Advances in Non-Contrast Enhanced Perfusion Assessment

By David Alsop, PhD, Director of MRI Research, Beth Israel Deaconess Medical Center and Associate Professor of Radiology, Harvard Medical School, and Ajit Shankaranarayanan, PhD, Senior Scientist, Applied Science Laboratory

Brain tissue perfusion, often referred to as Cerebral Blood Flow (CBF), is a key measure of tissue function and the state of its vascular supply. In normal states of vascular regulation, perfusion is correlated with tissue metabolic activity. In cases of vascular injury or occlusion, perfusion may be more reflective of vascular disease.

Perfusion imaging typically requires administration of a contrast agent, or tracer, but a special technique of magnetic resonance imaging (MRI) permits the imaging of perfusion without any contrast. This technique uses spatially selective radio frequency (RF) pulses to invert the water spins of inflowing arterial blood. Since this inversion "labels" the inflowing blood spins, the technique has become known as Arterial Spin Labeling (ASL). Relative to contrast CT and MR perfusion techniques, ASL can achieve reduced vascular contamination and may provide more accurate quantification when flow is elevated or in lesions with a compromised blood-brain barrier.

ASL perfusion imaging acquires two images. The labeled image is acquired a short wait after the inflowing arterial spins are inverted. This wait gives time for the labeled blood to pass through the arteries and arterioles and enter the tissue. A control image is acquired with the identical imaging sequence, but without inverting the arterial spins. Subtracting the labeled image from the control image produces an ASL perfusion weighted image, which can then be converted to a quantitative image which reflects cerebral blood flow.

In early implementations, clinical ASL often suffered from low sensitivity, motion artifact, image distortions, underestimation of slow flow, and vascular contamination. Recognizing the potential of ASL, GE Healthcare scientists collaborated with investigators at Beth Israel Deaconess Medical Center (Boston, Mass.) to evaluate potential solutions to some of ASL's limitations and to develop a more robust 3D technique.

Description

The collaboration targeted three major improvements over early ASL implementations:

- Pulsed continuous labeling;
- Background suppression; and
- 3D fast spin echo (FSE) acquisition.

Pulsed continuous labeling: Early in the development of ASL, it was appreciated that continuously inverting blood just before it entered the imaged volume would provide a major signal increase compared to labeling the inflowing blood with a single inversion at a single time point. Practical approaches, however, to achieving continuous labeling with more standard clinical hardware were not available until pulsed continuous labeling (pCASL)[1] was invented. pCASL uses many short RF pulses to continuously invert spins just before they enter the volume of interest to decrease signal loss from decay of labeled blood. This labeling approach excellently approximates the continuous inversion of spins but uses a lower RF duty cycle that is more compatible with clinical hardware. The approach also causes less magnetization transfer saturation for improved quantification and higher sensitivity.

Background suppression: Arterial spin labeling has a very small effect on a typical MR image. The perfusion effect can only be seen after subtracting the label and control images that are roughly 100 times larger. Any motion or other changes in these bright images can overwhelm the perfusion sensitive difference with artifacts and noise. Fortunately, a technique first reported by GE scientist Tom Dixon and later evaluated in ASL perfusion by researchers at the National Institutes of Health can greatly improve ASL image robustness.[2] This technique employs additional inversion pulses in the labeling sequence that can suppress the static tissue signal intensity in the label and control images while leaving the perfusion sensitive component almost unaffected.

3D FSE imaging: Early work with ASL relied on echo-planar imaging to minimize noise and artifacts from motion and other image fluctuations. With the use of background suppression, alternative sequences with reduced signal loss and distortion in the presence of magnetic field non-uniformity can be used. Volumetric 3D fast spin echo imaging offers high sensitivity and excellent image quality. To speed image acquisition, a short spiral gradient pattern was used to read out each echo in the FSE train. This yields an acquisition of the center of k-space with every shot, which helps improve image robustness while providing whole brain perfusion images in approximately five minutes. This acquisition is called 3D ASL.

Advantages of the 3D ASL approach include:

- No need for IV access or contrast administration;
- Isotropic 3D whole-brain acquisition;
- More coverage and/or higher resolution in a shorter scan time versus other ASL techniques;
- Exquisite image quality, demonstrating robustness to motion and susceptibility; and
- Inlined and automatic reconstruction for the analysis of perfusion sensitive images.

