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Case Series

Radiology Section

# Applications of Arterial Spin Labelling Sequence in Neuroimaging, Case Depictions with Examples: A Case Series

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## ABSTRACT

Since many neurological diseases are associated with altered regional cerebral flow, Arterial Spin Labelling (ASL) image being a non invasive non contrast sequence, is increasingly being used and incorporated in routine protocols as an adjuvant sequence to study the regional alterations in cerebral perfusion or Cerebral Blood Flow (CBF). It demonstrates increased or decreased regional CBF in various brain pathologies reliably without the use of intravenous contrast material. In this case series (seven cases), ASL is increased (increased CBF) in cases of high-grade tumour, highly cellular tumours, encephalitis, tumour recurrence, acute phase of Posterior Reversible Encephalopathy Syndrome (PRES), and decreased in cerebral infarct, periinfarct ischaemic penumbra, thereby making an effort to emphasise the significance and utilisation of ASL in adjunct to the other routine Magnetic Resonance Imaging (MRI) sequences.

**Keywords:** Cerebral perfusion, Diffusion-weighted image, Magnetic resonance imaging

## INTRODUCTION

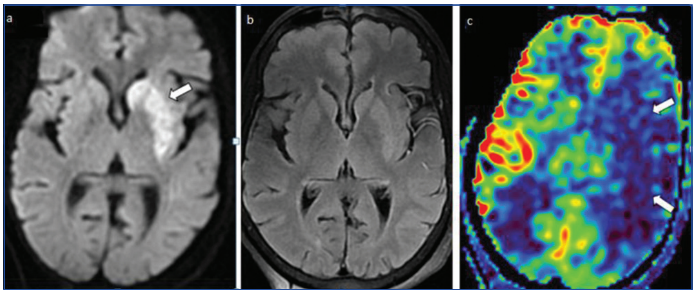
Tissue perfusion by definition means supplying nutrients and oxygen to the tissue through blood flow. ASL is a unique non ionising, non invasive sequence in MRI whereby it uses magnetically labeled blood water protons as endogenous tracers to study the regional tissue perfusion [1,2]. ASL provides more reliable information about the alterations in tissue perfusion both qualitatively and also quantitatively [3], the other imaging techniques available for studying tissue perfusion, blood velocities and blood transit times are Positron Emission Tomography (PET), Single-Photon Emission Computed Tomography (SPECT), CT perfusion and Dynamic Susceptibility Contrast (DSC), MRI which uses extraneous radioactive tracers and intravenous contrast material.

The ASL is unique and novel with advantages of being non invasive, it can be can be done in patients of renal dysfunction, and in situations where i.v. gadolinium is contraindicated, can be done in paediatric cases, ASL also have few disadvantages such as limited spatial resolution, poor signal to noise to ratio, overestimation of hypoperfusion in physiologically hypoperfused areas, etc. The present case series is of seven cases that shows the use of ASL in imaging which can be a valuable tool that can demonstrate occlusion/thrombosis in the affected vessel, stroke, stroke mimics, tumour recurrence and encephalitis.

## CASE SERIES

### Case 1

A 52-year-old male patient presented in the emergency department with a history of acute onset left-side chest pain and was found to have major coronary artery blockade and underwent coronary artery bypass graft. On postoperative day 4, the patient developed loss of speech and sudden onset weakness of right upper and lower limbs. Based on clinical evaluation, the patient was suspected of cerebral stroke and referred for MRI scan. MRI Diffusion-Weighted Image (DWI) and Fluid Attenuated Inversion Recovery (FLAIR) images showed acute infarct in left basal ganglia within window period (note diffusion- FLAIR mismatch) and left ASL image showed large perfusion defect or hypoperfusion in the left cerebral hemisphere which was out of proportion to infarct in DWI image that is Diffusion- ASL mismatch, suggestive of large periinfarct ischaemic penumbra in left cerebral hemisphere [Table/Fig-1a-c], thereby ASL provided valuable information regarding the reversible yet potentially salvageable tissue if treated appropriately in time. This information provided by the ASL could have been very valuable in cases suitable or not contraindicated for thrombolytic agents.

