Arterial spin-labeling (ASL) is capable of demonstrating hyperperfusion in a clinical population. Our clinical imaging experience has shown that ASL is very sensitive to pathologic states manifesting as focal, regional, and global hyperperfusion. With the availability of fully processed ASL cerebral blood flow (CBF) maps at our institution within minutes of acquisition, timely assessment of brain perfusion in a wide range of diseases is now possible.

In Part 1 of this series, we described the technique, artifacts, and pitfalls related to the application of ASL into a routine clinical neuroimaging protocol. Part 2 focused on patterns of focal and global hyperperfusion on ASL CBF maps. Here we describe various causes of focal and global hyperperfusion, including tumor, infarct, seizure, vascular malformations, and various other neurologic disorders (Table).

Perfusion MR imaging, particularly dynamic susceptibility contrast (DSC) MR imaging, has been established as a valuable adjunct imaging technique for the evaluation of brain tumors. Specifically, perfusion techniques may be useful in directing surgical biopsy and resection, helping differentiate recurrent tumor versus radiation necrosis, and in distinguishing between neoplasm and infection such as toxoplasmosis. Many studies exist in the literature establishing the validity of DSC MR imaging in tumor imaging. A recent study by Wolf et al found a 0.83 correlation between ASL and DSC MR imaging in measuring CBF within the tumor region. ASL maps consistently show elevated signal intensity in enhancing tumors such as high-grade gliomas and meningiomas, and studies have shown that perfusion MR imaging techniques can distinguish among high-grade gliomas, low-grade gliomas, and metastasis on the basis of various patterns of flow.

The methods for data acquisition and analysis are described in detail in Part 1 of this series. We identified common patterns of hyperperfusion on the basis of a retrospective analysis of 3000 clinical pulsed ASL cases acquired consecutively during a 12-month period.

### Discussion

#### Hyperperfusion Patterns Encountered with Clinical Spin-Tag Perfusion Imaging

**Focally Increased Signal Intensity.** Focally increased signal intensity may be produced by true hyperperfusion or by artifact such as motion or intravascular spin-label. ASL is sensitive in depicting hyperperfusion in a number of conditions related to stroke, tumor, seizure, or loss of autoregulatory function of blood vessels. The regional hyperperfusion implicated in hypertensive encephalopathy, posterior reversible encephalopathy syndrome (PRES), and related syndromes can be readily disclosed by ASL, which on serial follow-up can demonstrate the waxing and waning time course often observed in these conditions. Relative high signal intensity may also occur in a regional or lobar distribution under normal physiologic conditions, such as with visual cortex activation in the occipital lobes.

**Luxury Perfusion.** Localized autoregulatory dysfunction occurs in the setting of stroke and is often visualized on con-

---

**Table: Hyperperfusion patterns on clinical spin-tag perfusion imaging**

| Hyperperfusion Pattern | Causes |
|------------------------|--------|
| Focal                  | Luxury perfusion |
|                        | Reperfusion |
|                        | Spontaneous recanalization |
|                        | Thrombolytic-induced recanalization |
|                        | Seizure activity (ictal or peri-ictal) |
|                        | Tumor |
|                        | Vascular malformation |
|                        | Localized autoregulatory dysfunction |
|                        | PRES |
|                        | Migraine |
|                        | Postendarterectomy |
|                        | Inflammation |
|                        | Infarction |
| Global                 | Young age |
|                        | Robust CBF |
|                        | Hypercapnia |
|                        | Post-carotid endarterectomy |
|                        | Post-anoxic insult |

**Note:** PRES indicates posterior reversible encephalopathy syndrome; CBF, cerebral blood flow.
Conventional MR imaging as intravascular enhancement in the infarcted territory. Sluggish transit of intravascular arterial spins may account for the focal high ASL signal intensity often apparent in areas of acute infarct. Other causes of focal autoregulatory dysfunction include the PRES and post-carotid endarterectomy hyperperfusion syndrome. ASL is very sensitive to states of hyperperfusion, which are depicted as focal areas of signal-intensity increase in the region of luxury perfusion (Fig 1). In severe cases of PRES, initial hyperperfusion may give way to infarction and subsequent bilateral parieto-occipital perfusion deficits. Concomitant parenchymal hemorrhage may create susceptibility artifact and contribute to the appearance of hypoperfusion.

Reperfusion. Because it is not subject to artifacts due to the recirculation of tracer, ASL is well suited for the serial assessment of brain perfusion in the setting of acute stroke and can provide important prognostic information regarding reperfusion. Restoration of flow to regions of the ischemic core or penumbra can be seen as high signal intensity on ASL following spontaneous recanalization of clot, administration of systemic or transcatheter thrombolytics, or extracranial-to-intracranial bypass. These areas of reperfusion can be distinguished from stagnant intravascular spin-label because they often correspond to anatomic structures such as the basal ganglia, thalamus, insula, or a cortical gyrus. Figure 2 demonstrates focal hyperperfusion in the left middle cerebral artery (MCA) territory 12 hours following the administration of systemic thrombolytic agents, whereas spontaneous reperfusion of an infarcted territory is shown in Fig 3.