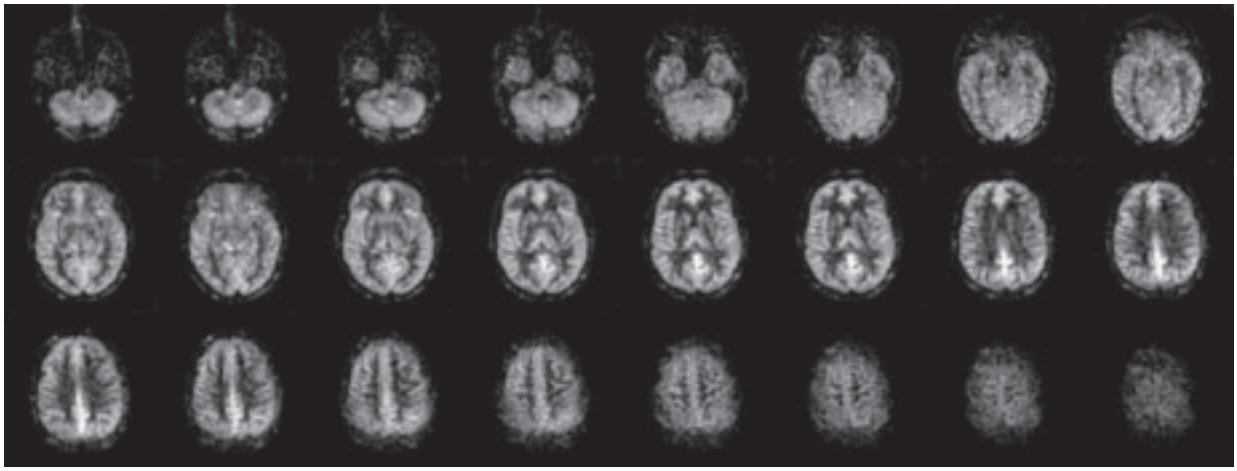


Figure 1. 3D ASL whole brain perfusion images acquired on the Discovery MR750 3.0T system: scan time 5:30 min, isotropic 4 mm voxels

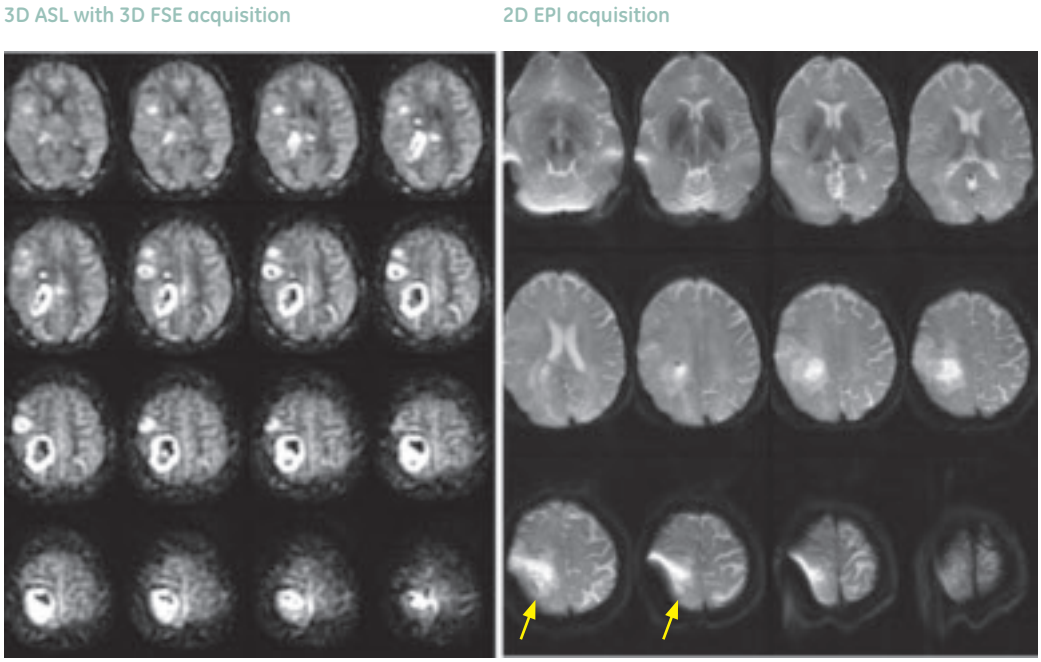


Figure 2. Comparison of 3D ASL scans with 2D EPI images in a patient with a surgical clip; note the significant reduction in susceptibility artifacts in FSE scans allowing for more robust image quality