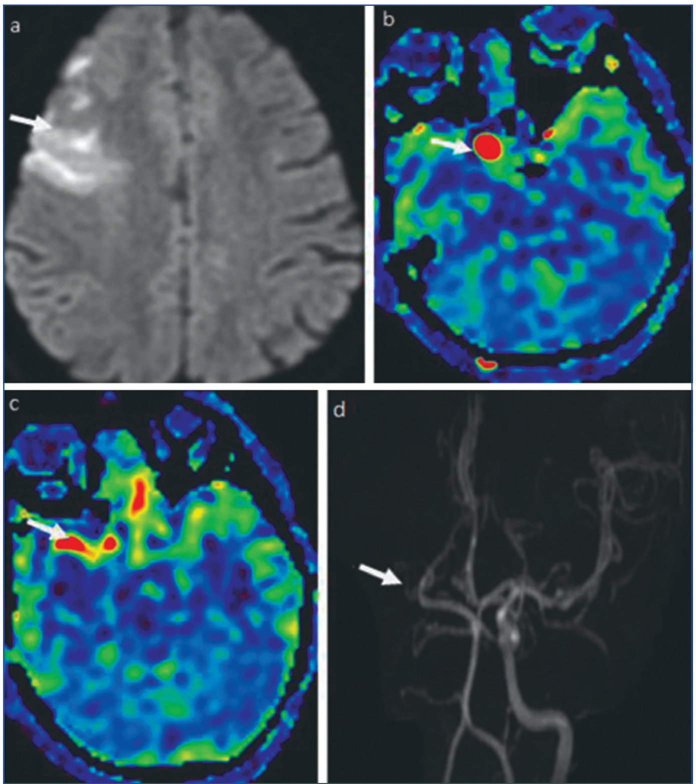



**[Table/Fig-1]:** Axial DWI image: a) Showing diffusion restriction in left basal ganglia (arrow) in left Middle Cerebral Artery (MCA) territory and FLAIR image; b) Showing no significant corresponding signal changes-s/o acute infarct in window period. 3D colour coding ASL; c) Image demonstrating large hypoperfusion in left cerebral hemisphere disproportionate to infarct volume (arrow), that is Diffusion-perfusion mismatch-s/o Peri-infract ischaemic penumbra or potentially salvageable tissue.

Since the patient was already on dual antiplatelet therapy, the physician didn't take risk of using thrombolytic agents, as they can cause complications associated with the use of thrombolytic agents and explained the same to the patient's relatives hence, the patient was put on observation and advised for physiotherapy on follow-up.

### Case 2

A 48-year-old male patient presented with a history of acute onset right upper and lower limb weakness, the patient was diabetic and hypertensive for four years with a family history of diabetes, hypertension, and coronary artery disease. The diagnosis of cerebral stroke was made clinically and advised for MRI scan. DWI image showed acute infract in the right high frontal lobe and ASL images showed abnormal signal in the course of right Internal Cerebral Artery (ICA) and Middle Cerebral Artery (MCA) and MRI. Time Of Flight (TOF) image show absent flow-related enhancement in right ICA and MCA, suggestive of complete occlusion confirming the findings on ASL [Table/Fig-2a-d]. Thus, ASL also demonstrates occlusion/thrombosis in the affected vessel. The patient underwent thrombolysis and power was gradually improving on follow-up with no postthrombolytic complications.

