however, ASL examination can be performed immediately when needed. Third, SPECT examinations are generally unavailable outside working hours or on weekends, and the timing of ictal SPECT examinations is often delayed. Fourth, while SPECT facilities are not installed in all hospitals dealing with neuroemergencies, 1.5-T MR machines are widely provided.

The present study has some limitation. First, the degree of ATA visualization may differ between the (peri) ictal and interictal

states. On 3-T pCASL, ATA is visualized when labeled blood flow stagnates in the artery due to changes in hemodynamics associated with steno-occlusion or a giant aneurysm of the internal carotid artery.<sup>[1,19]</sup> However, the precise mechanism of ATA delineation on 1.5-T PASL has not yet been elucidated. In the present study, the ATA depiction during the (peri) ictal state tended to be stronger than that at the interictal state, and this was particularly noticeable in the artery that feeds the ictal hyperperfused area. Therefore, ATA cannot be completely eliminated by creating a subtraction image. However, ATA that is not completely removed exists in the subarachnoid space, as shown in Patients 1, 3, and 4 on SIACOM; therefore, it can be distinguished from increased CBF in the parenchyma. Second, since there is a difference in the velocity of CBF between (peri) ictal and interictal periods<sup>[22]</sup> it should always be borne in mind that it may not be possible to obtain a complete subtraction image of CBF on SIACOM, which is susceptible to ATT.<sup>[1,8-10,19,22,23]</sup> However, this possibility was not clearly seen in our four patients. Third, it is practically difficult to obtain interictal ASL data and subsequent SIACOM during and immediately after the initial treatment. In the present study, interictal ASL data were obtained in the outpatient clinic on averaged 3.5 months after the epileptic ictus. When the (peri) ictal ASL images are superimposed directly on the anatomical MR images, in that case, ATA can be distinguished in the subarachnoid space while ATA cannot be deleted.

## CONCLUSION

Although it is necessary to examine several patients in the future, SIACOM can mostly eliminate the depiction of ATA, which is one of the weakest points of 1.5-T PASL, and clearly demonstrate the pathophysiology of epileptic seizures.

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## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Akiyama T, Morioka T, Shimogawa T, Haga S, Sayama T, Kanazawa Y, *et al.* Arterial spin-labeling magnetic resonance imaging with dual post-labeling delay in internal carotid artery steno-occlusion: Validation with digital subtraction angiography. *J Stroke Cerebrovasc Dis* 2016;25:2099-108.
2. Alsop DC, Detre JA, Golay X, Günther M, Hendrikse J, Hernandez-Garcia L, *et al.* Recommended implementation of arterial spin-labeled perfusion MRI for clinical applications: A consensus of the ISMRM perfusion study group and the European consortium for ASL in dementia. *Magn Reson Med* 2015;73:102-16.
3. Bambach S, Smith M, Morris PP, Campeau NG, Ho ML. Arterial spin labeling applications in pediatric and adult neurologic disorders. *J Magn Reson Imaging* 2022;55:698-719.
4. Chen G, Lei D, Ren J, Zuo P, Suo X, Wang DJ, *et al.* Patterns of postictal cerebral hyperperfusion in idiopathic generalized epilepsy: A multi-delay multiparametric arterial spin labelling perfusion MRI study. *Sci Rep* 2016;6:28867.
5. Dolui S, Vidorreta M, Wang Z, Nasrallah IM, Alavi A, Wolk DA, *et al.* Comparison of PASL, PCASL, and background suppressed 3D PCASL in mild cognitive impairment. *Human Brain Mapp* 2017;38:5260-73.
6. Fukuma K, Kajimoto K, Tanaka T, Takaya S, Kobayashi K, Shimotake A, *et al.* Visualizing prolonged hyperperfusion in post-stroke epilepsy using postictal subtraction SPECT. *J Cereb Blood flow Metab* 2021;41:146-56.
7. Funakoshi Y, Shono T, Kurogi A, Kono S. Osteosarcoma of the temporal bone occurring 40 years after radiotherapy: A technical case report. *Surg Neurol Int* 2021;12:152.
8. Goto K, Shimogawa T, Mukae N, Shono T, Fujiki F, Tanaka A, *et al.* Implications and limitations of magnetic resonance perfusion imaging with 1.5-Tesla pulsed arterial spin labeling in detecting ictal hyperperfusion during non-convulsive status epilepticus. *Surg Neurol Int* 2022;13:147.
9. Haga S, Morioka T, Shimogawa T, Akiyama T, Murao K, Kanazawa Y, *et al.* Arterial spin labeling perfusion magnetic resonance image with dual postlabeling delay: A correlative study with acetazolamide loading <sup>123</sup>I-Iodoamphetamine single-photon emission computed tomography. *J Stroke Cerebrovasc Dis* 2016;25:1-6.
10. Haga S, Morioka T, Kameda K, Takahara K, Amano T, Tomohara S, *et al.* Subtraction of arterial spin-labeling magnetic resonance perfusion images acquired at dual post-labeling delay: Potential for evaluating cerebral hyperperfusion syndrome following carotid endarterectomy. *J Clin Neurosci* 2019;63:77-83.
11. Hirsch LJ, Fong MW, Leitinger M, LaRoche SM, Beniczky S, Abend NS, *et al.* American Clinical Neurophysiology Society's standardized critical care EEG terminology: 2021 version. *J Clin Neurophysiol* 2021;38:1-29.
12. Kanazawa Y, Morioka T, Arakawa S, Furuta Y, Nakanishi A, Kitazono T. Nonconvulsive partial status epilepticus mimicking recurrent infarction revealed by diffusion-weighted and arterial spin labeling perfusion magnetic resonance images. *J Stroke Cerebrovasc Dis* 2015;24:731-8.
13. Kanazawa Y, Arakawa S, Shimogawa T, Hagiwara N, Haga S,

