Arterial Spin Labeling (ASL) perfusion MRI

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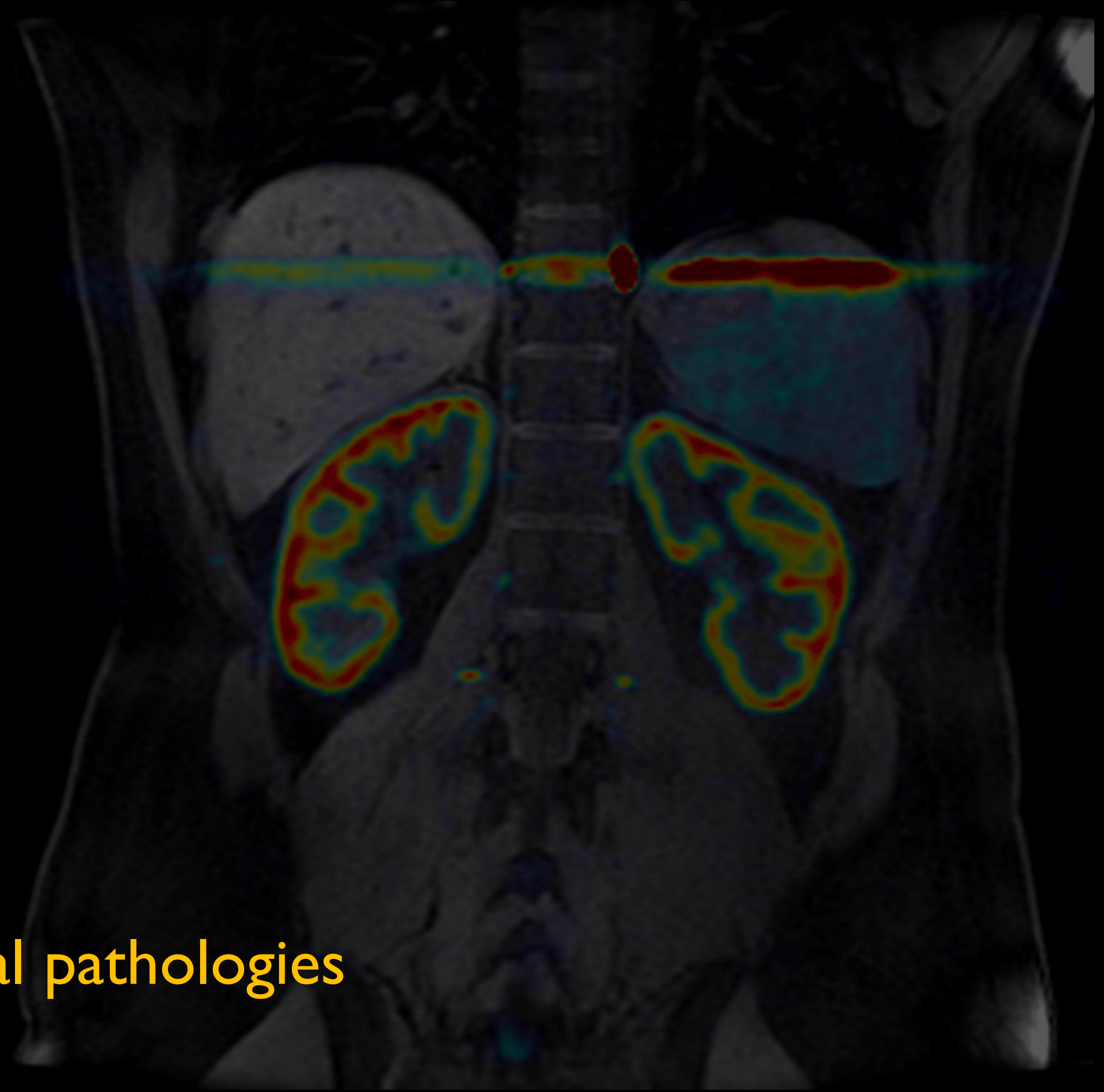
Nottingham, UK

Outline



Background

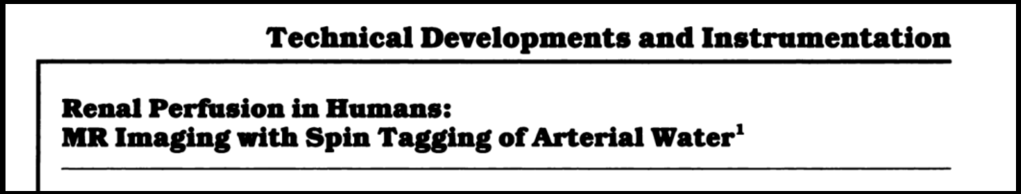
Arterial Spin Labeling

- Basics of ASL
- Labeling methods
- ASL quantification
- Background suppression?
- Motion management
- Imaging readouts

Applications of perfusion MRI in renal pathologies

Perfusion and Arterial Spin Labeling (ASL)

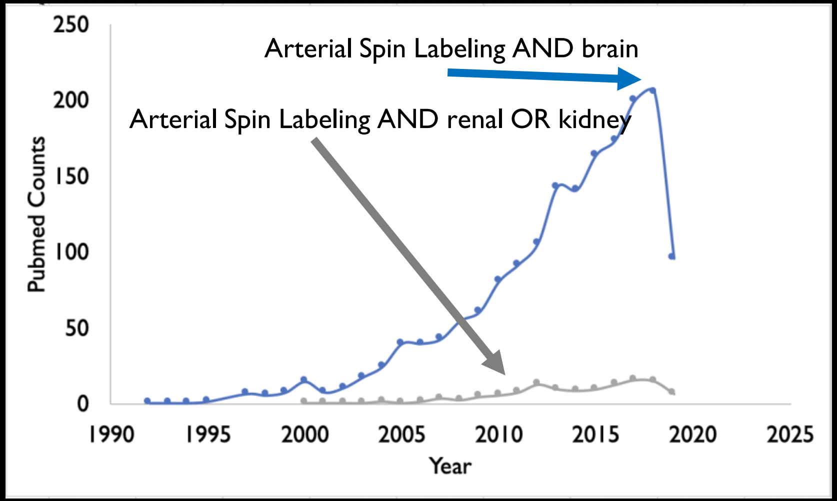
- Perfusion is an extremely relevant physiological parameter
- Usually measured with contrast agents (I for CT, Gd for MRI, $^{15}O\text{-}H_2O$ for PET) and/or ionizing radiation
    - Repeatability?
    - Counter-indicated in patients with renal failure, pregnancy …
    - Mix between perfusion and vessel permeability
- Is there a totally non-invasive alternative?


Technical Developments and Instrumentation

Renal Perfusion in Humans:
MR Imaging with Spin Tagging of Arterial Water[1]

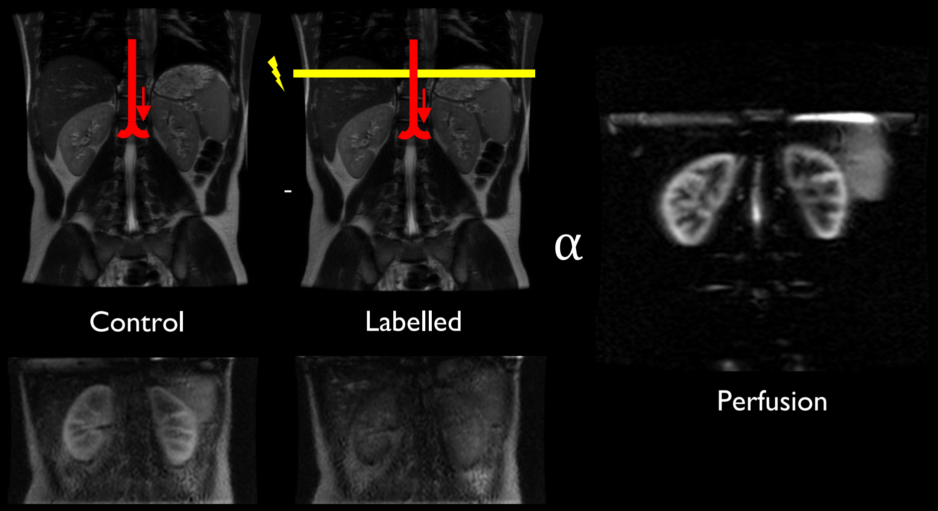
Arterial Spin Labeling (ASL)

