Perfusion Quantification and Application of ASL in Clinical Research

Perfusion Module Lecture 3

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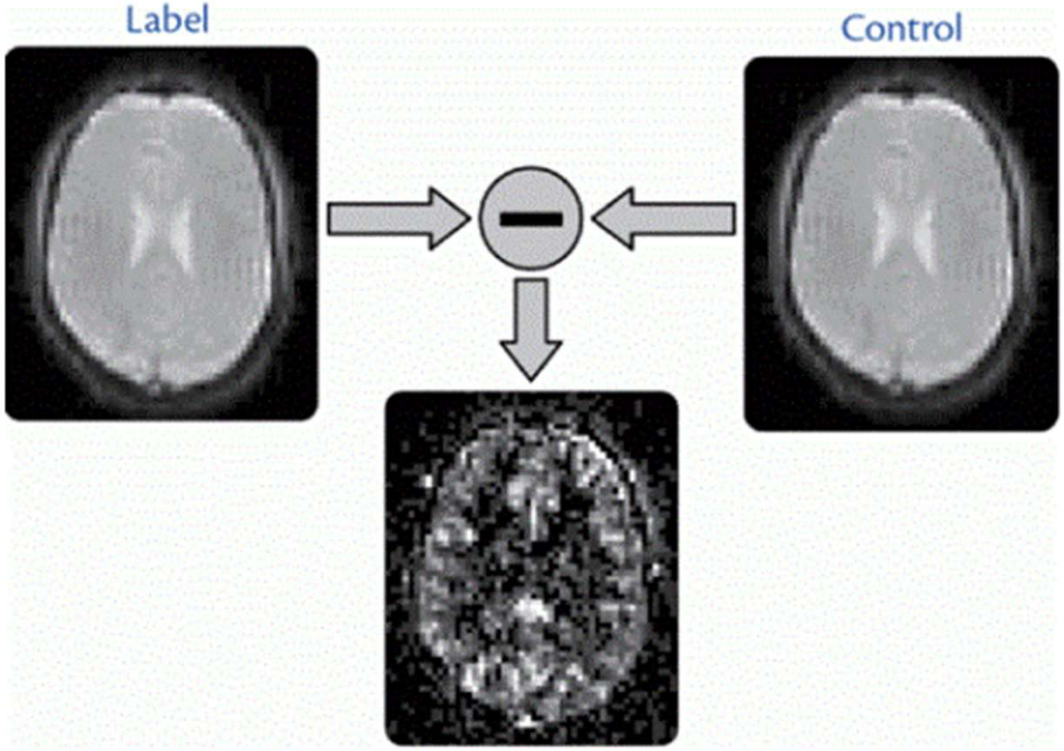
A perfusion-weighted image can be created through subtraction process



Perfusion-Weighted Image (AU)

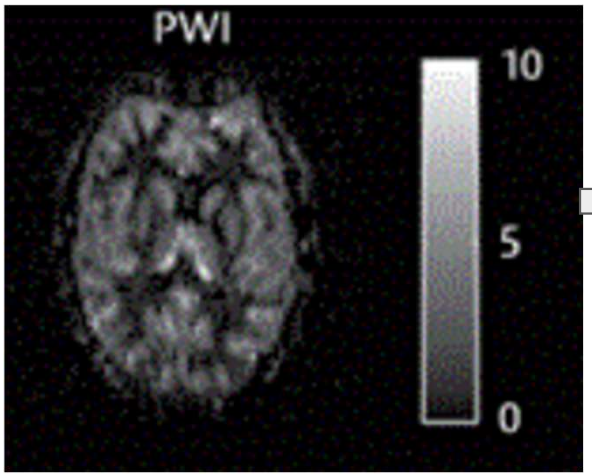
- Labeled blood water bolus will have **negative longitudinal magnetization**, thus reduce the MR signal in the label image.
- Typical signal difference between label and control image: **~ 1% - 2%**.
- The subtraction creates a **perfusion-weighted image** (unitless).

$$S_{\text{label}} = S_{\text{static}} - S_{\text{blood}}$$

$$S_{\text{control}} = S_{\text{static}} + S_{\text{blood}}$$

Roadmap: From a perfusion-weighted image to a calibrated CBF image

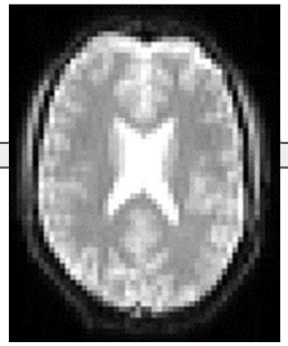
Perfusion-Weighted Image (AU)



Post processing
(Tutorial 1)