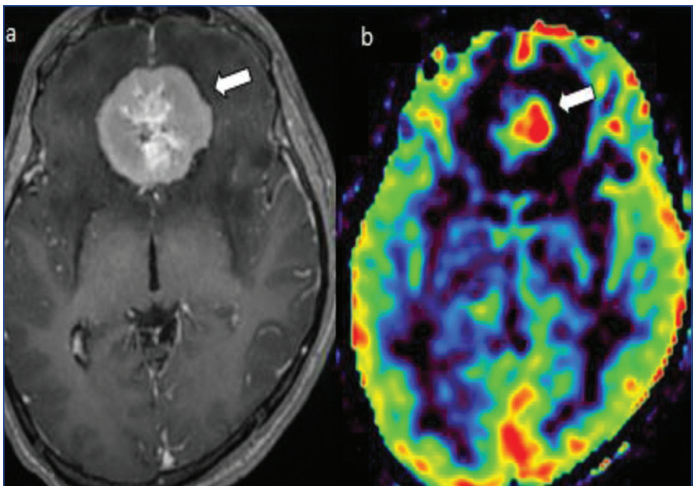



**[Table/Fig-2]:** Axial DWI image: a) Showing acute infract in the right middle frontal gyrus (arrow). ASL image; b,c) Showed abnormal signals in the course of the cavernous segment of the right internal carotid artery and right mainstream MCA- Suggestive of complete occlusion/thrombosis which is correlated and confirmed with MRI-TOF angiography; d) MRI-TOF image demonstrating, non visualisation of right ICA and MCA (arrow in figure 2d)-suggestive of complete occlusion/thrombosis.

## Case 3

A 38-year-old male patient presented to the emergency department with complaints of seizure-like activity followed by a fall in his residence, he sustained injury over right parieto-temporal region with three episodes of vomiting and loss of consciousness, intubated elsewhere in the hospital and was referred here for further management. In this hospital, neurosurgeon evaluated clinically and suspected the patient of having brain space-occupying lesion and advised MRI brain.

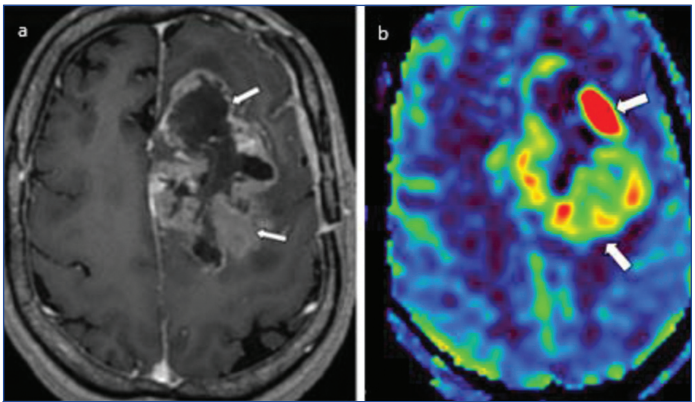
Postcontrast axial T1 and ASL images showed well-defined oval shaped avidly enhancing lesion (with spoke wheel pattern) in the midline basi frontal region and on ASL, the lesion showed increased perfusion in the centre-imaging features, consistent with frontal meningioma [Table/Fig-3a,b]. He was operated and the meningioma was excised uneventfully. During the postoperative follow-up, the patient was stable and subsequently discharged.




**[Table/Fig-3]:** Axial contrast enhanced image: a) Showing well-defined extra-axial round avidly enhancing lesion in the mid line basifrontal region. Note classic spoke wheel pattern (arrow) and 3D ASL image; b) Demonstrating increased cerebral perfusion in the lesion-imaging features s/o basifrontal meningioma.

## Case 4

A 65-year-old male patient presented two months back with Generalised Tonic Clonic Seizures (GTCS) and loss of consciousness. He was diabetic, hypertensive, and a smoker with no significant family history. He underwent MRI brain outside the hospital, which was suggestive of glioblastoma multiformae, and was referred here for further management. Detailed evaluation was done and he underwent excision biopsy and postoperative histopathology report showed grade i.v. glioblastoma multiformae. Preoperative contrast-enhanced MRI scan showed thick peripheral irregular heterogeneously enhancing mass lesion (central non enhancing area representing necrosis) causing mild mass effect and midline shift to the right side and on ASL the lesion showed increased thick ring of peripheral perfusion [Table/Fig-4a,b]- s/o high-grade glioma. Patient was put on adjuvant radiotherapy and concurrent timozoalmide 100 mg and the patient is on regular follow-up.



