# Arterial Spin Labeling

Bradley MacIntosh and Guocheng Jiang

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# Learning Objectives

- ASL has been around for over two-decades and is still going strong
- Non-invasive and quantitative, but unique ASL-CBF contrast
  - ASL using a 3 Tesla MRI scanner is the most common application
- There are several ASL image analysis software options, but we are biased to using tools from the FMRIB Software Library
- Showcase diverse applications of the ASL researches across the lifespan and diseases.

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# Lecture 2 – How does ASL perfusion MRI work?

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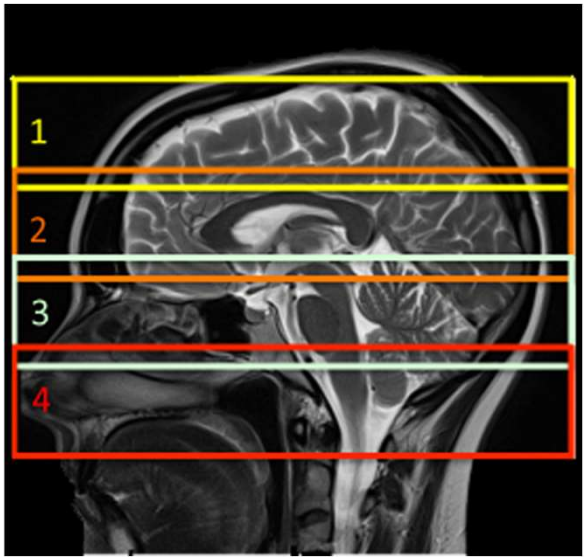
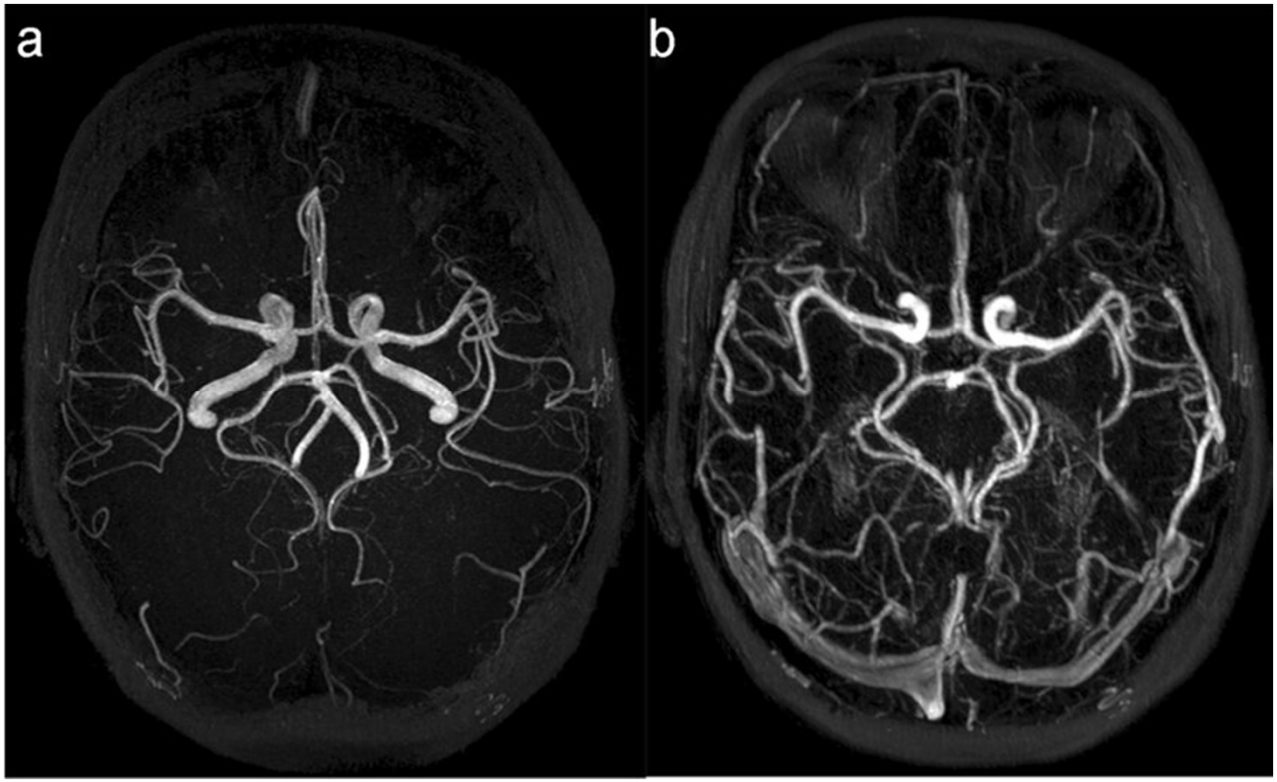
# ASL relies on a few principles to give perfusion contrast