Seizure Activity. Seizure activity can mimic acute stroke in both imaging findings and clinical presentation. In the absence of restricted diffusion or a discrete lesion on conventional MR imaging, focally increased signal intensity on ASL may represent either a complex partial seizure in the postictal state (Fig 4) or clot lysis and late reperfusion in the setting of subacute stroke. Often the clinical history will allow differentiation of these 2 entities. Ictal single-photon emission CT has been shown to be 90% sensitive in the depiction of hyperperfusion in the ictal phase of temporal lobe epilepsy. In addition, in a meta-analysis by Lee et al, late postictal hyperperfusion was found in the epileptogenic zone in more than half of patients with seizures. ASL has advantages in that both anatomic and perfusion MR images can be obtained in the same setting. The mechanism of hyperperfusion due to seizure activity is not completely understood but may be related to transient loss of autoregulatory function in the surrounding vasculature or to the release of excitatory neurotransmitters such as glutamate in areas of increased neuronal firing. In the seizure evaluation, ASL complements the traditional evaluation with electroencephalography (EEG), anatomic imaging, and nuclear medicine studies.

Subdural Hematoma. Subdural hematomas can also show hyperperfusion in the adjacent cortex on pulsed arterial spin-labeling (Fig 5). This may be secondary to compression of the cortical venous outflow or malfunction of the local cerebral regulatory mechanisms secondary to trauma.

Tumor. Tumor evaluation with ASL has been studied, and correlations between flow and tumor grade have been made. The ability to quantify perfusion with ASL potentially allows monitoring of tumor response to therapy. Additionally, ASL can help distinguish areas of tumor recurrence from areas of radiation necrosis. Other cerebral perfusion methods that rely on dynamic bolus techniques require large-bore intravenous access devices and adequate renal function. In patients with metastatic disease or primary neoplasms who

---

**Fig 1.** Luxury perfusion. Asymmetric intravascular enhancement of the cortical vessels in a large infarcted left MCA territory (ellipse) on the postcontrast T1-weighted images. ASL CBF map demonstrates hyperperfusion in the left caudate, insula, and frontal lobe (arrow). The posterior parietal regions are hypoperfused.

**Fig 2.** Reperfusion. An 80-year-old woman presenting with right hemiparesis met the criteria for systemic thrombolytics. ASL CBF map acquired approximately 12 hours after tissue plasminogen activator administration reveals localized hyperperfusion within the left MCA territory (arrow). Perfusion is otherwise preserved throughout the left hemisphere.
have undergone extensive chemotherapy or in patients with renal insufficiency, routine follow-up examinations with large-bore intravenous devices may not be practical. Additionally, because ASL requires no contrast, the complication of nephrogenic systemic fibrosis can be avoided. Surgical craniotomy closure devices can hinder perfusion evaluation secondary to susceptibility artifacts. As modifications in closure device materials are made, perfusion imaging evaluation adjacent to the craniotomy site is likely to improve.

Figures 6–8 demonstrate high-flow states on ASL associated with meningioma, glioblastoma multiforme, and ependymal metastases, respectively. Perfusion and T1-weighted enhancement mismatches may be used to indicate diffusely infiltrating tumors such as gliomatosis cerebri (Fig

1430 Deibler | AJNR 29 | Sep 2008 | www.ajnr.org

Fig 3. Hyperperfused stroke territory on ASL. A 73-year-old woman with atrial fibrillation and embolic infarcts in the left posterior cerebral artery and posterior watershed territories. Punctate areas of restricted diffusion are seen (left, yellow arrow). ASL map (right) shows gyral hyperperfusion in the left hemisphere (white arrow). Hyperperfusion is also seen in the right posterior watershed territory.

Fig 4. Hyperperfused seizure territory. A 6-year-old boy with a history of Landau-Kleffner syndrome who presented with complex partial seizures causing paresis of the right face and upper extremity. ASL shows regional hyperperfusion in the left parietal hemisphere associated with the ictal phase of seizure activity (arrows). EEG confirmed almost continuous seizure activity within the left hemisphere. Findings of the diffusion-weighted sequence were normal (not shown). Symptoms improved on antiepileptic medications and a course of intravenous immunoglobulin.