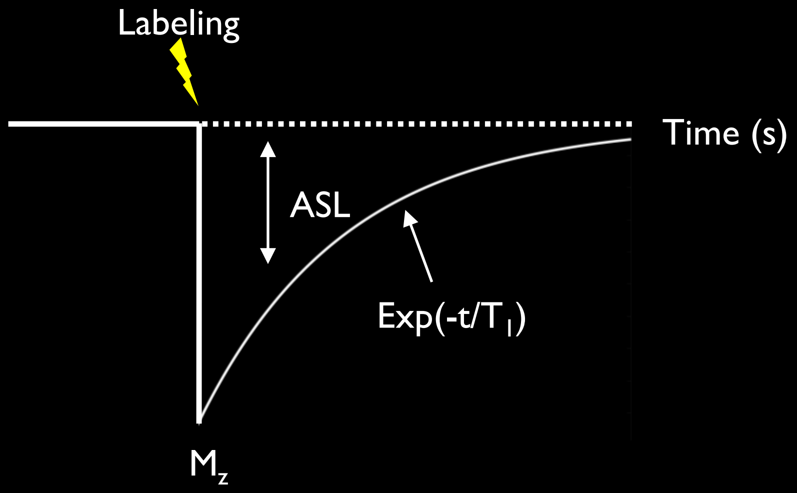
- Originally proposed in 1992 (Williams, Detre et al., PNAS)
- 1^{st} renal report in 1995
- Renal applications have seen a slow development compared to brain
- But the past few years have seen increase in interest and developments for renal perfusion imaging with ASL



Basics of ASL

- Basic idea is to use arterial blood water as an endogenous tracer (compared to exogenous contrast agents)
  - High permeability / freely diffusible
  - Widely available
- ASL uses radiofrequency (RF) pulses to modify the longitudinal magnetization of arterial blood
- Typical ASL experiment
  1. Apply RF
  2. Wait for delivery and exchange of the labeled bolus to the tissue of interest
  3. Image (labeled image)
  4. Repeat 1-3 without modifying arterial blood magnetization (control image)
  5. Subtract the label from the control $dM = M_{control} - M_{label}$
- The label decays with the longitudinal relaxation time T_1
- Two main "families" of labeling methods
  - Labeling using RF spatial selectivity
  - Labeling using velocity selectivity

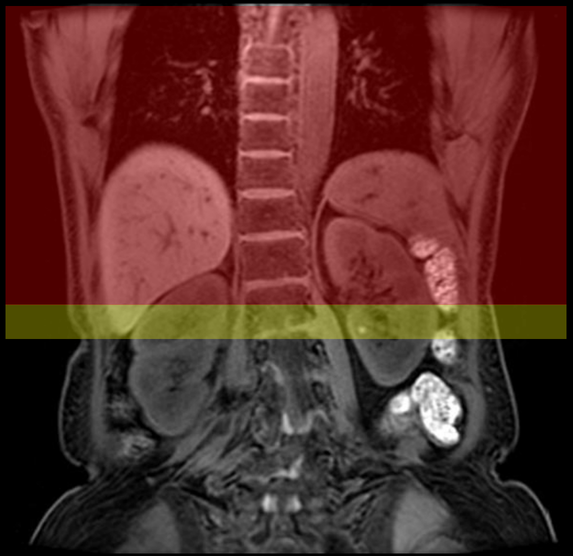




Flow-Sensitive Alternating Inversion Recovery (FAIR)

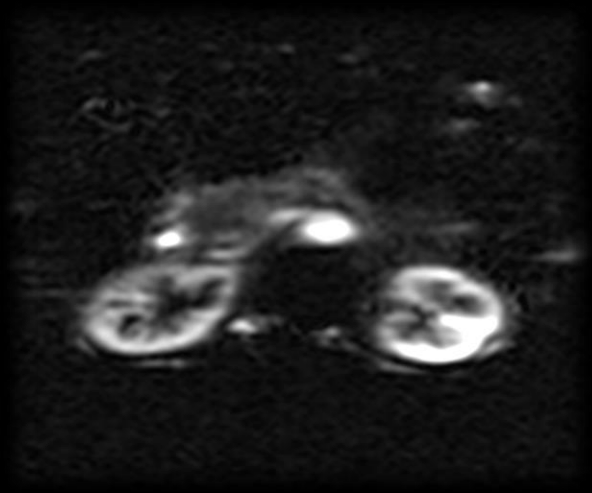
Kwong et al., MRM 1995 ; Kim., MRM 1995 ;Wong et al., MRM 1998

- Uses a selective / global inversion
- Usually using adiabatic RF pulses for robust inversion (Hyperbolic-Secant, FOCI)

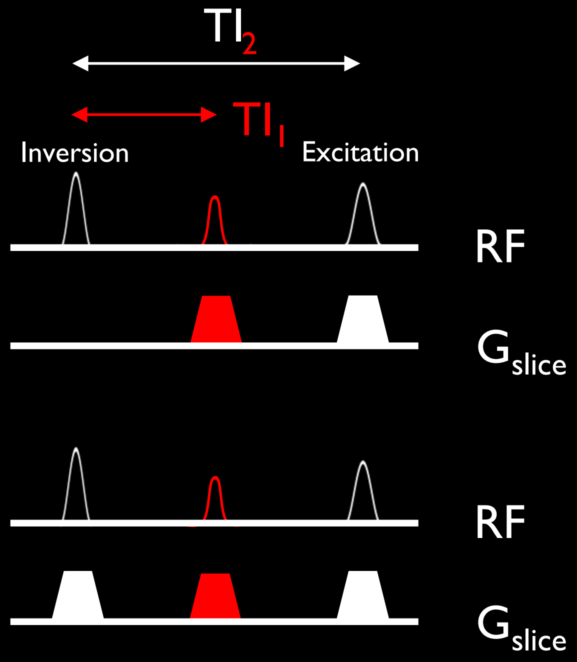


Selective (control) inversion

Global (label) inversion



Perfusion-weighted



- One of the most popular pulsed labeling methods
- Easy to implement, low SAR, high labeling efficiency (>0.95), no MT effects
- Usually, saturation pulses are added to better define the bolus for quantification (Q2TIPS, QUIPSS II)