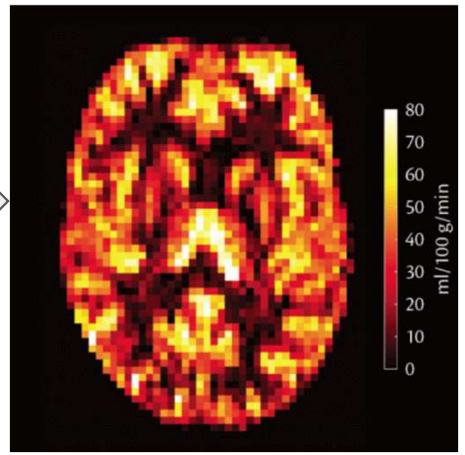
Motion Correction
Registration
Spatial smoothing

Calibration
(Lecture 3)



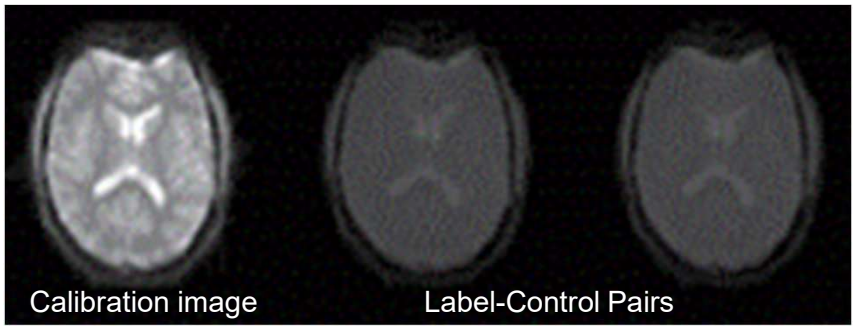
Calibration Images
Kinetic Modeling

Calibrated CBF Map
(ml/100g/min)

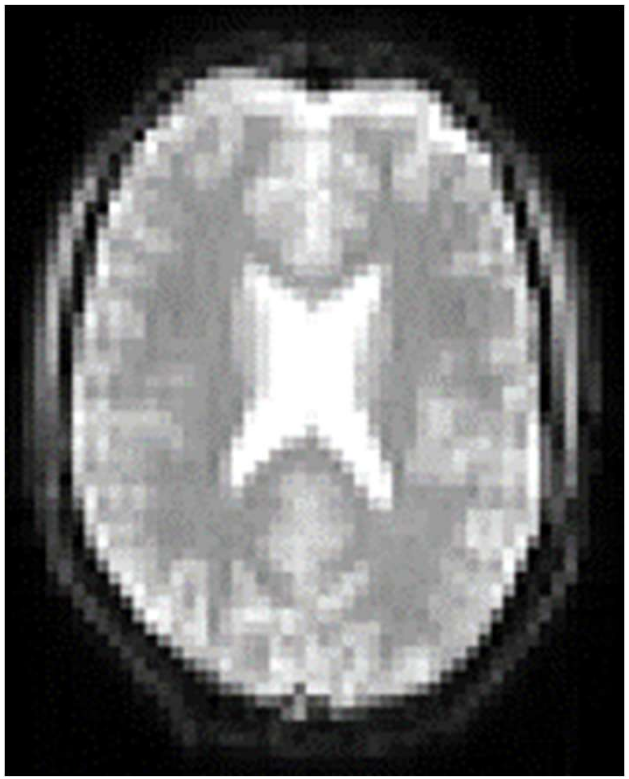


How to get a measure of perfusion in absolute unit from ASL?

- Voxel intensities in a perfusion-weighted image varies due to different scanners, readout techniques, patient positioning, etc.
- The **calibration** process estimates the arterial blood magnetization as an approximation of tracer concentration, and is used kinetic model to obtain a CBF value in absolute units in **ml (blood) /100g (tissue) / min**.
    - Voxelwise calibration is recommended;
    - A **perfusion calibration (M0) image**, is acquired to know the baseline tissue magnetization.



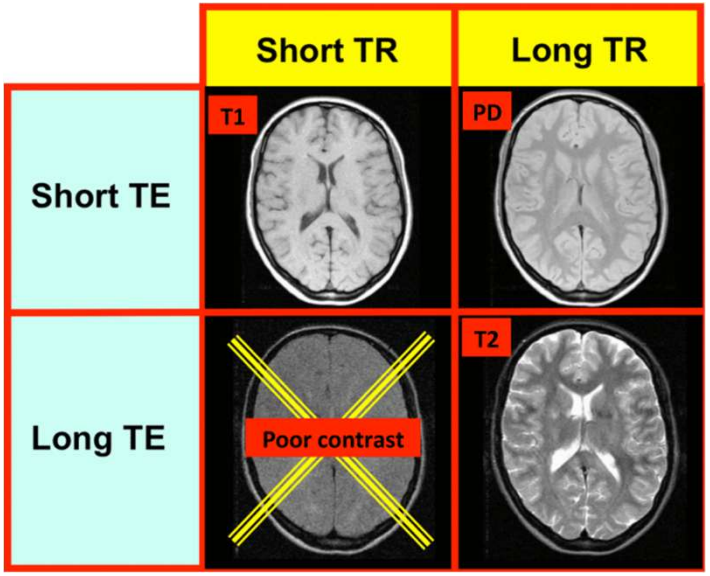
Proton-density-weighted MR image is used as the M0 image