The 3D ASL sequence has since been tested by several global research sites on over 1,000 clinical cases in a realistic clinical environment. The results are very encouraging: the sequence – including the ability to consistently generate excellent diagnostic quality images in clinically acceptable scan times. Applications to stroke and cerebrovascular disease, brain tumors, and dementia are currently the subject of several pending or scheduled articles.

Based upon the initial experience with this 3D ASL technique, the authors see several potential clinical applications:

- Situations where contrast administration is a concern (e.g. pediatrics, patients with compromised kidney function);
- Assessment of brain tumor vascularity and recurrence;
- Rule out ischemic injury or detect reperfusion;
- Differential diagnosis of dementias; and
- Assessment of inflammation and infection.

With 3D ASL, GE Healthcare aims to introduce a new ASL technique that is robust, fast, patient-friendly, and provides tangible clinical value. ■

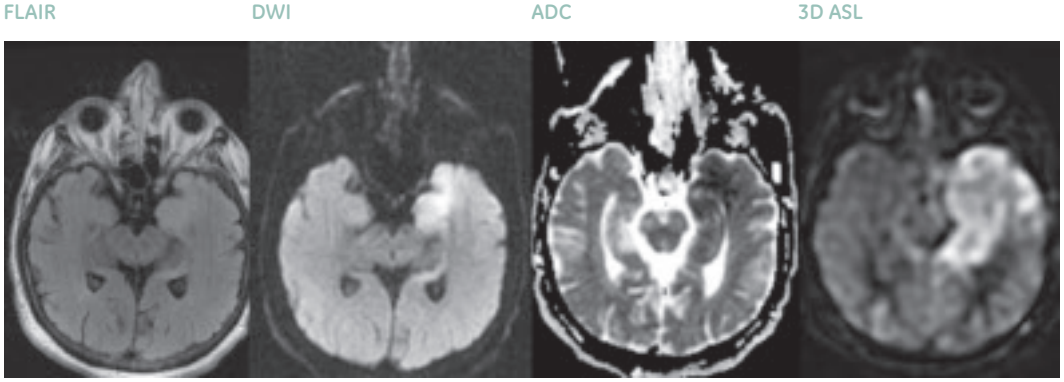


Figure 3. Images acquired on a Signa HDxt 1.5T system of a 59-year-old patient with HSV-1 encephalitis affecting the medial temporal lobe

References:

1. Garcia et al ISMRM 2005, Dai et al 2008
2. (Dixon et al 1991, Mani et al 1997, Ye et al 1998)

The Researchers' Perspective

Ever wonder what happens before a new product is launched? Here's what the inventor of the technique we now know as 3D ASL and his GE scientist collaborator have to say about the teamwork, the process, and the satisfaction of ushering a good concept to the clinical setting.