(Pseudo)-Continuous Arterial Spin Labeling

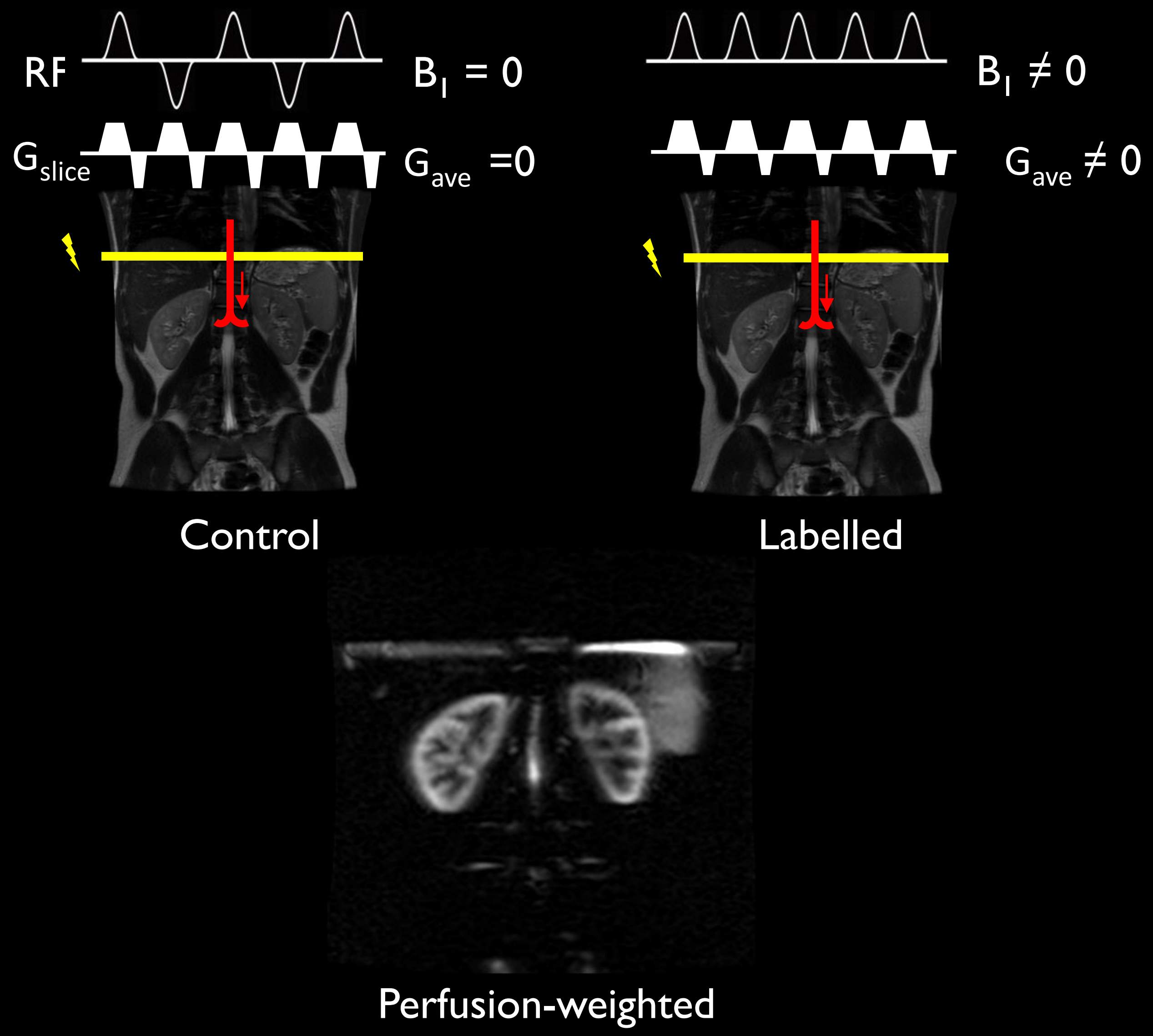
Williams et al., PNAS 1992 ; Detre et al., MRM 1992 ; Alsop and Detre, Radiology, 1996 ; Dai et al., MRM 2008

- Original ASL implementation (Williams et al, Detre et al, 1992): continuous RF for flow-driven adiabatic inversion *(Dixon et al., MRM 1986)*

- CASL → PCASL by using short, repeated RF pulses and gradients to achieve higher efficiency and lower hardware demands

- PCASL is the most popular and recommended ASL implementation for brain applications *(Alsop et al., MRM, 2015)*

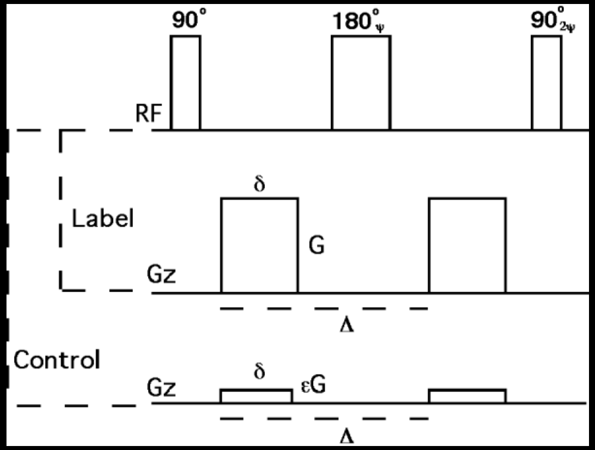
- Requires optimization of labeling parameters (B_1, G_{max}, G_{av}, G_{max}/G_{av}) depending on the typical flow velocity profiles and expected B_0 variations *(Zhao et al., MRM 2016 ; Echeverria-Chasco et al., ISMRM 2019 #4954)*



Velocity-selective Arterial Spin Labeling

Wong et al., MRM 2006

- Uses velocity-selectivity to achieve spin labeling
- Based on the use of flow-sensitizing gradients (e.g. Stejskal-Tanner diffusion gradients)
  - The dephasing/rephasing gradients will attenuate moving spins while static spins will mostly remained untouched



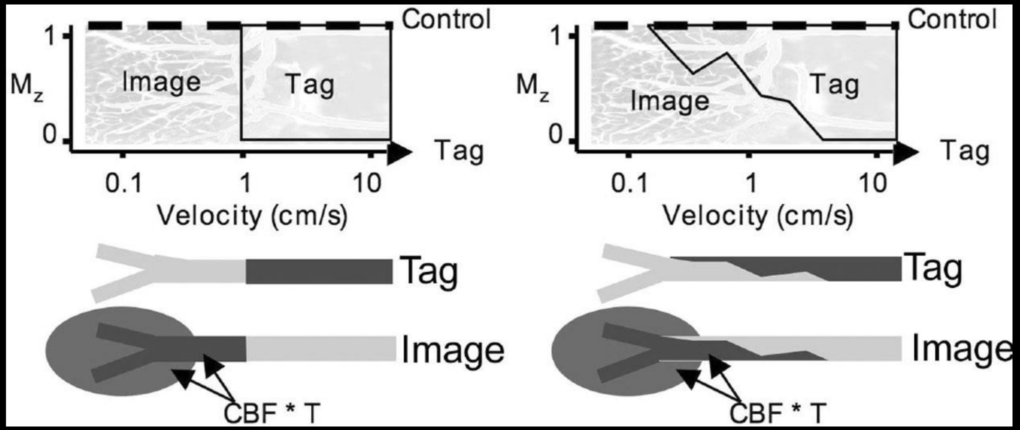
Duhamel et al., MRM 2003

- The gradient parameters (amplitude, duration and spacing) determines the cutoff velocity and directionality …
- …But also a diffusion-weighting

- **Transit-time insensitive**
- **Labeling closer to the tissue of interest**

- Very few renal applications so far

Bones et al., ISMRM 2019 #4948



Wong et al., MRM 2006

Summary of labeling methods

Spatially-selective ASL

Pulsed ASL (e.g. FAIR)

- Single inversion of a large volume
- Various "geometrical" implementations

✓ High-efficiency (>0.95)
✓ Low SAR
✓ Easy implementation

✗ Unknown bolus duration
✗ Lower theoretical SNR
✗ Requires careful planning

(Pseudo)-Continuous ASL

- Long train of RF pulses to achieve labeling of flowing spins
- Uses shaped RF + gradient to define a labeling plane

✓ Higher theoretical SNR
✓ Defined bolus
✓ Compatible with volumetric imaging

✗ High(er) SAR
✗ Lower labeling efficiency (≈0.8)
✗ Velocity and B_0 dependence

➔ Most used methods in renal ASL

Velocity-selective ASL

- Uses velocity to selectively label flowing blood
- Achieved with the use of dephasing gradients that define a velocity cutoff

✓ Transit-time independence
✓ No concern about labeling position
✓ Allows labeling very close to the tissue

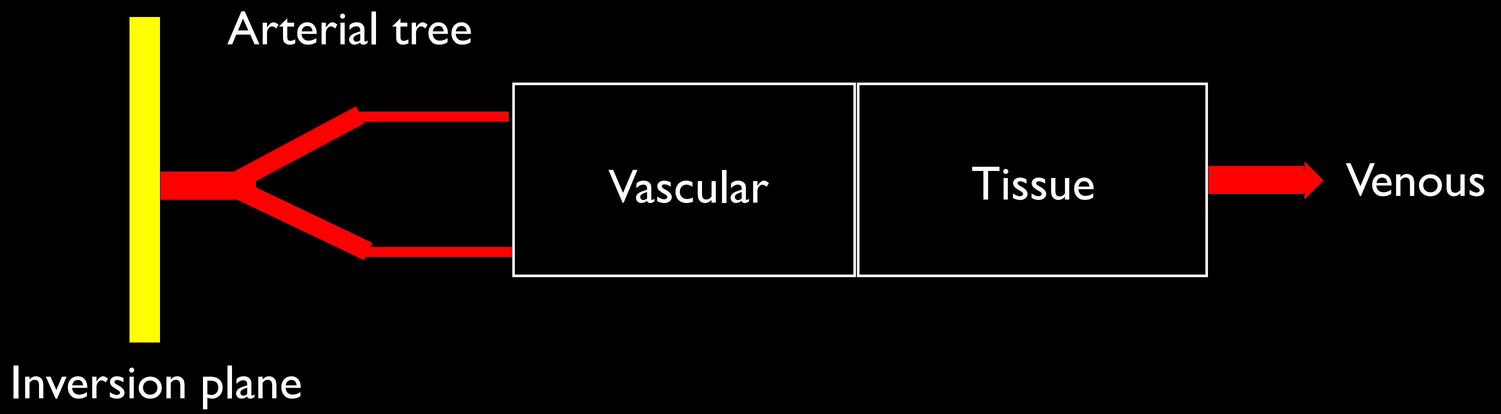
✗ B_0 / B_1 sensitive
✗ ½ SNR (saturation based technique)
✗ No perfect cutoff
✗ Additional diffusion-weighting