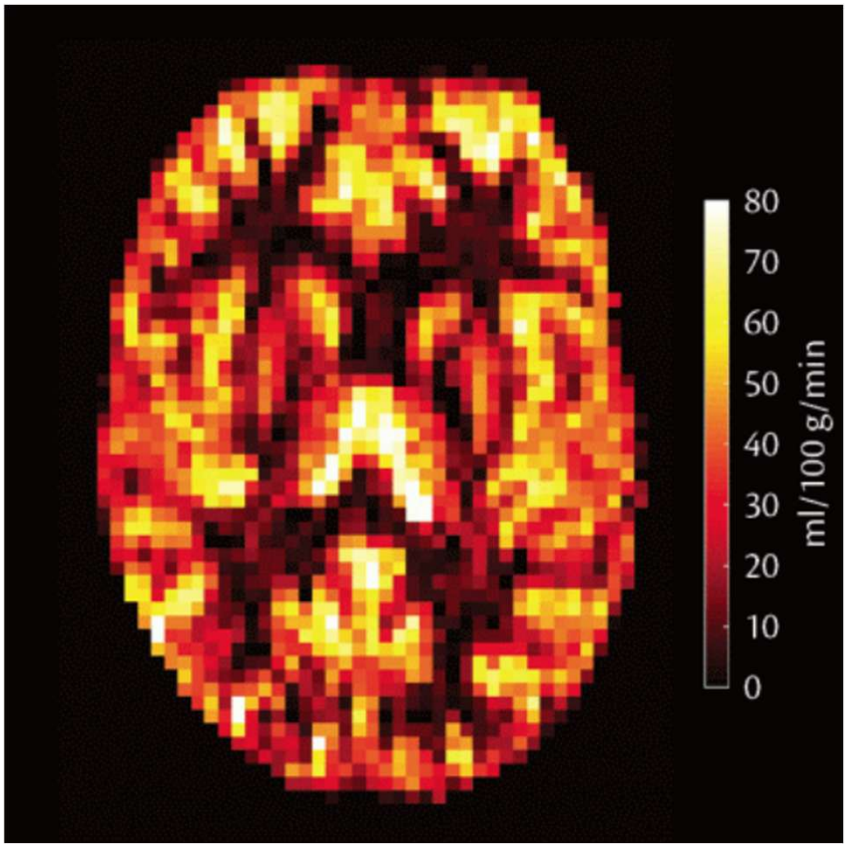
- Signals in the **proton-density-weighted (PDw) images** are dominated by the amount of water in the tissue.

- **Long TR:** Minimizing the T1 effect. (TR > 4.0s)
- **Short TE:** Minimizing the T2 effect.

- No background suppression, no labeled blood-water bolus.



Quantification of cerebral blood flow using kinetic model



Kinetic model provides an equation of MRI signal and perfusion (CBF), describing the amount of labeled blood water that accumulates in the voxel in a given amount of time and give quantitative measure of CBF.