Spin tagging




Out of volume preparation

Time of flight MR angiography

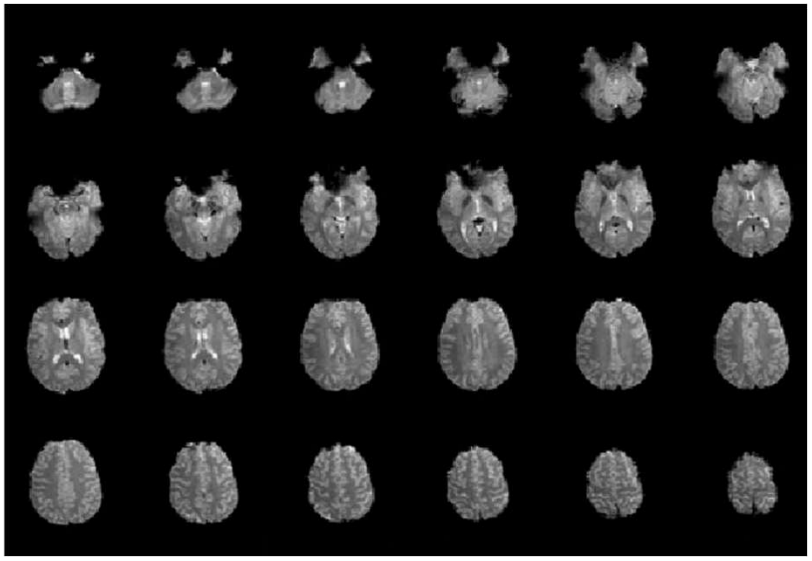



https://mriquestions.com/motsa.html

# ASL relies on a few principles to give perfusion contrast

Rapid multi-slice imaging

**Functional MRI**



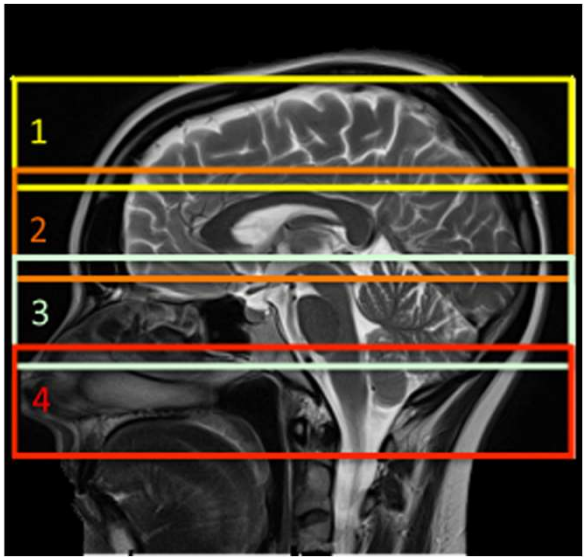
**Diffusion MRI**

Echo planar imaging

https://mriquestions.com/motsa.html

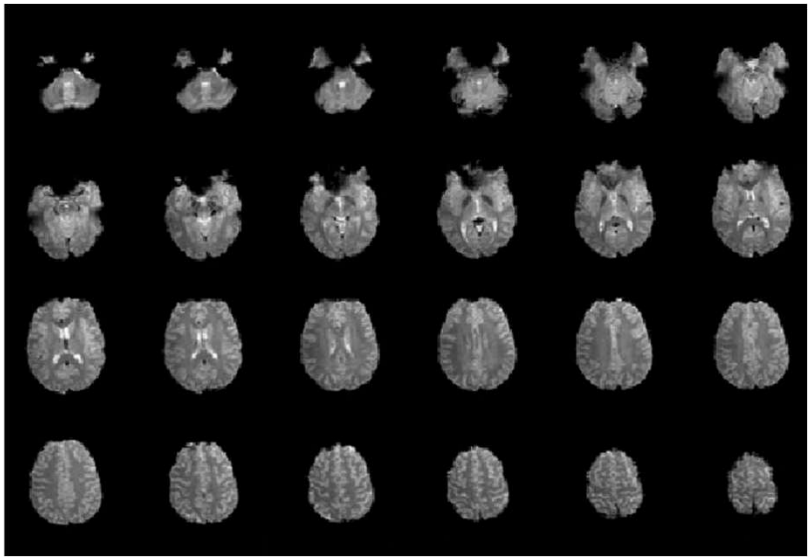
# ASL relies on a few principles to give perfusion contrast