Still in development phases

Blood-flow quantification from ASL

Alsop and Detre, JCBFM 1996 ; Buxton et al., MRM 1998 ; Parkes et al., JMRI 2005

- Strength of ASL: capabilities for absolute quantification (in physiological units of mL/100g/min)
- Several levels of model complexity, all based on modification of the Bloch equations to include the effect of labeling and flow



- Simplest model ➔ One compartment model

→ No separation between vascular and tissue compartments
→ Requires PLD > ATT to be valid
→ Considers $T_{1,blood}=T_{1,tissue}$

  - More robust (does not require additional measurements) but less accurate

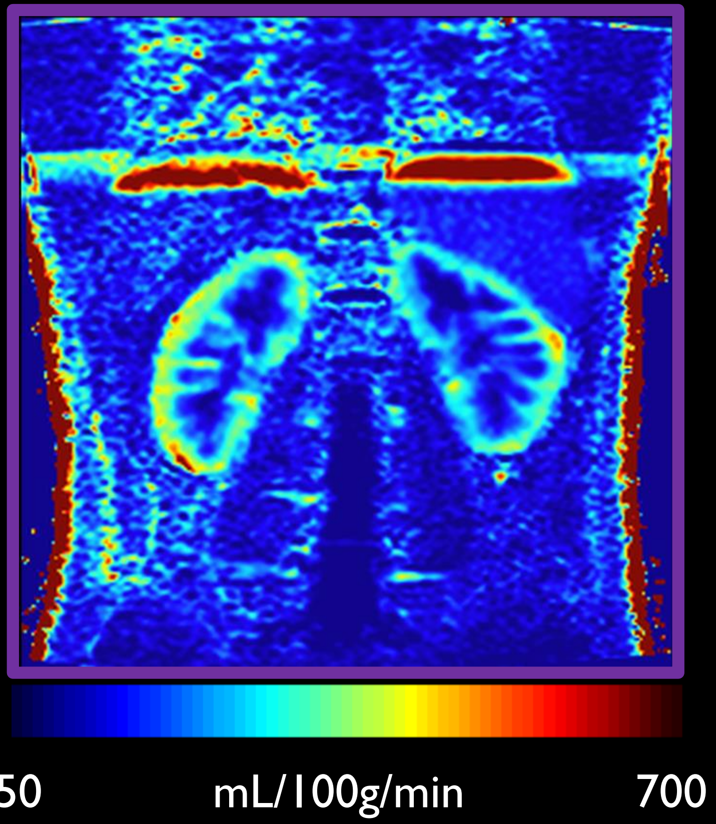
- Alternative ➔ Two-compartment model

→ Considers the difference of T_1 between blood and tissue
→ Also considers the effect of arterial transit-time (ATT)

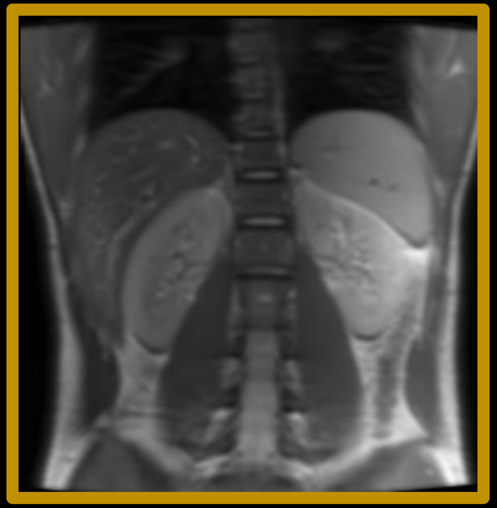
  - More accurate in specific cases (e.g. renal fibrosis affecting tissue T_1 ; prolonged ATT) but requires more measurements

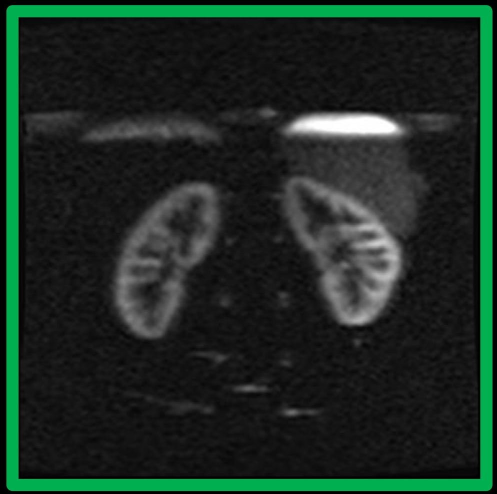
Blood-flow quantification from ASL – single compartment model

$$RBF = \frac{6000.\lambda.(M_{control} - M_{label}).\exp(\frac{PLD}{T_{1,b}})}{2.\alpha.T_{1,b}.M_0.(1-\exp(-\frac{\tau}{T_{1,b}}))}$$



- RBF = renal blood-flow (in mL/100g/min)
- λ = Blood-tissue partition coefficient (0.9)
- α = ASL Labeling efficiency (0.6 – 0.8)
- M_0 = fully-relaxed magnetization
- τ = Labeling duration (usually 1-2s)
- PLD = post-labeling delay (1-2s)
- $T_{1,b}$ = longitudinal relaxation time of blood (≈1.3s at 1.5T, 1.6s at 3T)





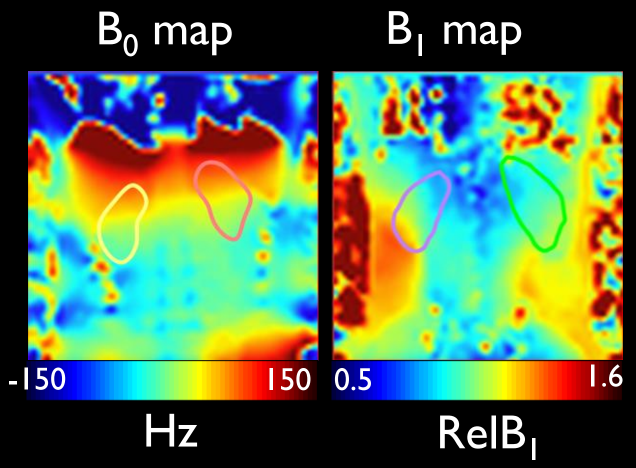
Specific challenges pertaining to renal imaging

• Respiratory motion

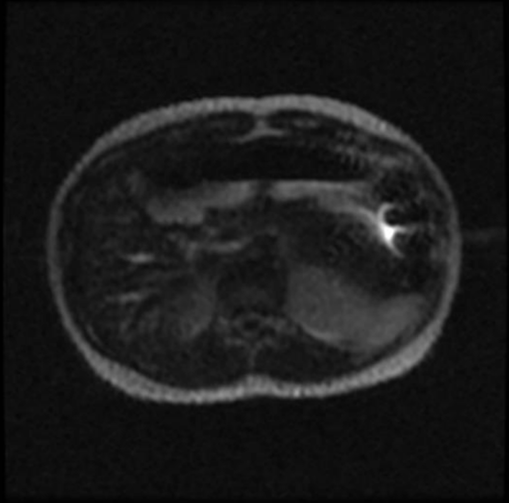
- S/I kidney motion of a few cms during breathing
- Creates errors when subtracting control/label

• Off-resonance/B_1 effects

- Dielectric (B_1) and field inhomogeneities (B_0) are more important in the abdomen
- Impacts labeling efficiency + imaging quality