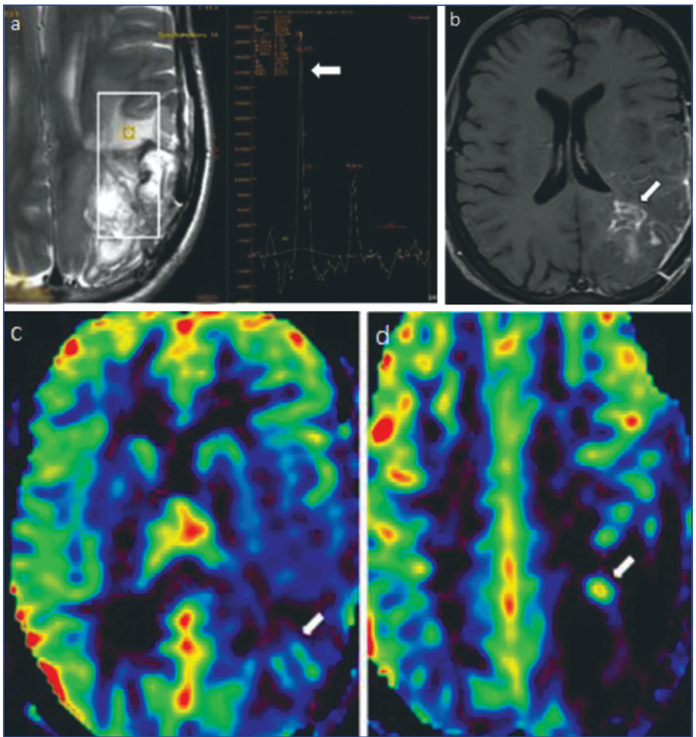

**[Table/Fig-4]:** Axial postcontrast image: a) Showing thick irregular nodular peripheral enhancement noted in left deep paramedian high frontal lobe and on ASL image; b) The lesion showing increased peripheral perfusion- imaging features s/o high grade glioma/gliobstoma multiformae.

## Case 5

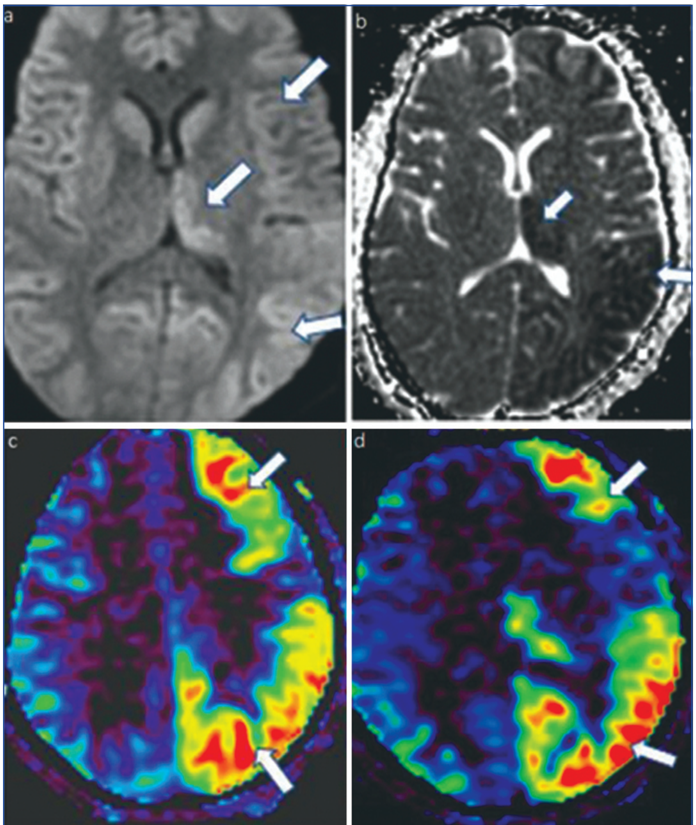
A 46-year-old male patient presented with first episode of GTCS with no similar episode in the past. No significant past history or family history and was diagnosed to have a left parieto-occipital lobe space-occupying lesion and raised the possibility of oligodendroglioma based on MRI, subsequently patient underwent surgical excision and the specimen was sent for histopathological examination and was diagnosed as oligodendroglioma WHO grade III. Patient had received adjuvant radiotherapy of 54cGY for two months. Later, the patient had a fall and headache, was referred for MRI brain imaging for further evaluation. MRI images revealed heterogeneously hyperintense lesion with perilesional oedema and patchy postcontrast enhancement. On ASL the lesion showed increased perfusion. MRI spectroscopy revealed choline peak [Table/Fig-5a-d]; hence, imaging features suggestive of tumour recurrence. ASL with additional sequences helped to differentiate between tumour recurrence from postoperative and postradiation induced changes. In radiation induced necrosis there will be cerebral hypoperfusion at the site on ASL though there might be heterogeneous enhancement.