Spin tagging




Out of volume preparation

Rapid multi-slice imaging



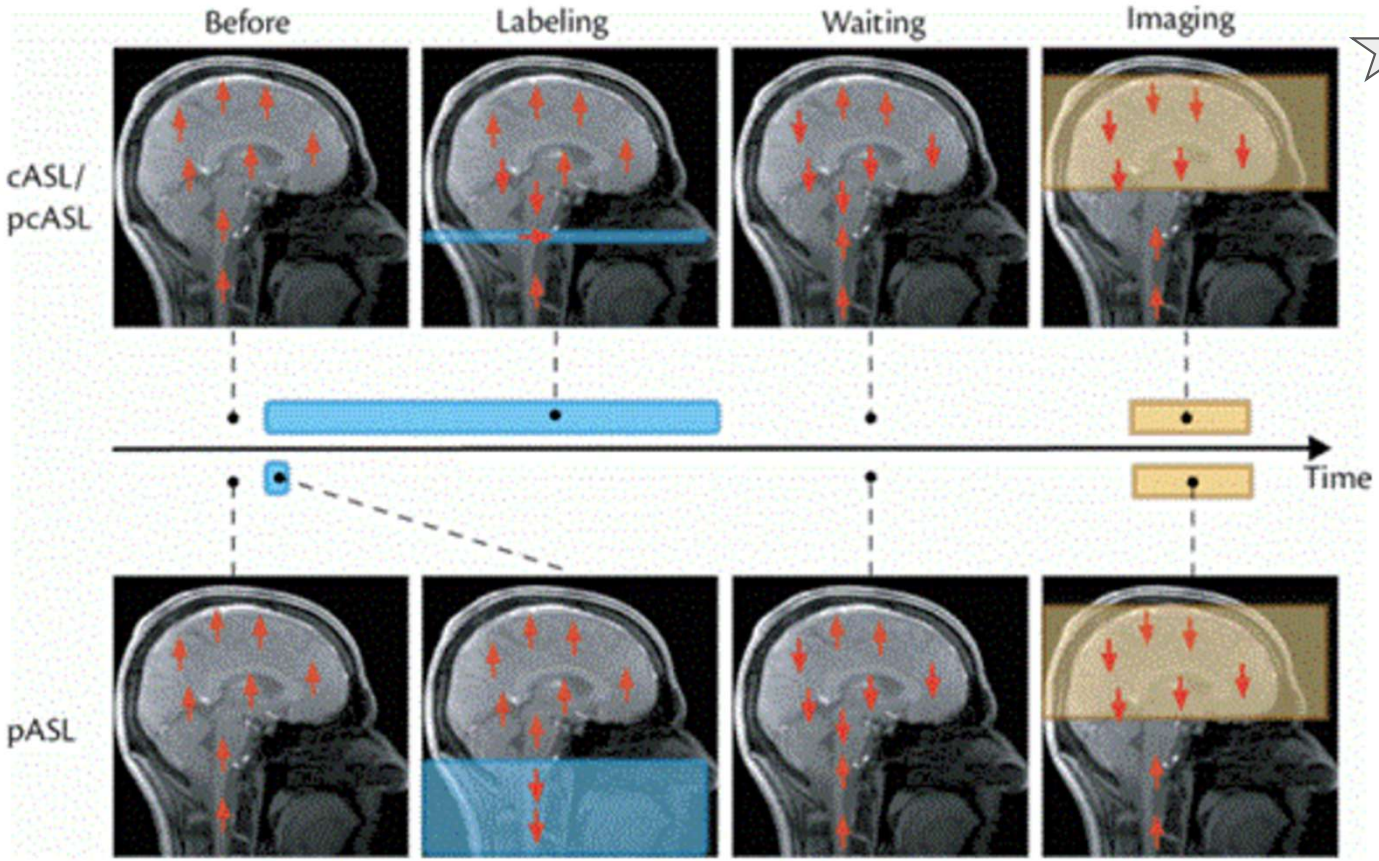
Echo planar imaging

Control and Tag pairs

Serial imaging

https://mriquestions.com/motsa.html

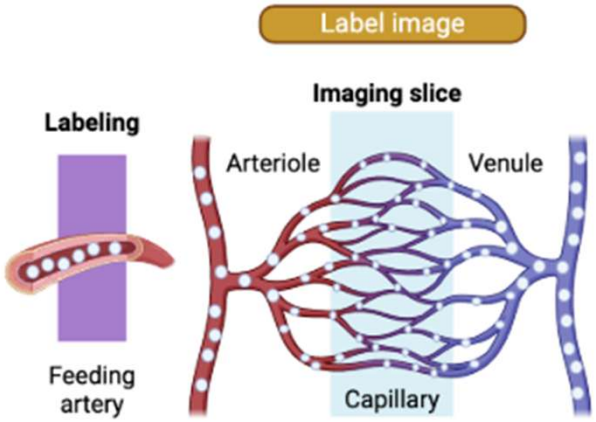
# Three stages of a typical ASL experiment: Labeling, Waiting, and Imaging