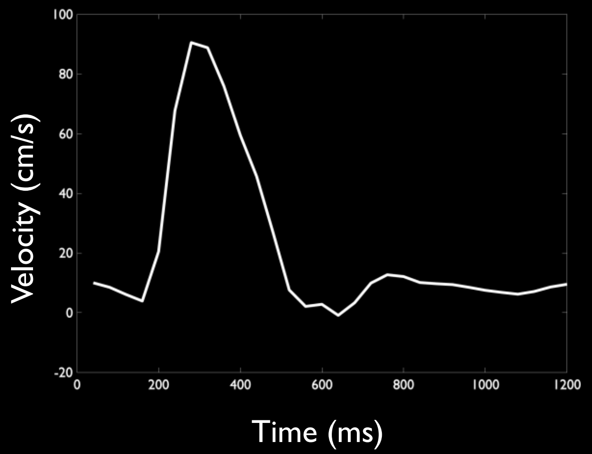
• Physiological motion



- Peristalsis
- Cardiac-related noise
- Food/fluids moving through the GI tract

• Highly pulsatile flow

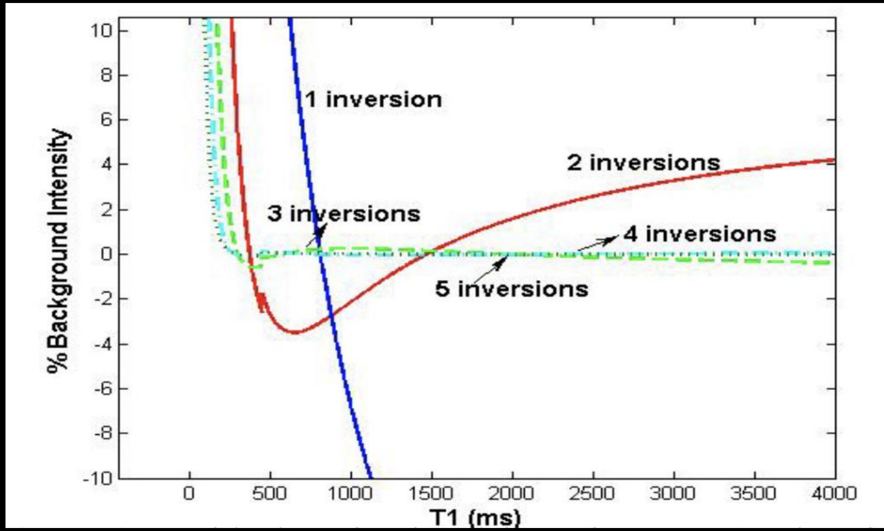
- The abdominal aorta has a strong pulsatile profile
- Affects labeling efficiency (especially in PCASL)

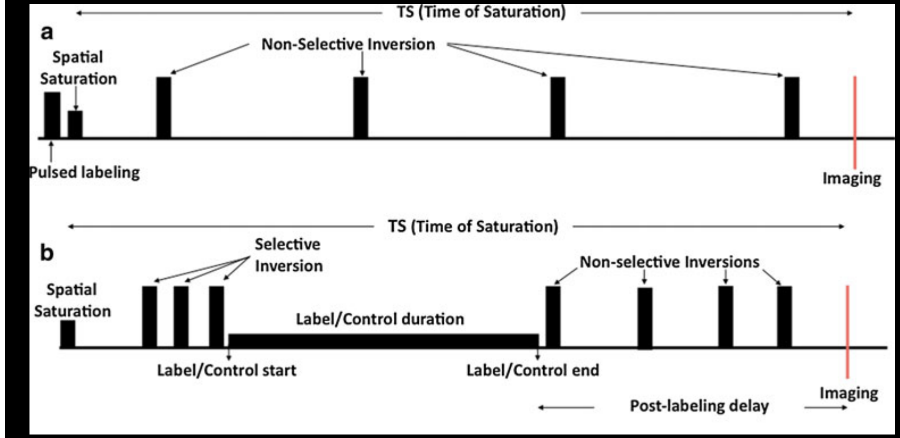


Reduction of motion-sensitivity with background suppression

- ASL signal ≈ 1-2% of relaxed magnetization
- Sensitive to physiological fluctuations as well as patient motion
- The use of multiple inversions can reduce static tissue signal by 100-fold for a wide range of T_1

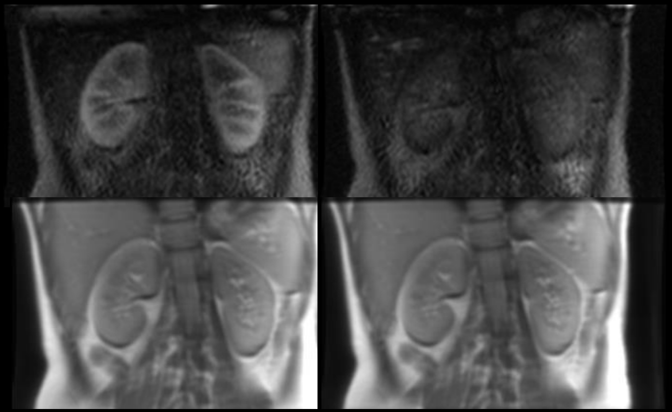
Mani et al., MRM 1997
Ye et al., MRM 2000





Maleki et al., MAGMA, 2012

Background suppressed



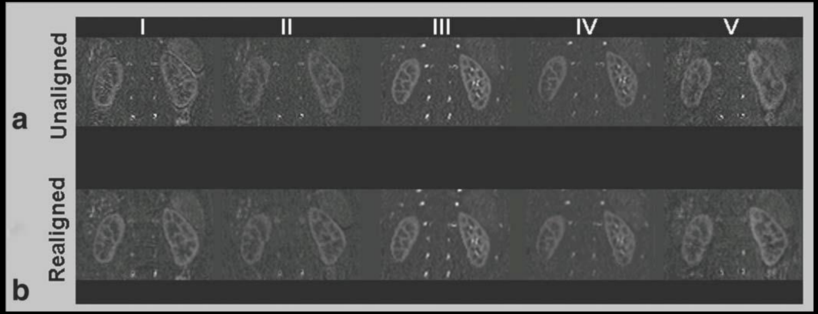
Unsuppressed

- Reduction of global labeling efficiency due to imperfect inversions (≈5% / inversion) *Garcia et al., MRM, 2005*
- Requires careful optimization of timings

Motion management in abdominal (renal) ASL

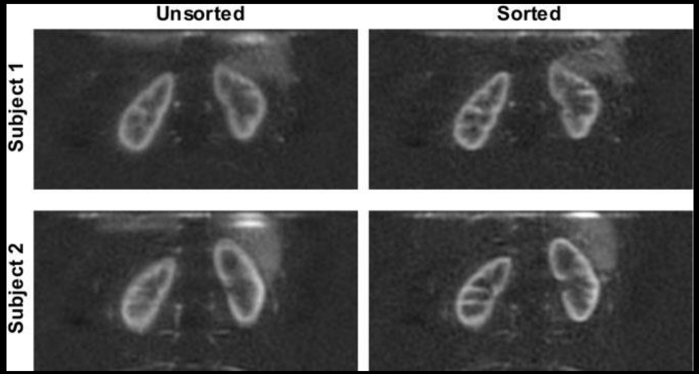
The long ASL preparation makes usual triggering strategies difficult

- Retrospective motion-correction
  - Rigid realignment
  - Works w/ 2D and 3D data



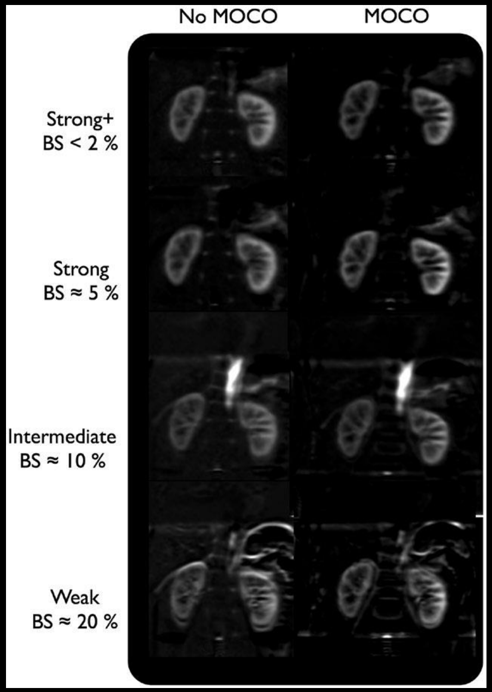
Gardener and Francis, MRM 2010
Nery et al., MRM 2019