Signal decay during the PLD due to relaxation

Signal difference

ml/100g/min

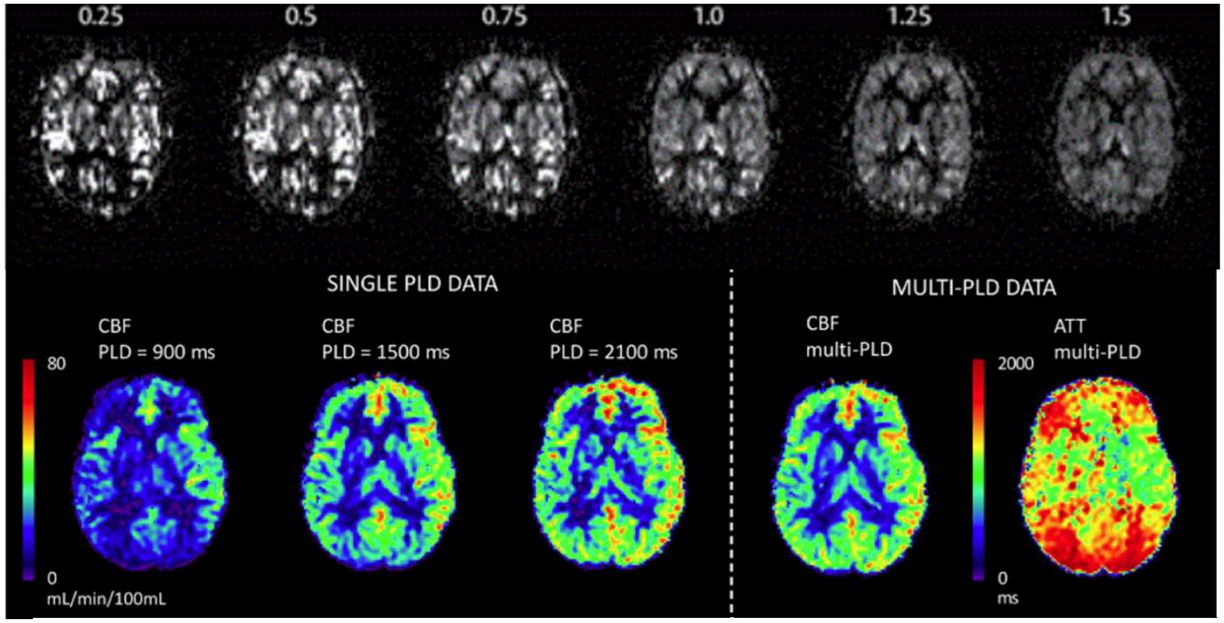
$$CBF = \frac{6000\lambda(S_{\text{control}} - S_{\text{label}})e^{PLD/T_1}}{2\alpha T_1 S_{PD}(1-e^{-\tau/T_1})}$$

How good is labeling process?

Baseline magnetization

- **T1**: T1 time of arterial blood (1.65s at 3.0T)
- **Tau**: Labeling duration (1.80s)
- **Alpha**: Labeling efficiency (0.85)
- **S(PD)**: Signal from PDw calibration image
- **Lambda**: Whole brain partition coefficient (0.9 ml blood/ml tissue)

Multiple PLD pcASL imaging allows us to estimate the arterial transit time (ATT) and cerebral blood flow simultaneously (2024)



PCASL:

$$SI_{control} - SI_{label} = \begin{cases} = 0 & 0 < LD + PLD < ATT \\ \dfrac{2 \cdot \alpha \cdot \alpha_{BS} \cdot T_{1b} \cdot M_{0a} \cdot CBF \cdot e^{-\frac{ATT}{T_{1b}}} \cdot \left(1 - e^{-\frac{LD + PLD - ATT}{T_{1b}}}\right)}{6000} & ATT < LD + PLD < ATT + LD \\ = \dfrac{2 \cdot \alpha \cdot \alpha_{BS} \cdot T_{1b} \cdot M_{0a} \cdot CBF \cdot e^{-\frac{PLD}{T_{1b}}} \cdot \left(1 - e^{-\frac{LD}{T_{1b}}}\right)}{6000} & ATT < PLD \end{cases}$$

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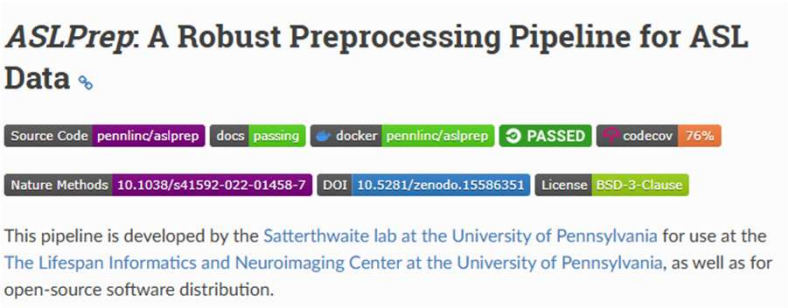
Recommendations for Quantitative Cerebral Perfusion MRI using Multi-Timepoint Arterial Spin Labeling: Acquisition, Quantification, and Clinical Applications

- Single PLD scans usually assume a fixed **arterial transit time (ATT)** value over the entire brain and assumes PLD > ATT.
- Multiple PLD ASL scans provide an **ATT map**: Time for arterial blood to travel from the labeling plane in PCASL, or the distal edge of the labeling slab in PASL, to the imaging voxel.