- Morioka T, *et al.* Arterial spin labeling magnetic resonance imaging for differentiating acute ischemic stroke from epileptic disorders. *J Stroke Cerebrovasc Dis* 2019;28:1684-90.
14. Matsuda H, Matsuda K, Nakamura F, Kameyama S, Masuda H, Otsuki T, *et al.* Contribution of subtraction ictal SPECT coregistered to MRI to epilepsy surgery: A multicenter study. *Ann Nucl Med* 2009;23:283-91.
  15. Murao K, Morioka T, Shimogawa T, Furuta Y, Haga S, Sakata A, *et al.* Various pathophysiological states of acute symptomatic seizures immediately after ischemic stroke, namely “onset seizures”, shown by complementary use of peri-ictal magnetic resonance imaging and electroencephalography. *Neurol Clin Neurosci* 2017;5:169-77.
  16. O'Brien TJ, So EL, Mullan BP, Hauser MF, Brinkmann BH, Bohnen NI, *et al.* Subtraction ictal SPECT coregistered to MRI improves clinical usefulness of SPECT in localizing the seizure focus. *Neurology* 1998;50:445-54.
  17. Ohtomo S, Otsubo H, Arai H, Shimoda Y, Homma Y, Tominaga T. Hyperperfusion in the thalamus on arterial spin labelling indicates non-convulsive status epilepticus. *Brain Commun* 2020;3:fcaa223.
  18. Shimogawa T, Morioka T, Sayama T, Haga S, Kanazawa Y, Murao K, *et al.* The initial use of arterial spin labeling perfusion and diffusion-weighted magnetic resonance images in the diagnosis of nonconvulsive partial status epilepticus. *Epilepsy Res* 2017;129:162-73.
  19. Shimogawa T, Morioka T, Akiyama T, Haga S, Arakawa S, Sayama T. Sequential changes of arterial spin-labeling perfusion MR images with dual postlabeling delay following reconstructive surgery for giant internal carotid artery aneurysm. *Surg Neurol Int* 2017;8:222.
  20. Shirozu N, Morioka T, Tokunaga S, Shimogawa T, Inoue D, Arihiro S, *et al.* Comparison of pseudocontinuous arterial spin labeling perfusion MR images and time-of-flight MR angiography in the detection of periictal hyperperfusion. *eNeurologicalSci* 2020;19:100233.
  21. Soldozy S, Galindo J, Snyder H, Ali Y, Norat P, Yağmurlu K, *et al.* Clinical utility of arterial spin labeling imaging in disorders of the nervous system. *Neurosurg Focus* 2019;47:E5.
  22. Takahara K, Morioka T, Shimogawa T, Haga S, Kameda K, Arihiro S, *et al.* Hemodynamic state of periictal hyperperfusion revealed by arterial spin-labeling perfusion MR images with dual postlabeling delay. *eNeurologicalSci* 2018;12:5-18.
  23. Tokunaga S, Morioka T, Shirozu N, Tsurusaki Y, Arihiro S, Shimogawa T, *et al.* Arterial spin-labeling perfusion MR images with dual postlabeling delay reveals hemodynamic changes in dural arteriovenous fistulas following endovascular surgery. *Interdiscip Neurosurg* 2020;21:100733.
  24. Wakisaka K, Morioka T, Shimogawa T, Murao K, Kanazawa Y, Hagiwara N, *et al.* Epileptic ictal hyperperfusion on arterial spin labeling perfusion and diffusion-weighted magnetic resonance images in posterior reversible encephalopathy syndrome. *J Stroke Cerebrovasc Dis* 2016;25:228-37.
  25. Young CO, Etchbehere EC, Souza EM, Brunetto SQ, de Oliveira Santos A, Lima MC, *et al.* Clinical usefulness of SISCOP-SPM compared to visual analysis to locate the epileptogenic zone. *Front Neurol* 2020;11:467.

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