- BS + Data sorting
  - Discarding based on respiratory sensors (bellows)



Robson et al., MRM 2009

- BS + Motion-correction
  - Non-rigid realignment
  - Heavy BS (<2% static tissue)

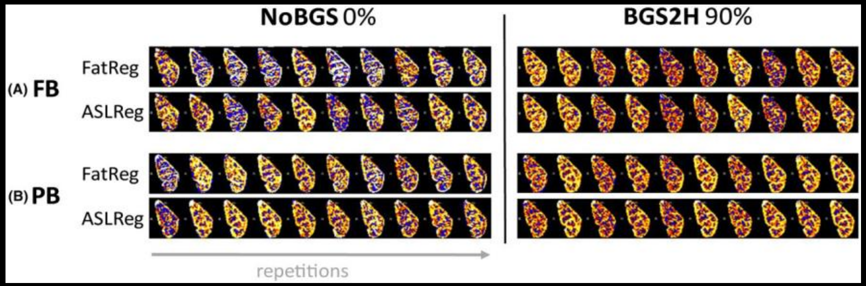


Taso et al., MRM 2019

- Echo-navigators
  - 2D low-resolution navigator + bSSFP

Tan et al., MRM 2014

- BS + Fat navigators + MC



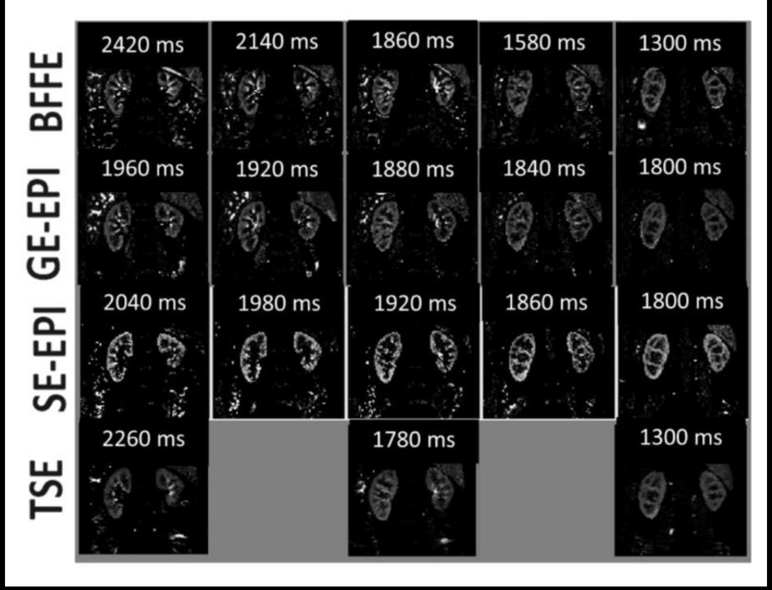
Bones et al., MRM 2019

Imaging sequences for renal ASL

(More or less) any sequence can be prepared with ASL

What are the pre-requisites for a good imaging module for (renal) ASL?

- High SNR / tSNR
- Robust to field inhomogeneities
- Fast → Multi-slice capabilities?
- Stability




diagnostics

MDPI

Article

Evaluation of 2D Imaging Schemes for Pulsed Arterial Spin Labeling of the Human Kidney Cortex

Charlotte E. Buchanan, Eleanor F. Cox and Susan T. Francis *

Candidates for 2D imaging?

- Echo-Planar Imaging (EPI)
- Balanced SSFP
- Single-shot FSE/TSE (HASTE, SSFSE)

How about volumetric encoding?

- GRASE *(Nery et al., MRM 2019; Cai et al., JMRI 2017)*
- Segmented RARE/FSE *(Robson et al., Acad Radiol 2016 ;Taso et al., MRM 2019)*

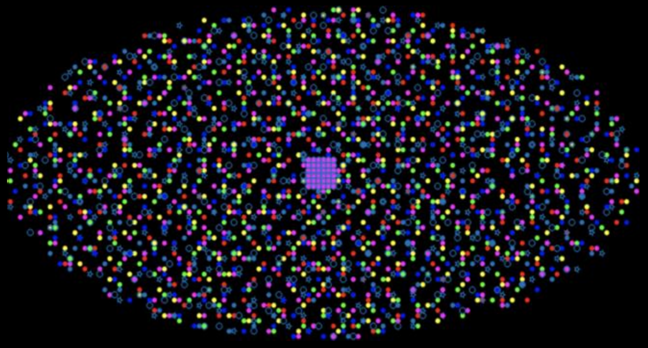
Towards 3D renal perfusion measurement with ASL

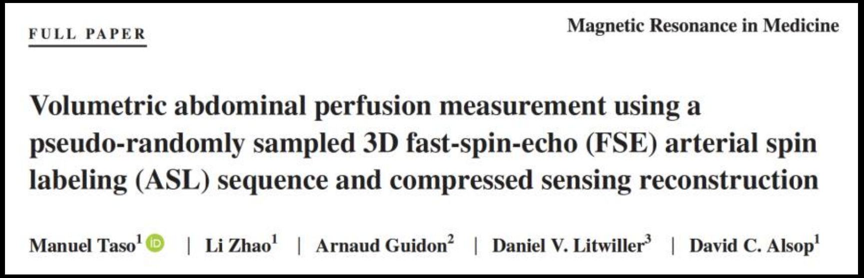
- Segmented FSE with sparse pseudo-random sampling (VD-Poisson disk)
- Compressed-Sensing reconstruction

k-space sampling operator, Reconstructed image, Regularization term

$$m(x,y,z,t) = argmin\|DFSm - y\|_2^2 + \lambda_1\|\Psi m(x,y,z)\|_1 + \lambda_2\|\mathrm{TV}m(t)\|_1$$

Fourier transform operator, ESPIRiT maps, Acquired data, Spatial wavelet transform operator, Temporal TV transform operator




FULL PAPER

Magnetic Resonance in Medicine

Volumetric abdominal perfusion measurement using a pseudo-randomly sampled 3D fast-spin-echo (FSE) arterial spin labeling (ASL) sequence and compressed sensing reconstruction

Manuel Taso[1] | Li Zhao[1] | Arnaud Guidon[2] | Daniel V. Litwiller[3] | David C. Alsop[1]