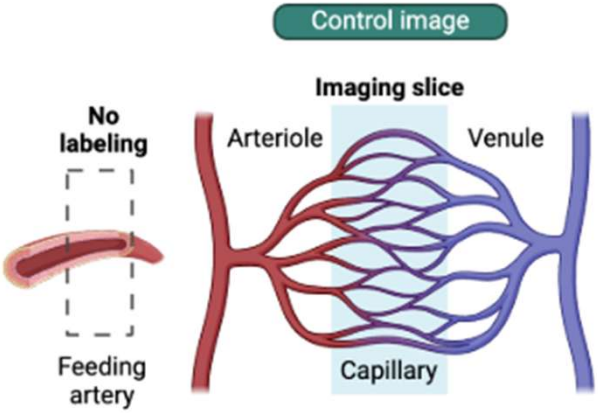


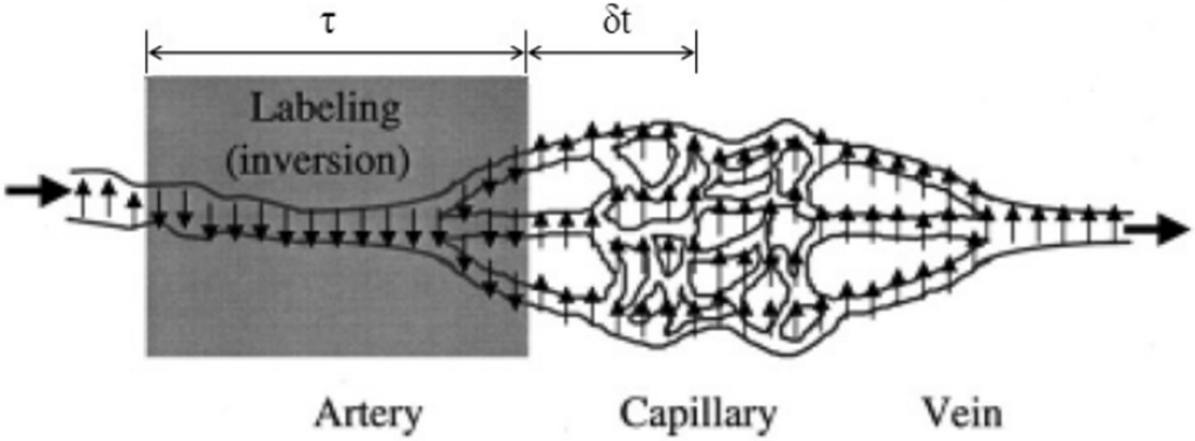

In **continuous ASL (cASL) and pseudo-continuous ASL (pcASL),** a continuous RF pulse will be applied, and proton magnetization will be inverted as blood travel through the labeling plane

In **pulsed ASL (pASL),** a short RF pulse (~10 ms) is used to invert all the magnetization of blood water in the labeling plane.

# ASL is a non-invasive measurement of cerebral blood perfusion




- **Spin**: Hydrogen (proton) nuclei.
- **Arterial spin labeling**: To (magnetically) label the hydrogen nuclei in the arterial blood.
- An RF field will alter the magnetization of hydrogen nuclei within water that pass through the labeling plane (neck).

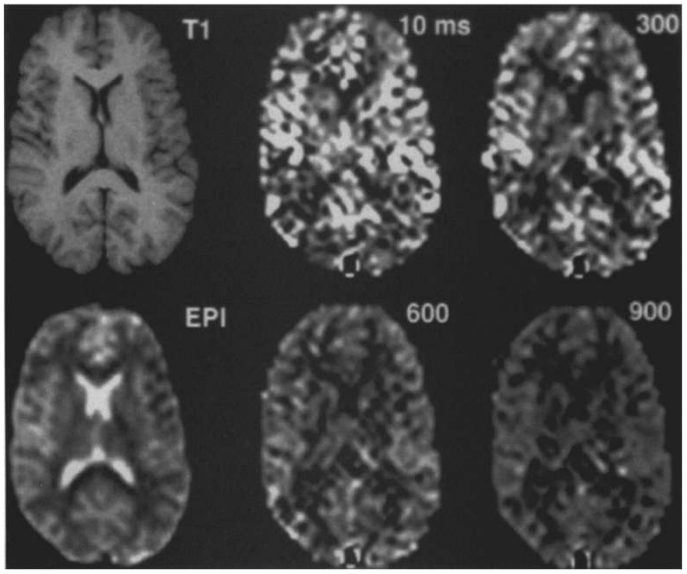
# Theory, principles, and applications of ASL date back 2 decades

*Two of the classic ASL papers*

1996 JCBFM

Reduced Transit-Time Sensitivity in Noninvasive Magnetic Resonance Imaging of Human Cerebral Blood Flow