Different software tools and the major vendors

Softwares: ASLPrep, BASIL (OxfordASL), ExploreASL

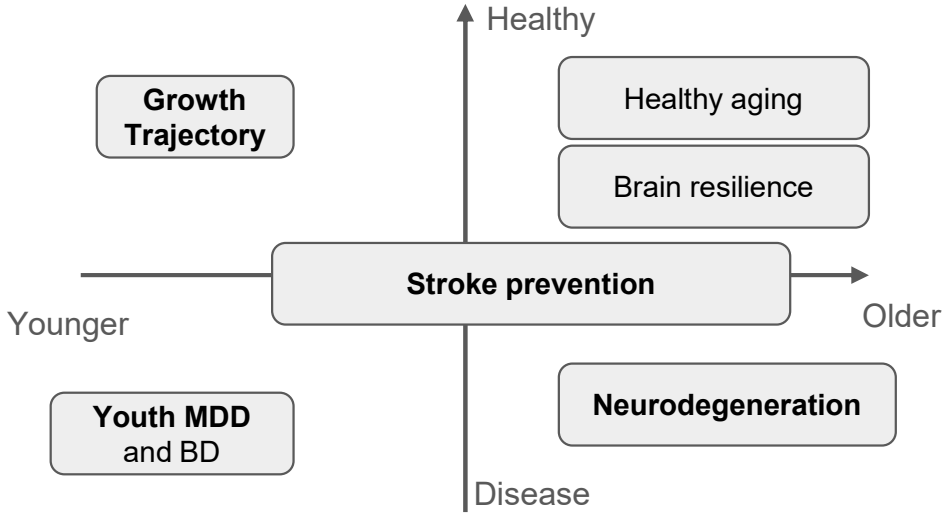


Major Vendors: GE, Philips, Siemens

** Names are sorted alphabetically, thus not representing popularity or priority to use.

Example applications of pcASL imaging on selected clinical topics

1. **(Psychiatry)** Adolescent perfusion with mood disorders;
2. **(Neurodevelopmental)** Adolescent perfusion for males and females;
3. **(Cardiovascular)** Stroke and secondary stroke prevention
4. **(Neurodegenerative)** Pathophysiology of genetic frontotemporal dementia



1. ASL-CBF and mood disorders in the adolescent brain

Imaging Acquisition

Neuroimaging was acquired via MRI using a Philips Achieva (Philips Healthcare, Cambridge, Massachusetts, USA) 3T scanner with an 8-channel head receiver coil. Structural high-resolution T1-weighted images were collected for anatomical registration. CBF was measured using pseudo-continuous arterial spin labeling (ASL) scans. Anatomical T1-weighted images were acquired using high-resolution fast-field echo imaging (repetition time/echo time/inversion time = 9.5/2.3/1400 ms, field of view 240 × 191 mm, spatial resolution 0.94 × 1.17 × 1.2 mm, flip angle 8°, 256 × 164 × 140 matrix, and scan duration 536 seconds). The ASL images were obtained with single-shot two-dimensional echo-planar imaging (repetition time/echo time = 4000/9.7 ms, 64 × 64 × 18 matrix, spatial resolution 3 × 3 × 5 mm, 1650 ms labeling duration, post-label delay of 1600 ms for the most inferior slice [ascending slice order], 30 control-tag pairs, and scan duration of 248 seconds). An ASL reference volume was acquired with a repetition time of 10 seconds to determine the initial magnetization used for quantification.

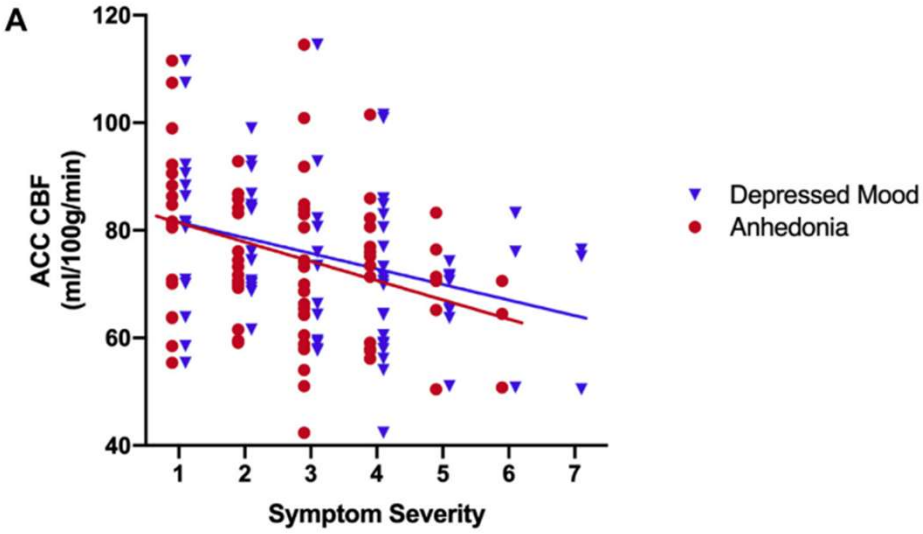
NEW RESEARCH

Check for updates

Cerebral Blood Flow and Core Mood Symptoms in Youth Bipolar Disorder: Evidence for Region–Symptom Specificity