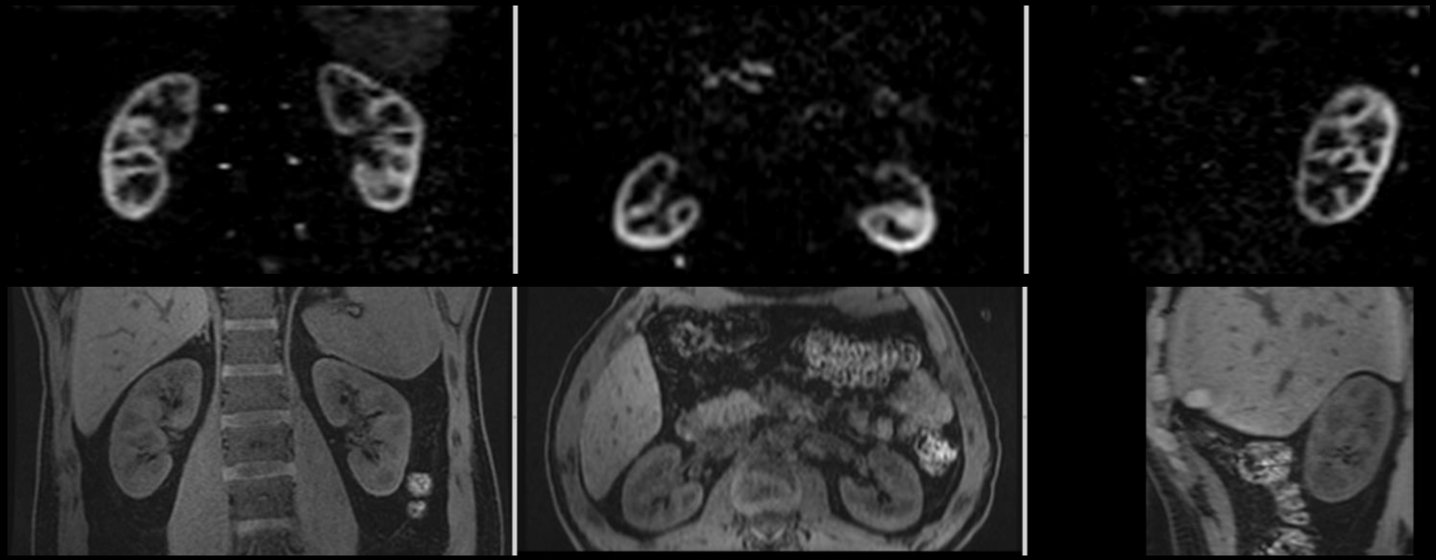
BART

➔ Power-pitch @ 5pm

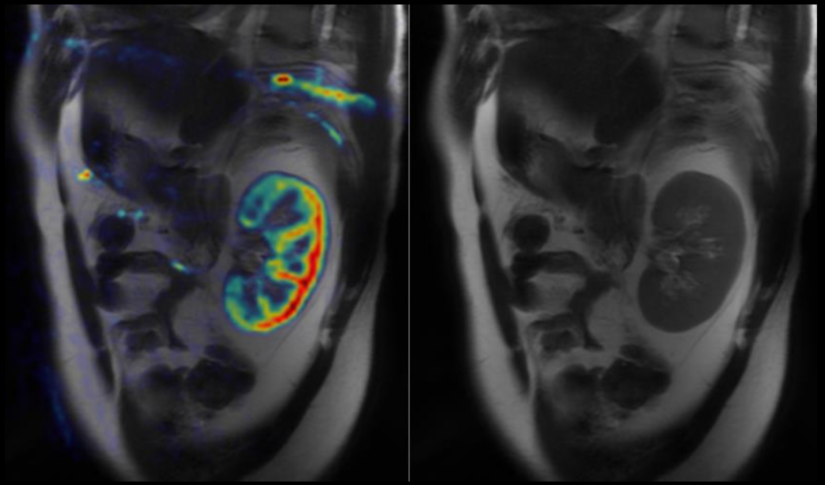
2.7mm isotropic ASL in ≈5 minutes

ASL

T_1-Dixon

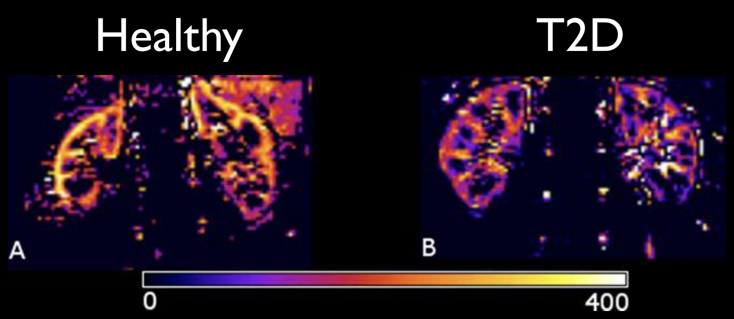


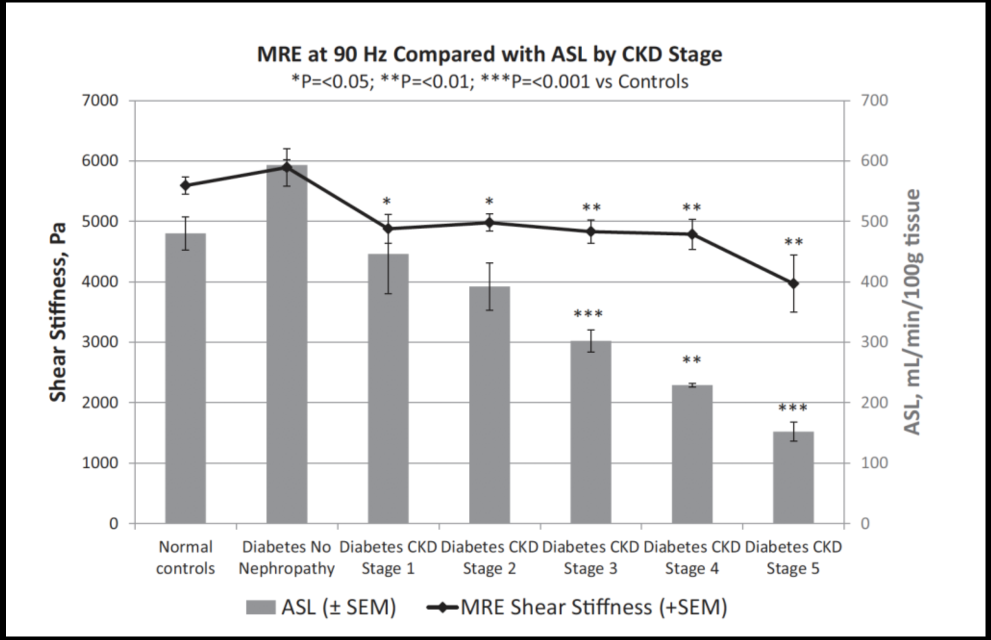
Long-axis reformat



Renal applications of ASL perfusion: CKD

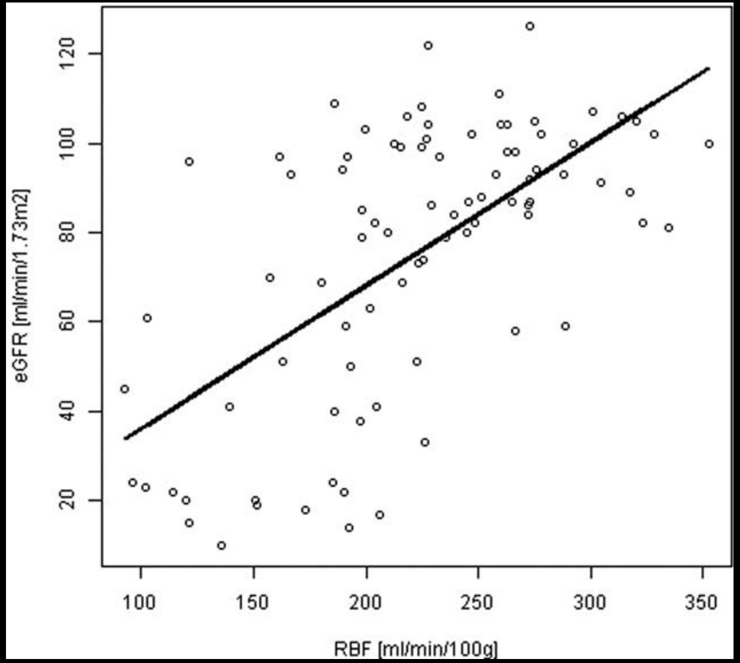
- Chronic Kidney Disease: progressive alteration of renal function
- One of the most important complications of type 2 diabetes
- Stage defined by the estimated Glomerular Filtration Rate (eGFR)





Brown et al., Nephrol Dial Transplant 2019

- eGFR is correlated to RBF
- Perfusion alteration increases with increased CKD severity
- Perfusion alteration is also encountered in diabetics w/o nephropathy (hyperfiltration)

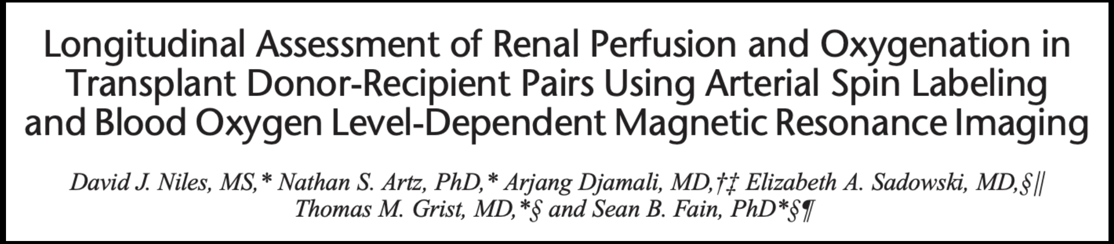


Mora-Gutiérrez et al., JMRI 2017

Renal applications of ASL perfusion: renal transplants

Several questions arise for renal transplantations

- What happens to the donor remaining kidney?
- How does the transplanted kidney behave?