*D. C. Alsop and *†J. A. Detre



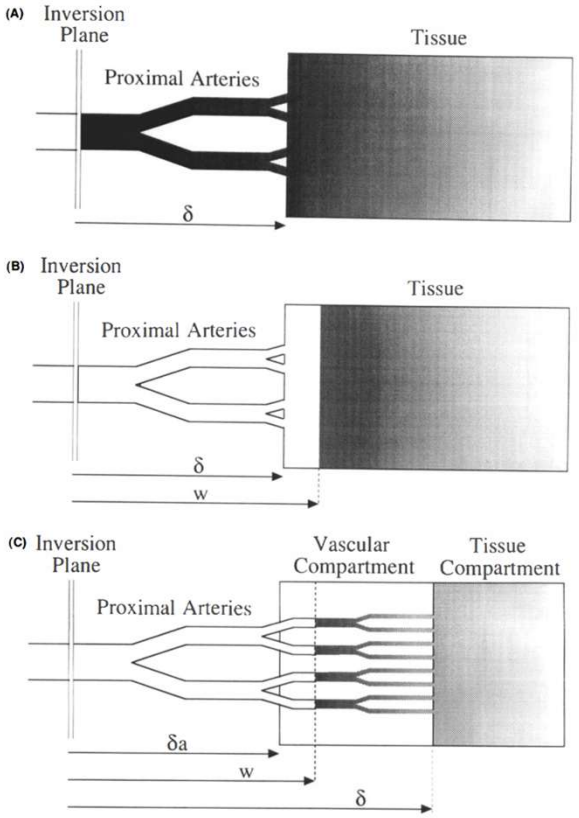




**FIG. 1.** Schematic diagrams of the continuous arterial tagging perfusion imaging models. **A:** In previous implementations, arterial spins are inverted as they pass the inversion plane. Tagged spins gradually relax back towards equilibrium as they diffuse into the tissue. δ is defined as the transit time from the inversion plane to the tissue. **B:** When a delay of duration, w, is introduced, the proximal artery signal is eliminated, and uninverted spins may enter the tissues before imaging. If δ increases, fewer uninverted spins arrive in the tissue resulting in an increase in signal. This increase largely cancels the loss of signal resulting from increased $T_1$ decay of tagged spins before they arrive in the tissue. **C:** In a more complex model, the contribution of intraluminal spins is explicitly accounted for by separating the "tissue" seen in **(a)** and **(b)** into a vascular compartment and a true tissue compartment. A second transit time, δa, from the inversion plane to the arterial vascular compartment, is defined.

https://journals.sagepub.com/doi/pdf/10.1097/00004647-199611000-00019

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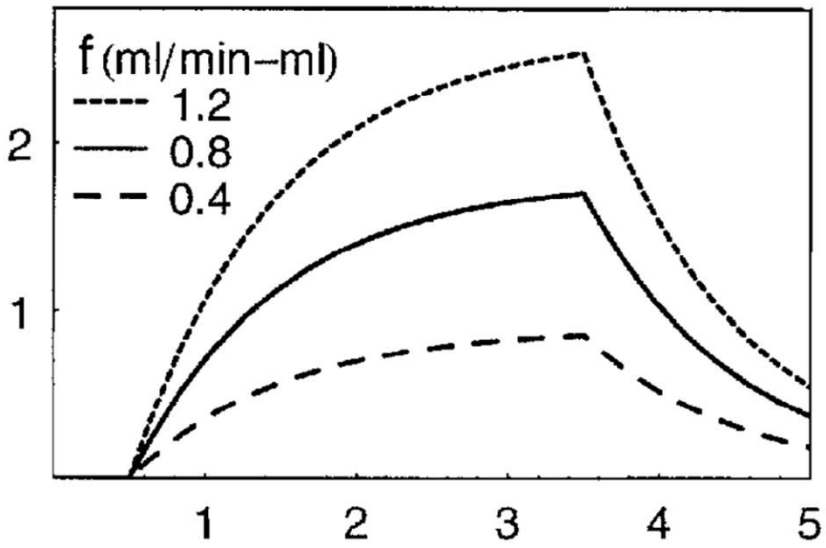
*Two of the classic ASL papers*

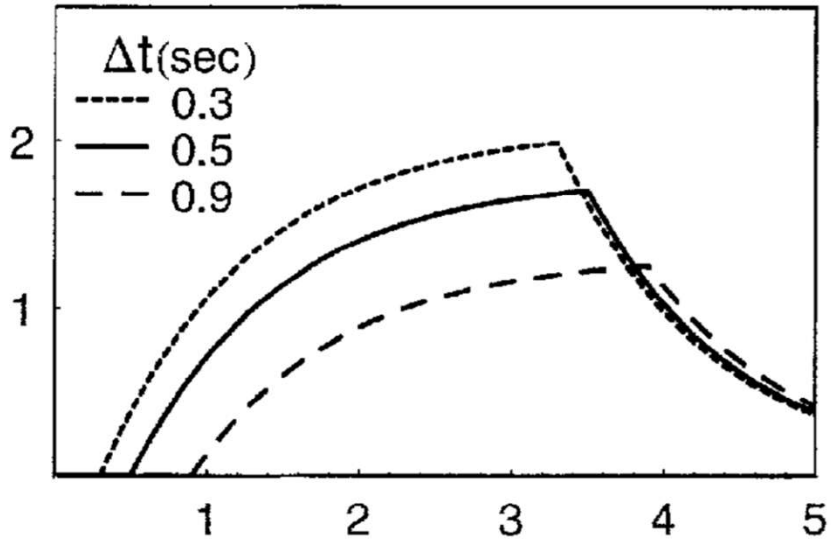
1998 Magnetic Resonance in Medicine

**A General Kinetic Model for Quantitative Perfusion Imaging with Arterial Spin Labeling**

Richard B. Buxton, Lawrence R. Frank, Eric C. Wong, Bettina Siewert, Steven Warach, Robert R. Edelman