## Case 6

A 32-year-old female patient presented to the emergency department with eight episodes of GTCS, up rolling of eyeballs, 30 minutes apart, tongue bite, and severe headache. The C-reactive protein of the patients was raised (1.2) and was clinically suspected of having encephalitis. The MRI study revealed subtle gyral diffusion restriction in left cerebral hemisphere and anteromedial thalamus with corresponding increased cerebral perfusion on ASL [Table/Fig-6a-d]. Imaging features were s/o encephalitis. Patients Cerebrospinal Fluid (CSF) analysis was s/o Meningoencephalitis. Hence, in this case inflammation of brain parenchyma as in encephalitis, there will be hyperperfusion of affected regions which is best demonstrated by ASL without using exogenous contrast material.



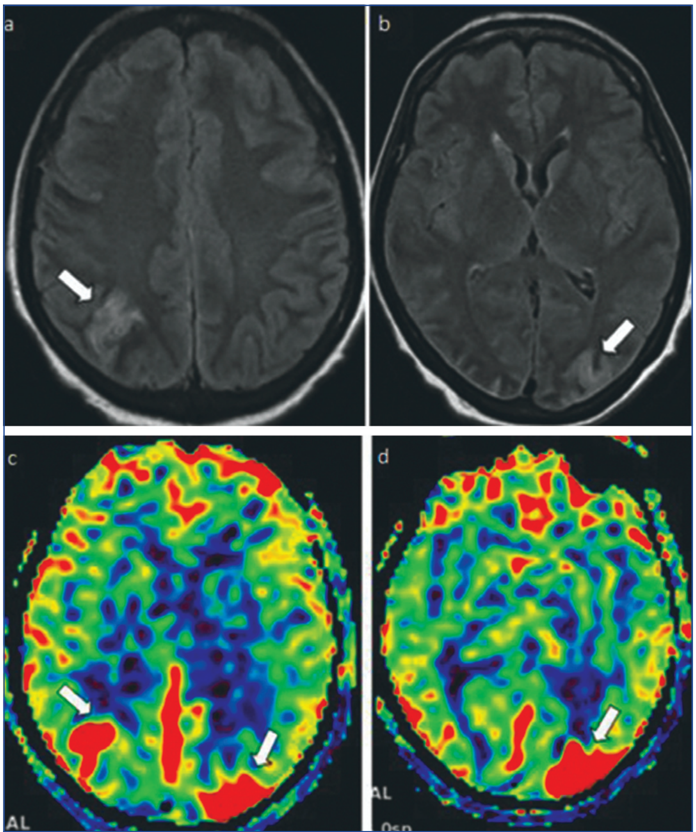
**[Table/Fig-5]:** Cropped T2 weighted axial image: a) Showing abnormal ill-defined hyperintense lesion with perilesional oedema in left parieto-occipital lobe. Axial postcontrast image: b) Showing patchy heterogeneous enhancement in left parieto-occipital lobe (arrow) ASL image c,d) Showing increased cerebral bold flow in the left parieto-occipital lobe in the postoperative site which is suggestive of tumour recurrence and on MR spectroscopy, left parieto-occipital lobe lesion shows increased choline peak (arrow in figure 5a) consistent with recurrence of glial tumour.