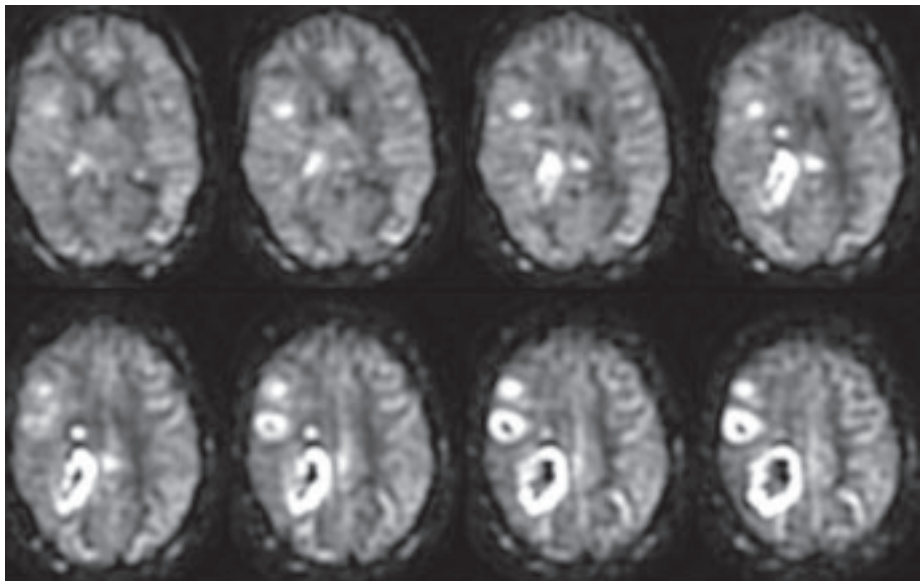
After putting together his own pilot sequence, Dr. Alsop admits his prototype wasn't as sophisticated or as flexible as he envisioned the sequence could potentially be. The prototype still got the attention of former GE ASL Scientist, Ehud Schmidt, who'd developed a reputation for his work in ASL. "GE realized this wasn't just a researcher's toy and had the potential for wide-spread use," Dr. Alsop says. Schmidt connected Dr. Alsop to Ajit Shankaranarayanan, PhD and senior scientist at GE's Global Applied Science Lab (Menlo Park, CA), "We found his idea impressive, but we needed to work together to get it into an environment where people could easily use it," he says.

Dr. Alsop began collaborating with Dr. Shankaranarayanan and his team to incorporate GE's developments in spiral acquisitions. "We worked together – testing and proving different aspects – and created a new prototype that was flexible to use and, as important, easier to use for the technologists."

A key benefit GE Healthcare provided was the large network of clinical sites that could evaluate the new prototype. "Dr. Alsop had the initial prototype in one or two sites, but by the end of 2007, our new prototype was sent to 15 different institutions in the US, Europe, Japan, and APAC," says Dr. Shankaranarayan. While GE helped coordinate the clinical evaluations, Dr. Alsop and Dr. Shankaranarayanan worked together to implement technical changes based on clinical feedback.

"We anticipate this will be a long-term collaboration with Dr. Alsop," adds Dr. Shankaranarayanan, "with our mutual goal to expand perfusion imaging to other areas of the body."

Dr. Alsop agrees that this type of collaboration is necessary for the betterment of healthcare. "Our institution is, in general, interested in technology transfer. By acts of Congress, NIH researchers are obligated to transfer their technology to commercial ventures."



David Alsop

David Alsop, PhD, is currently director of MRI Research within the Center for Advanced Imaging at Beth Israel Deaconess Medical Center and associate professor of Radiology at Harvard Medical School. Dr. Alsop received his PhD in Physics from the University of California (Berkeley, CA). His research interests include techniques for rapid Magnetic Resonance Imaging (MRI), high field MRI, perfusion imaging, neuro-imaging, aging and dementia, cancer, and stroke. Dr. Alsop serves as Associate Editor and member of the Editorial Board of *Magnetic Resonance in Medicine*.

Ajit Shankaranarayanan

Ajit Shankaranarayanan, PhD and senior scientist joined GE in 2001 following completion of his PhD from Case Western Reserve University, Cleveland, OH. Some of his research interests include non-contrast perfusion imaging, real-time imaging, motion insensitive imaging and he has worked on a number of novel projects spanning several clinical specialties including neurology and cardiology. In his current role as a senior scientist, he leads multi-disciplinary collaborations with several luminary academic institutions including Beth Israel Deaconess Hospital (Dr. David Alsop), UCSD (Dr. Anders Dale), and Stanford (Dr. Dwight Nishimura). These collaborations have resulted in the development and evaluation of promising new techniques to perform true 3D motion insensitive imaging, robust whole brain non-contrast perfusion imaging, and high-resolution diffusion imaging. The projects have helped cement GE's role as an innovator in MRI technology for the diagnosis of various neuro and cardiac diseases while expanding GE's already impressive application portfolio.