Mikaela K. Dimick, BA, Simina Toma, MD, MSc, Bradley J. MacIntosh, PhD, Anahit Grigorian, MSc, Lisa Fiksenbaum, PhD, Eric A. Youngstrom, PhD, Andrew D. Robertson, PhD, Benjamin I. Goldstein, MD, PhD, FRCP(C)

FIGURE 1 Anterior Cingulate Cortex Cerebral Blood Flow and Depression Symptoms

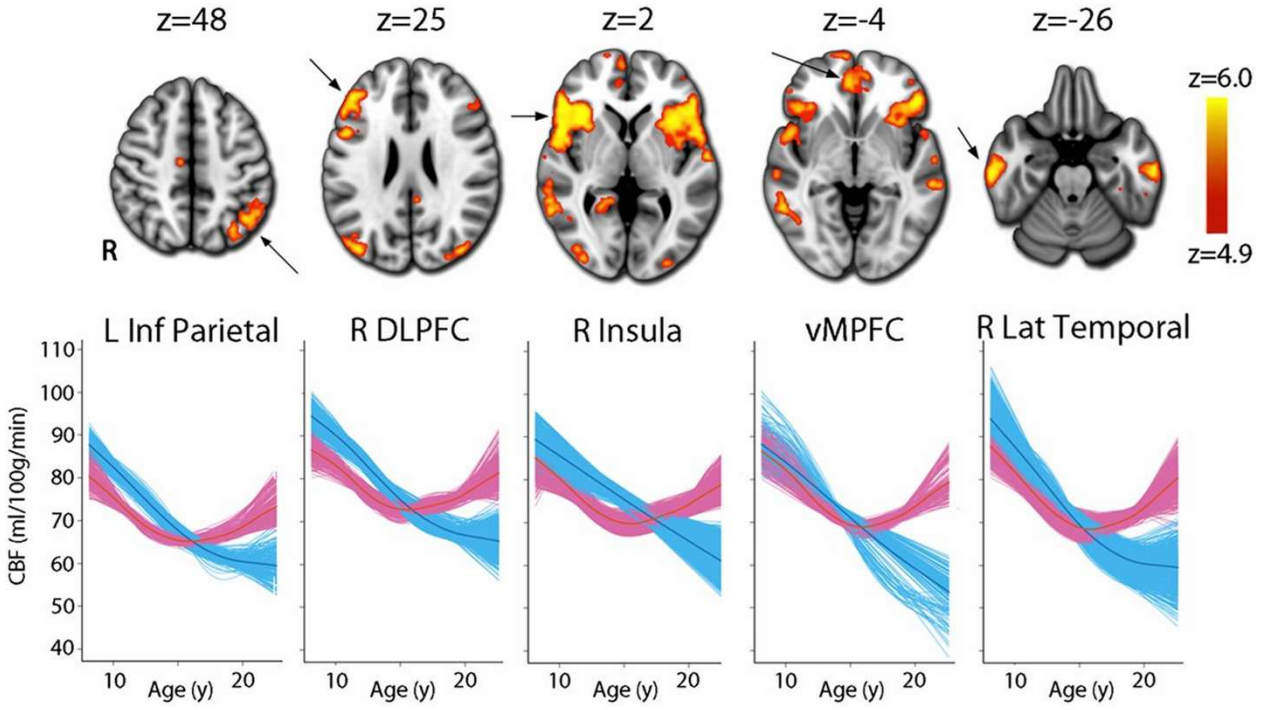


DOI: 10.1016/j.jaac.2022.04.010

2. ASL helps delineating sex-specific growth curves for CBF during youth

Impact of puberty on the evolution of cerebral perfusion during adolescence

Theodore D. Satterthwaite[a,b,1], Russell T. Shinohara[b,c], Daniel H. Wolf[a,b], Ryan D. Hopson[a], Mark A. Elliott[b,d], Simon N. Vandekar[a], Kosha Ruparel[a], Monica E. Calkins[a], David R. Roalf[a], Efstathios D. Gennatas[a], Chad Jackson[a], Guray Erus[b], Karthik Prabhakaran[a], Christos Davatzikos[b], John A. Detre[e], Hakon Hakonarson[f], Ruben C. Gur[a,b,g], and Raquel E. Gur[a,b]



Red-yellow masks indicated brain region showing significant sex difference on the CBF trajectory.