**[Table/Fig-6]:** DWI image: a,b) Note subtle gyral diffusion restriction in left cerebral cortex and left anteromedial thalamus (arrows) ASL; c,d) Demonstrating increased perfusion in corresponding areas of left cerebral cortex and anteromedial thalamus (arrows)- s/o encephalitis.

## Case 7

A 49-year-old female case of dilated cardiomyopathy with severe left ventricle dysfunction with status post Percutaneous Transluminal Coronary Angioplasty (PTCA) and mitral valve replacement. The patient was drowsy and irritable and clinically suspected of hypoxic-ischaemic encephalopathy and was referred for an MRI brain scan. Axial FLAIR images showed mild gyral oedema with subtle diffusion restriction (not shown here) in bilateral parieto-occipital lobes and ASL coloured mapping showed increased perfusion in corresponding bilateral high parieto-occipital lobes [Table/Fig-7a-d] suggestive of acute phase of PRES. Thus, differentiating PRES from hypoxic ischaemic encephalopathy wherein in the later there will be cerebral hypoperfusion on ASL.



**[Table/Fig-7]:** Axial FLAIR images: a,b) Note mild gyral hyperintensities representing gyral oedema seen in right partial lobe and left occipital lobe (arrows) with corresponding increased cerebral perfusion in ASL images (arrows in figure 7c and figure 7d) Imaging features are suggestive PRES.

## DISCUSSION

The ASL is the resultant or outcome image of subtraction of magnetically tagged images from control images thereby eliminating static tissue signal and hence the remaining signal is a relative measure of perfusion proportional to CBF [4]. DSC and Dynamic Contrast-Enhanced (DCE) are the other methods to study tissue perfusion. There are different types of techniques that are described to achieve ASL and are classified based on magnetic labeling such as pulsed ASL, continuous ASL, pseudo-continuous ASL, and velocity-selective ASL. Continuous ASL was the first intimal method but due to its limitation, pseudo-continuous ASL and velocity selective ASL were developed to overcome the limitations of continuous ASL [4,5]. The ASL image is interpreted as hyperperfused as in luxury perfusion or restoration of perfusion in previous ischaemic penumbra after intravascular thrombolysis [6] and as hypoperfused as in abscess, postictal state, granulomas and as mixed perfusion states depending on the stage of disease activity [7]. The introduction of ASL in routine stroke protocol has been a significant milestone in neuroradiology. The very important role of ASL in stroke patients is identifying ischaemic penumbra that is DWI-ASL mismatch in other words diffusion-perfusion mismatch wherein, the ASL deficit is larger than DWI deficit thereby suggesting potentially yet salvageable periinfarct ischaemic penumbra and hence helps in guiding appropriate timely management of stroke patients and thus determining the outcome [8,9]. It has been shown that focal hyperperfusion early after thrombolysis is associated with a smaller final infarct volume and with improved functional outcomes at 24 hours and three months even despite having a higher chance of parenchymal haemorrhage [10,11]. The focal and diffuse pathological perfusion deficits, post-thrombolysis reperfusion/luxury reperfusion, and perfusion diffusion mismatch can all be depicted on the ASL method [12,13]. Other most commonly used application after stroke is in the radiological evaluation of suspected brain tumour.