Fig 5. Hyperperfusion underlying a subdural hematoma. Axial T2-weighted image (left) demonstrates an acute-to-subacute left cerebral convexity hematoma (yellow arrows). Postcontrast image (center) shows compression of underlying vessels (ellipse). ASL CBF map (right) shows intense gyral hyperperfusion in the left parietal and occipital lobes (white arrow).
9). On ASL, artifact must be excluded as a cause of the perceived absence of increased flow within a tumor because local susceptibility artifact, blood products, or masking effect may obscure hyperperfused foci within lesions.

**Vascular Malformations.** Localized hyperperfusion may occur in the setting of vascular malformations, depending on the size and type of vessels involved and the rate of flow through the lesion. Hyperperfusion can be seen in both arteriovenous malformations and venous angioma (Fig 10). In addition to assessing flow within the lesion itself, various states of hyperemia and ischemia in adjacent regions occurring in both the pre- and postoperative settings may be disclosed with ASL.12,13

**Localized Autoregulatory Dysfunction.** PRES and PRES-like syndromes can occur spontaneously or in association with
uncontrolled hypertension, eclampsia, and cyclosporine toxicity and as a complication of certain chemotherapeutic regimens. A loss of autoregulatory control occurs in these syndromes, and initial attempts to maintain perfusion pressure result in arteriolar vasoconstriction. Hyperperfusion follows and results in reversible edema, more commonly in the vertebrobasilar vascular territories likely because of the relatively fewer perivascular sympathetic nerves in this area. Figure 11 demonstrates changes with time in a 31-year-old patient with PRES, including initial vasoconstriction and hypoperfusion followed by rebound hyperperfusion. ASL is a robust technique in the evaluation of hyperperfusion syndromes due to its repeatability and its strength in depicting high-flow states. Figure 12 demonstrates a case of post-endarterectomy hyperperfusion syndrome in a patient who had recently undergone ipsilateral carotid endarterectomy. This is a
well-described phenomenon using other perfusion techniques and is presumed to result from loss of autoregulatory function.

Globally Increased Signal Intensity

Increases in signal intensity on ASL maps commonly occur on a global scale and may be secondary to physiologic, pathologic, or artifactual causes. Pediatric patients and healthy adults with robust brain perfusion are examples of individuals with true physiologic increases in global CBF. Disease states such as hypocapnia and anoxia can result in loss of autoregulatory control and striking hyperperfusion, which might have the appearance of a “superscan.” Finally, artifacts must be excluded when one is confronted with higher than expected global signal intensity.

Robust CBF. Wide variations in global CBF may occur within the clinical population, even among healthy individuals. Although the normal range of gray matter CBF in the literature varies between 40 and 70 mL/100 g per minute,18 diffusely intense ASL signal intensity may be seen in some healthy individuals with global gray matter CBF values exceeding 100 mL/100 g per minute. Performing ASL at higher field strengths predisposes to improved signal-to-noise ratio and less decay of the spin tag due to prolongation of T1 at 3T, yielding high-
quality ASL maps in a larger percentage of cases. Furthermore, ASL in children consistently demonstrates increased global CBF, a phenomenon discussed in detail in Part 1 of this series.1

Global Cerebral Hyperperfusion. Global cerebral hyperperfusion has been reported to occur as a complication of embolic stroke, carotid endarterectomy, and head injury.17,19 Acute restoration of flow above normal perfusion pressures may lead to loss of autoregulation and may result in elevated global CBF. Postischemic cerebral hyperemia is a phenomenon that is known to occur and appears to be mediated by trigeminal neural input.20 Figure 13 demonstrates a case of paradoxically high global CBF in the setting of restricted diffusion in multiple vascular territories following cardiopulmonary arrest.

Hypercapnia. Hypercapnia is a potent cerebral vasodilatory stimulus. Many studies in clinical research and practice have used hypercapnia challenge to produce global increases in CBF and determine cerebral vascular reserve.18,21 Research
studies have shown that even small elevations in end-tidal carbon dioxide (CO₂) on the order of 5-8 mm Hg are capable of producing measurable increases in global CBF. In the clinical population, common conditions that can result in arterial blood gas disturbances include chronic obstructive pulmonary disease, adult respiratory distress syndrome, and pulmonary edema. Increases of 30 mm Hg or more from baseline can occur in these patients and may significantly increase global CBF. Figure 14 demonstrates a case of unusually high global CBF for age in a patient with severe pulmonary edema and marked hypercapnia (PCO₂ = 76) on arterial blood gas analysis on the day of the MR imaging.

Conclusion
The unique property of repeatability in ASL naturally lends itself to the evaluation of pathologic states with dynamic perfusion anomalies, such as infarct, tumor, seizure, and vascular instability. In our experience, ASL has been quite sensitive to states of increased CBF, which have often led to the creation of CBF maps with high signal-to-noise ratios. In summary, Parts 1 (techniques and artifacts), 2 (hypoperfusion patterns), and 3 (hyperperfusion patterns) of this review series describe our current experience with ASL based on the largest clinical sample to date. As MR imaging manufacturers begin to offer this new imaging technique and it is incorporated into clinical practice, knowledge of the typical artifacts, hypoperfusion, and hyperperfusion patterns will aid in the interpretation of perfusion images.