The developmental pattern of CBF change differed significantly between males (blue) and females (pink) in multiple regions within heteromodal association cortex

https://www.pnas.org/doi/full/10.1073/pnas.1400178111

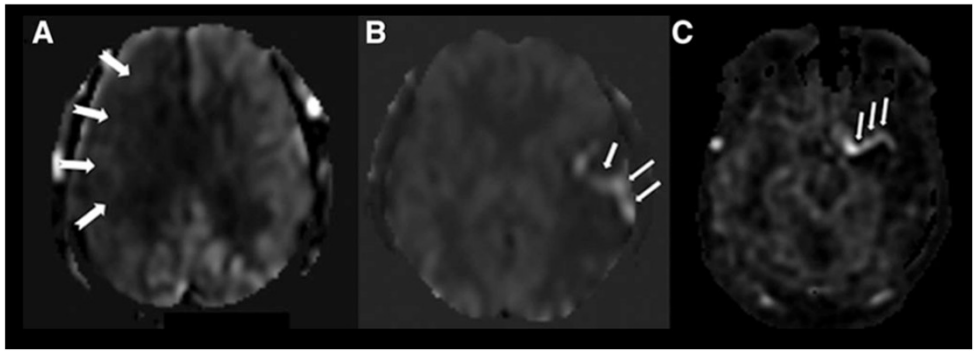
3. ASL studies in advancing stroke and cerebrovascular assessments

RESEARCH ARTICLE | Originally Published 13 November 2019 | Check for updates

Regional Arterial Spin Labeling Perfusion Defect Is Associated With Early Ischemic Recurrence in Patients With a Transient Ischemic Attack

Ki-Woong Nam, MD, MSc, Chi Kyung Kim, MD, PhD, Sang-Bae Ko, MD, PhD, Byung-Woo Yoon, MD, PhD, Roh-Eul Yoo, MD, and Chul-Ho Sohn, MD, PhD | AUTHOR INFO & AFFILIATIONS

Stroke • Volume 51, Number 1 • https://doi.org/10.1161/STROKEAHA.119.026556



Among the patients had transient ischemic attack, ASL predicts ischemic lesion recurrence: A. Decreased CBF, B. Increased ATT, C. Abnormal intra-arterial high-intensity signal

https://doi.org/10.1161/STROKEAHA.119.026556

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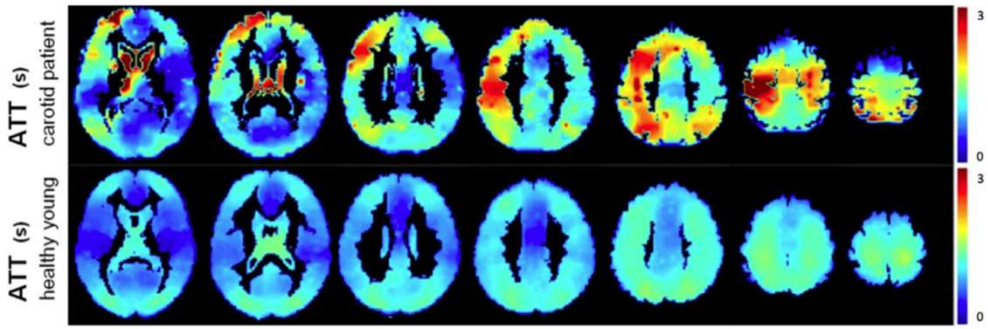
Recommendations for quantitative cerebral perfusion MRI using multi-timepoint arterial spin labeling: Acquisition, quantification, and clinical applications



ATT in patients with carotid artery occlusion was significantly higher (~1s longer) than the ATT in healthy controls.

https://doi.org/10.1002/mrm.30091

4. ASL helps reveal altered CBF in presymptomatic C9orf72, GRN or MAPT mutation carriers who had high risks of frontotemporal dementia