The main basic pathophysiology of any tumour is cell mitosis and angiogenesis. The angiogenesis is a key factor in histologic tumour grading, and tumour blood flow serves as an in-vivo marker of the tumour characteristic that can be measured with ASL [14,15]. With the increased tumour grade the vascularisation and perfusion increases which is measured by ASL has been shown to correlate with tumour grade [15,16]. ASL image without using exogenous contrast agents effectively differentiates tumour recurrence and postradiation induced changes. ASL shows hyperperfusion in case of tumour recurrence where as it shows hypoperfusion in areas of radiation induced changes or radiation induced necrosis which on other conventional and contrast imaging sequences, is difficult to distinguish between the aforementioned entities. Weber MA et al., found ASL to predict tumour response as early as six weeks following treatment, with improved accuracy over tumour volume measurements [17]. Perfusion imaging can also be used to target stereotactic biopsy sites at the most hyperperfused site in tumour for better tissue yielding [18]. Furthermore, there lot many studies can be found in the literature enumerating the diagnostic applications of ASL, here authors have briefed few previously published case reports/studies supporting present current case series [Table/Fig-8] [19-22].

| Author | Place of study | Observations |
|---|---|---|
| ElBeheiry AA et al., [19] | Egypt | Demonstrated ASL precisely detected ischaemic penumbra and provides reliable insight into outcome prediction. A significant positive correlation was noted between ASL and DSC in grading of brain glioma. |
| Kato A et al., [20] | Japan | Proximal bright vessel sign on ASL is compatible with susceptibility vessel sign on Susceptibility Weighted Image (SWI). |
| Fazeli S et al., [21] | United States | Showed increased ASL CBF in the majority (65%) of patients with PRES. |
| Cao Y et al., [22] | Peoples Republic of China | Cerebral perfusion increases during the acute stage in viral encephalitis and decreases when the condition improves. 3D-ASL provides a reference for diagnosis and follow-up of viral encephalitis in children. |
| Present study | India | Increased ASL CBF noted in high grade brain tumours, tumor recurrence, encephalitis , PRES and decreased ASL CBF in infarct and peri infarct ischaemic penumbra. |

**[Table/Fig-8]:** Showing few cases reports/studies along with present study enumerating different applications of ASL [19-22].
ASL: Arterial spin labelling; DSC: Dynamic susceptibility contrast; CBF: Cerebral blood flow; PRES: Posterior reversible encephalopathy syndrome

The ASL also helps in differentiating close mimics of brain pathologies like lymphoma and toxoplasmosis in immunocompromised patients in addition to other MRI sequences [4].

### Other Applications of ASL

A study done by Alsop DC et al., has showed significant decrease in cerebral perfusion in the temporal, parietal, frontal and posterior cingulate regions in patients of Alzheimer's disease [23]. Kimura H et al., showed that ASL and bolus perfusion techniques are comparable in evaluating meningioma and that CBF corresponds to vascularity as assessed at histopathological analysis [24]. Perfusion pattern in PRES varies depending on the time and duration usually in acute setting there will be hyperperfusion in the frontal and occipital lobes while there will be hypoperfusion in subacute phase in the same aforementioned areas [4]. In epilepsy CBF is elevated during ictus and suppressed in the interictal state. Pollock JM et al., described three patients found in a retrospective review to have migraine in whom focally increased perfusion was captured during the patient's symptoms with ASL imaging [4].

## CONCLUSION(S)

The ASL is a unique non invasive MRI sequence that uses endogenous blood flow tracer to study the regional alterations in CBF and an effective alternative tool to DSC MRI sequence to study the cerebral perfusion or CBF alterations both qualitatively and quantitatively in various brain pathologies and at times as a problem-solving tool. Present study demonstrated different applications of ASL like in stroke, stroke mimics, tumour recurrence, encephalitis, etc., thus, the present series emphasised the application and utilisation of ASL sequence in various brain pathologies and thereby, strongly recommend this novel MRI sequence to be added in stroke protocol and other MRI studies whenever needed.

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