ASL “kinetic model”



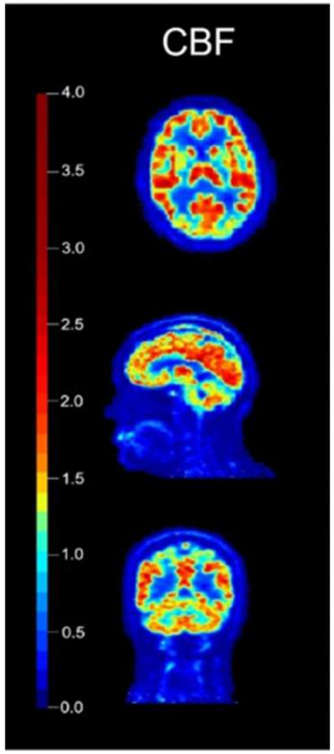

https://onlinelibrary.wiley.com/doi/10.1002/mrm.1910400308

# ASL remains primarily a research tool

2006 Stroke

## Comparative Overview of Brain Perfusion Imaging Techniques

Max Wintermark, MD; Musa Sesay, MD; Emmanuel Barbier, PhD; Katalin Borbély, MD, PhD; William P. Dillon, MD; James D. Eastwood, MD; Thomas C. Glenn, MD; Cécile B. Grandin, MD, PhD; Salvador Pedraza, MD; Jean-François Soustiel, MD; Tadashi Nariai, MD, PhD; Greg Zaharchuk, MD, PhD; Jean-Marie Caillé, MD; Vincent Dousset, MD; Howard Yonas, MD




**PET is the gold standard**

https://www.ahajournals.org/doi/full/10.1161/01.STR.0000177884.72657.8b

**TABLE 1. Overview of the Imaging Techniques Dedicated to Brain Hemodynamics**

| | Brain Perfusion Imaging Techniques | | | | | | |
|---|---|---|---|---|---|---|---|
| | PET | SPECT | XeCT | PCT | DSC | ASL | Doppler |
| Feasibility | Ionizing radiation | | | | Injection | | |
| Age range | Adults (and children for static exams) | Adults (and children) | Adults (and children) | Adults (and children) | Adults (and children) | Adults+children | Adults+children |
| Bedside | No | In some instances | No | No | No | No | Yes |
| Contrast material | $^{15}O_2$, $C^{15}O_2$, $H_2{}^{15}O$ | $^{133}Xe$, $^{99m}Tc$-HMPAO, $^{99m}Tc$-ECD, $^{123}I$-IMP (diffusible) | Stable xenon gas (diffusible) | Iodinated contrast material (nondiffusible) | gadolinium chelate (nondiffusible) | None (endogenous contrast) | None (endogenous contrast) |
| Radiation/study | 0.5–2 mSv | 3.5–12 mSv | 3.5–10 mSv | 2–3 mSv | None | None | None |
| Data acquisition | 5–9 min | 10–15 min | 10 min | 40 sec | 1 min | 5–10 min | 10–20 min |
| Data processing | 5–10 min | 5 min | 10 min | 5 min | 5 min | 5 min | None |
| Interpretation | | | | | | | |
| Mathematical model | Kety–Schmidt model | Principle of chemical microspheres for $^{99m}Tc$ tracers, Kety–Schmidt model for $^{133}Xe$ and $^{123}I$-IMP | Kety–Schmidt model | Meier–Zierler model | Meier–Zierler model | Meier–Zierler model | Other |
| Assessed parameters | CBV, CBF, rOEF, glucose metabolism | CBF | CBF | CBF, CBV, MTT, TTP, permeability map | CBF, CBV, MTT, TTP, permeability map | CBF | ICA BFV |
| Large vessels* | No influence on results | No influence on results | No influence on results | Influence results | Influence results | No influence on results | Not applicable |
| Quantitative accuracy | Yes | Yes for $^{133}Xe$ and $^{123}I$-IMP; no for the others tracers | Yes | Yes | Not in daily practice | Yes | Yes for hemispheric CBF |
| Including for low perfused areas† | Yes | Not applicable | Yes | Yes | Not applicable | Not <10 mL/min/100 g | Not applicable |
| Reproducibility | 5% | 10% | 12% | 10–15% | 10–15% | 10% | 5% |
| Brain coverage | Whole brain | Whole brain | 6-cm thickness | 4–5 cm thickness | Whole brain | Whole brain | One measurement for each hemisphere |
| Spatial resolution | 4–6 mm | 4–6 mm | 4 mm | 1–2 mm | 2 mm | 2 mm | Not applicable |
| Minimal time interval between 2 successive exams | 10 min | 10 min (split-dose technique for $^{99m}Tc$-HMPAO, $^{99m}Tc$-ECD and $^{123}I$-IMP) | 20 min | 10 min | 25 min | 0 min | 0 min |
| Clinical applications | | | | | | | |
| Clinical fields | Chronic cerebrovascular disorders | (Acute and) chronic cerebrovascular disorders | Acute and chronic cerebrovascular disorders | Acute and chronic cerebrovascular disorders | Acute and chronic cerebrovascular disorders | Chronic cerebrovascular disorders | Acute cerebrovascular disorders |
| | | Trauma | Trauma | Trauma | | Trauma | Trauma |
| | Dementia and psychiatric diseases | Dementia and psychiatric diseases | Vasospasm | Vasospasm | Vasospasm | Neurodegenerative disorders | Vasospasm |
| | Epilepsy | Epilepsy | Epilepsy | | | | |
| | Brain tumors | | | Brain tumors | Brain tumors | Brain tumors | |
| | Brain activation studies | Brain activation studies | | | | Brain activation studies | |
| Emergency setting | No | In some instances | Yes | Yes | Yes | Yes | Yes |