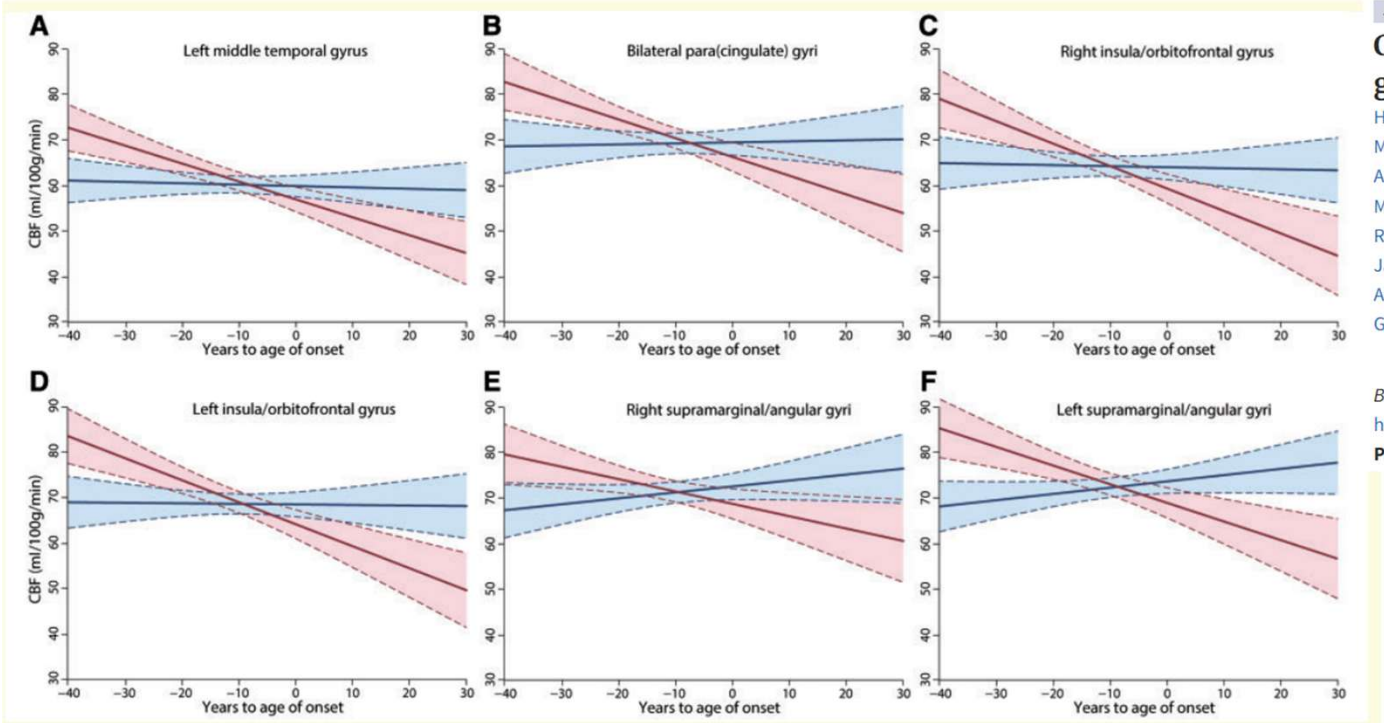


Figure 2 Linear mixed effects model regression lines for each of the six regions of interest plotting cerebral blood flow based on years to age of expected symptom onset in presymptomatic mutation carriers (red) and non-carriers (blue). Shaded areas represent the 95% confidence intervals.

JOURNAL ARTICLE

Cerebral perfusion changes in presymptomatic genetic frontotemporal dementia: a GENFI study

Henri J M M Mutsaerts , Saira S Mirza , Jan Petr , David L Thomas , David M Cash , Martina Bocchetta , Enrico de Vita , Arron W S Metcalfe , Zahra Shirzadi , Andrew D Robertson , Maria Carmela Tartaglia , Sara B Mitchell , Sandra E Black , Morris Freedman , David Tang-Wai , Ron Keren , Ekaterina Rogaeva , John van Swieten , Robert Laforce, Jr , Fabrizio Tagliavini , Barbara Borroni , Daniela Galimberti , James B Rowe , Caroline Graff , Giovanni B Frisoni , Elizabeth Finger , Sandro Sorbi , Alexandre de Mendonça , Jonathan D Rohrer , Bradley J MacIntosh , Mario Masellis ✉ , GENetic Frontotemporal dementia Initiative (GENFI)
Author Notes

Brain, Volume 142, Issue 4, April 2019, Pages 1108–1120,
https://doi.org/10.1093/brain/awz039
Published: 07 March 2019 **Article history ▾**

ASL may be a promising non-invasive imaging biomarker for the presymptomatic stages of genetic frontotemporal dementia.

https://doi.org/10.1093/brain/awz039

Summary of the ASL lectures

√ **ASL has been around for over two-decades and is still going strong:**

Perfusion-weighted imaging > pcASL > Multiple PLD pcASL > Velocity/Vessel-selective ASL > 7T ASL >…?

√ **Non-invasive and quantitative, but unique ASL-CBF contrast:**

Calibration using PDw images > Kinetic Modeling > Multiple PLD estimation of ATT > …?

√ **There are several ASL image analysis software options, but we are biased to using tools from the FMRIB Software Library**

BASIL, ASLPrep, > Software for Multiple PLD ASL, velocity-, and vessel-selective ASL analysis, > …?

√ **Showcase diverse applications of the ASL researches across the lifespan and diseases.**

Growth trajectory, aging trajectory, mood disorders, neurodegeneratives, stroke cares, > …?

Recommended readings and extensions

1. Alsop DC, Detre JA, Golay X, 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(1):102-116. doi:10.1002/mrm.25197

2. Woods JG, Achten E, Asllani I, et al. Recommendations for quantitative cerebral perfusion MRI using multi-timepoint arterial spin labeling: Acquisition, quantification, and clinical applications. Magn Reson Med. 2024;92(2):469-495. doi:10.1002/mrm.30091

Freely available datasource

- Human Connectome Project,
- OpenNeuro.org,
- Oxford Neuroimaging Primer dataset.
- OXASL - ASL-MRI analysis pipeline — oxasl 0.0.1 documentation

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