Acknowledgment
We thank Kathy Pearson for help with computer programming.

References
1. Deibler AR, Pollock JM, Kraft RA, et al. Arterial spin labeling in routine clinical practice, Part 1: Technique and artifacts. AJNR Am J Neuroradiol 2008;29:1228–34
2. Deibler AR, Pollock JM, Kraft RA, et al. Arterial spin-labeling in routine clinical practice, Part 2: Hypoperfusion patterns. AJNR Am J Neuroradiol 2008;29:1235–41
3. Wolf RL, Alop DC, McGarvey ML, et al. Susceptibility contrast and arterial spin labeled perfusion MRI in cerebrovascular disease. J Neuroimaging 2003;13:17–27
4. Warmuth G, Gunther M, Zimmer C. Quantification of blood flow in brain tumors: comparison of arterial spin labeling and dynamic susceptibility-weighted contrast-enhanced MR imaging. Radiology 2003;228:523–32
5. Weber MA, Gunther M, Lichy MP, et al. Comparison of arterial spin-labeling techniques and dynamic susceptibility-weighted contrast-enhanced MRI in perfusion imaging of normal brain tissue. Invest Radiol 2003;38:712–18
6. Schwartz RB. Hyperperfusion encephalopathies: hypertensive encephalopathy and related conditions. Neurology 2002;8:22–34
7. Elster AD, Moody DM. Early cerebral infarction: gadopentetate dimeglumine enhancement. Radiology 1990;177:627–32
8. Wagner WH, Cosman DW, Farber A, et al. Hyperperfusion syndrome after carotid endarterectomy. Ann Vasc Surg 2005;19:479–86
9. Lee SK, Lee SY, Yun CH, et al. Ictal SPECT in neocortical epilepsies: clinical usefulness and factors affecting the pattern of hyperperfusion. Neuroradiology 2006;48:678–84
10. Brown GG, Clark C, Liu TT. Measurement of cerebral perfusion with arterial spin labeling. Part 2. Applications. J Int Neuropsychol Soc 2007;13:526–38
11. Kim HS, Kim SY. A prospective study on the added value of pulsed arterial spin-labeling and apparent diffusion coefficients in the grading of gliomas. AJNR Am J Neuroradiol 2007;28:1693–99
12. Hacein-Bey L, Nour R, Pike-Spellman J, et al. Adaptive changes of autoregulation in chronic cerebral hypotension with arteriovenous malformations: an acetazolamide-enhanced single-photon emission CT study. AJNR Am J Neuroradiol 1995;16:1865–74
13. Young WL, Kader A, Ornstein E, et al. Cerebral hyperemia after arteriovenous malformation resection is related to “breakthrough” complications but not to feeding artery pressure: The Columbia University Arteriovenous Malformation Study Project. Neurosurgery 1996;38:1085–93, discussion 1093–85
14. Casey SO, McKinney A, Teksam M, et al. CT perfusion imaging in the management of posterior reversible encephalopathy. Neuroradiology 2004;46:272–76
15. Gupta V. Silent or non-clinical infarct-like lesions in the posterior circulation territory in migraine: brain hyperperfusion or hyperperfusion? Brain 2006;129:E39
16. Rogers LR. Cerebrovascular complications in cancer patients. Neurol Clin 2003;21:167–92
17. Macfarlane R, Moskowitz MA, Sakas DE, et al. The role of neuroeffector mechanisms in cerebral hyperperfusion syndromes. J Neurosurg 1991;75:845–55
18. Ito H, Kanno I, Ibaraki M, et al. Changes in human cerebral blood flow and cerebral blood volume during hypercapnia and hypocapnia measured by positron emission tomography. J Cereb Blood Flow Metab 2003;23:665–70
19. Muehlchlegel S, Voetsch B, Singhal AB. CT angiography and CT perfusion in post-CEA hyperperfusion syndrome. Neurology 2007;68:1437
20. Moskowitz MA, Macfarlane R, Tasdemiroglu E, et al. Neurogenic control of the cerebral circulation during global ischemia. Stroke 1990;21(11 suppl):III168–71
21. Noh U, Meadows GE, Kotajima F, et al. Cerebral vascular response to hypercapnia: determination with perfusion MRI at 1.5 and 3.0 Tesla using a pulsed arterial spin labeling technique. J Magn Reson Imaging 2006;24:1229–35

AJNR Am J Neuroradiol 29:1428–35 | Sep 2008 | www.ajnr.org 1435