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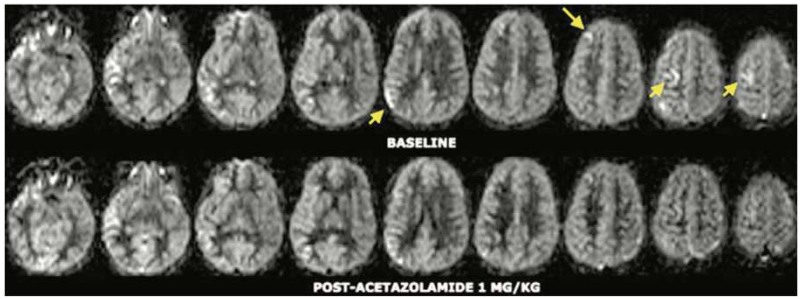


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MRI

Injection

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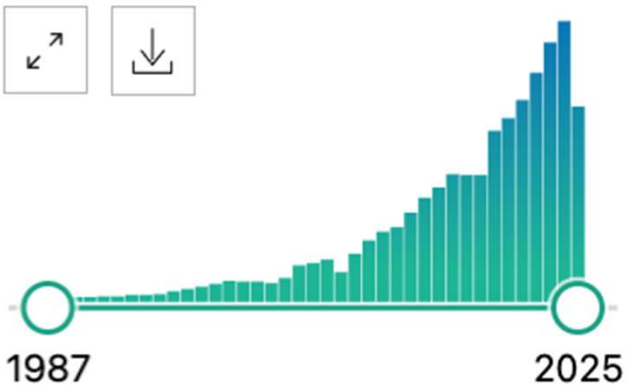
| | Epilepsy | Epilepsy | Epilepsy | | | | |
| | Brain tumors | | | Brain tumors | Brain tumors | Brain tumors | |
| | Brain activation studies | Brain activation studies | | | | Brain activation studies | |
| Emergency setting | No | In some instances | Yes | Yes | Yes | Yes | Yes |

https://www.ahajournals.org/doi/full/10.1161/01.STR.0000177884.72657.8b

# **DSC** versus **ASL**: Which MRI perfusion approach is more popular?

3,023 results

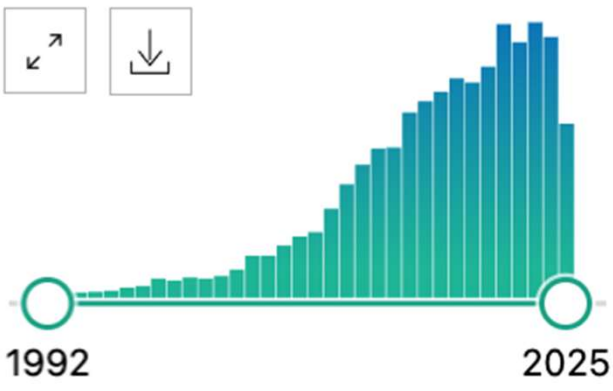
RESULTS BY YEAR




https://pubmed.ncbi.nlm.nih.gov/?term=%22dynamic+susceptibility+contrast%22+or+%28%22DSC%22+and+MRI%29&sort=pubdate

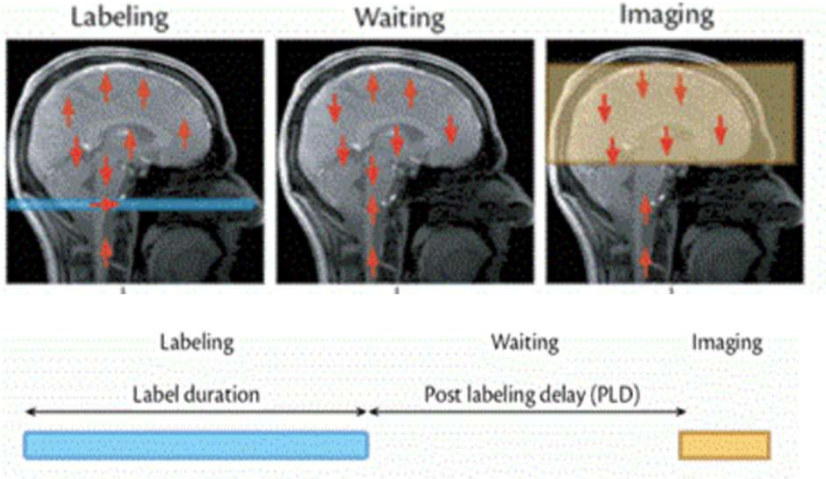
5,207 results

RESULTS BY YEAR




https://pubmed.ncbi.nlm.nih.gov/?term=%22arterial+spin+labeling%22+or+%28%22ASL%22+and+MRI%29+or+%22arterial+spin+tagging%22&sort=pubdate

# Pseudo-continuous ASL (pcASL) imaging was recommended in 2015 and this helped streamline neuroimaging research




**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**

David C. Alsop[1,*], John A. Detre[2], Xavier Golay[3], Matthias Günther[4,5,6], Jeroen Hendrikse[7], Luis Hernandez-Garcia[8], Hanzhang Lu[9], Bradley J. MacIntosh[10,11], Laura M. Parkes[12], Marion Smits[13], Matthias J. P. van Osch[14], Danny JJ Wang[15], Eric C. Wong[16,†], and Greg Zaharchuk[17]

- **pcASL** can be applied on clinical scanners without special hardwares.
- There is a well-defined labeling duration (LD) for perfusion quantification and to maximize the SNR.
- Relatively high labeling efficiency.

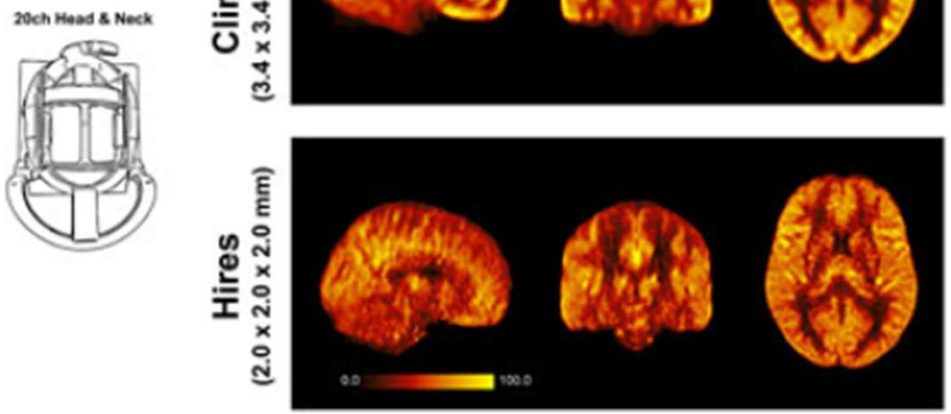
ISMRM | Perfusion STUDY GROUP

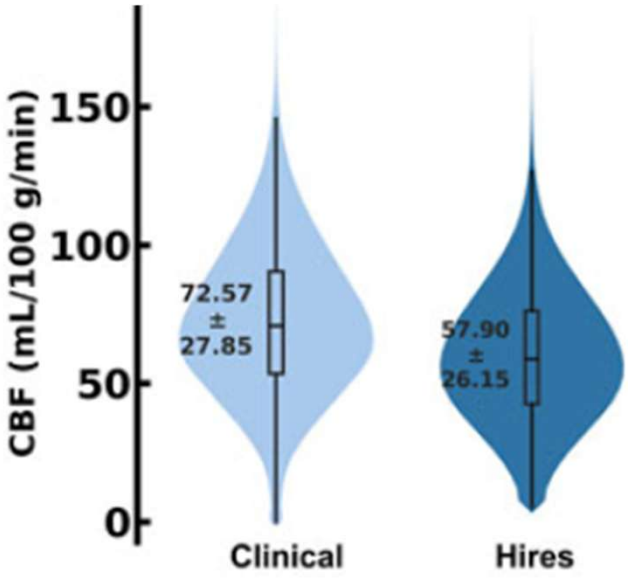
# ASL topics not discussed

**Spatial resolution** – can we push towards smaller voxel dimensions?

**Main magnetic field** – what is the status of ASL at 7 Tesla

**Pulse sequences** – time resolved angiography, vessel selective, velocity selective




https://www.frontiersin.org/journals/physiology/articles/10.3389/fphys.2023.1271254/full

# So What Is the **ASL-CBF** Signal Anyway?

- ASL-CBF signal depends on water, which is a freely diffusible tracer.
- ASL-CBF signal is a measure of tissue perfusion.
- ASL has its wrinkles that could include arterial transit time and partial volume error effects
  - Visually-inspect your ASL-CBF maps