Longitudinal Assessment of Renal Perfusion and Oxygenation in Transplant Donor-Recipient Pairs Using Arterial Spin Labeling and Blood Oxygen Level-Dependent Magnetic Resonance Imaging

David J. Niles, MS, Nathan S. Artz, PhD,* Arjang Djamali, MD,†‡ Elizabeth A. Sadowski, MD,§|| Thomas M. Grist, MD,*§ and Sean B. Fain, PhD*§¶*

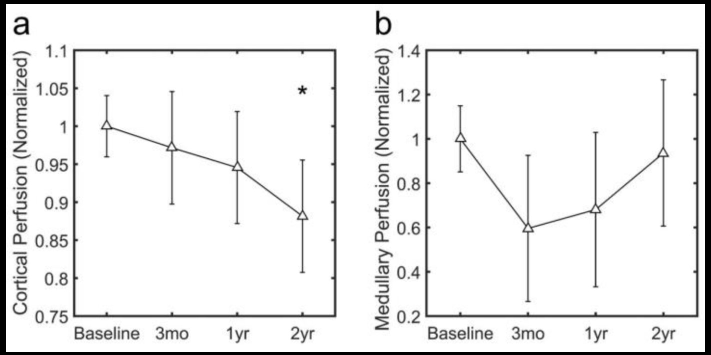
ASL-derived blood-flow was shown to be reduced in recipients with acute and chronic rejection *(Lanzman et al., Eur Radiol, 2010)*

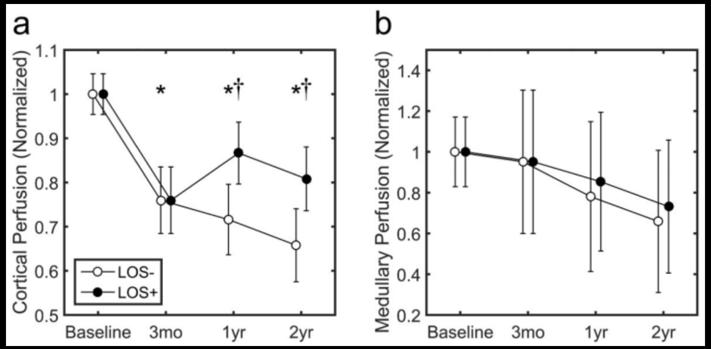
ASL can be used to monitor the evolution over time of both donor and recipient *(Niles et al., Invest Radiol 2016)*

→ ASL can be used to detect allograft dysfunction

→ Perspectives to study long-term outcomes of renal transplant

Donor



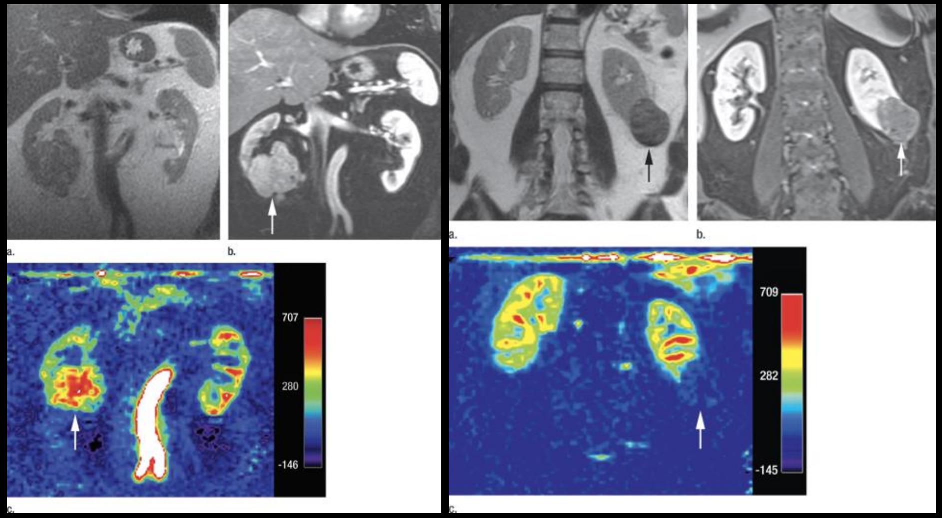


Transplant

Other renal applications of ASL perfusion

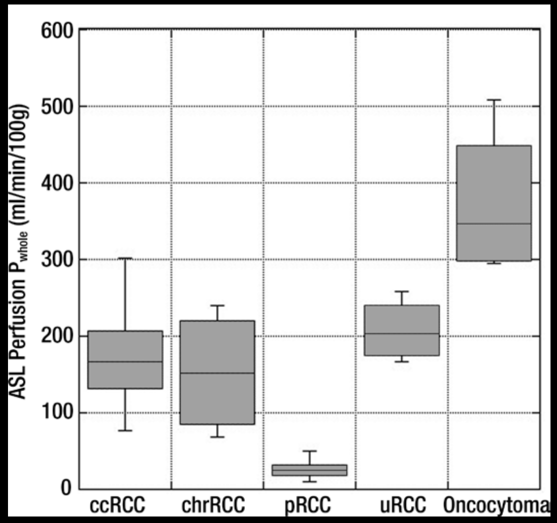
- Oncology (renal masses)
  - ASL can be performed in patients that can not receive Gd for DCE *(Pedrosa et al., Eur Radiol 2012)*
  - Different renal malignancies show different perfusion levels *(Lanzman et al., Radiology 2012)*
  - ASL is capable of detecting response to antiangiogenic therapy (*de Bazelaire et al., Clin Cancer Res 2008)*
- Inflammatory diseases
  - ASL has been successful in showing an increase in blood-flow related to inflammation in patients w/ lupus nephritis *(Rapacchi et al., MRI 2015)*

Lanzman et al., Radiology 2010

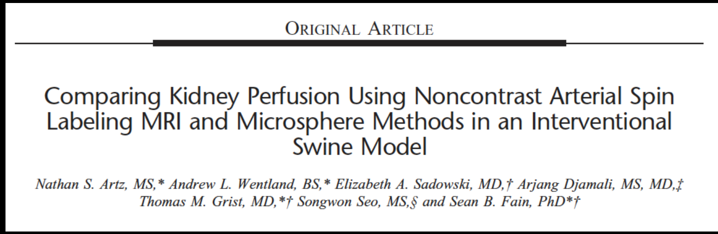


Oncocytoma

Papillary RCC

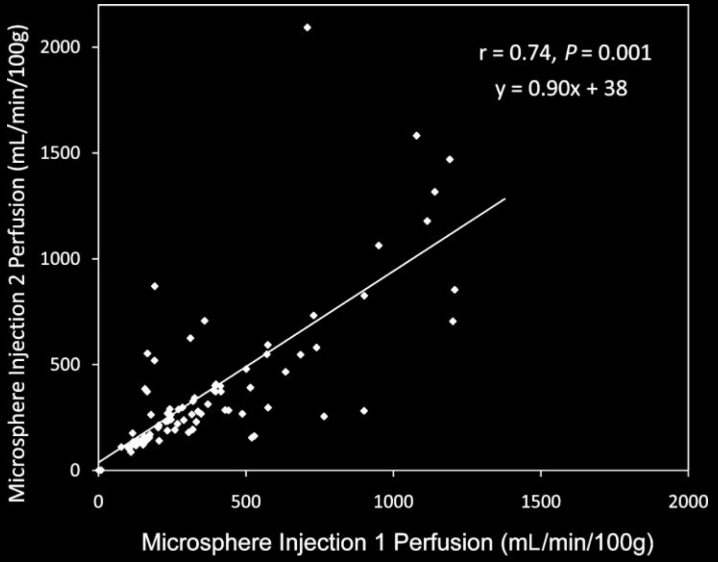


Renal applications of ASL perfusion: reproducibility and comparison against gold-standards

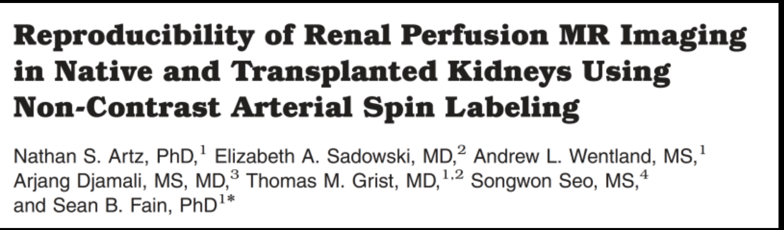

ORIGINAL ARTICLE

Comparing Kidney Perfusion Using Noncontrast Arterial Spin Labeling MRI and Microsphere Methods in an Interventional Swine Model

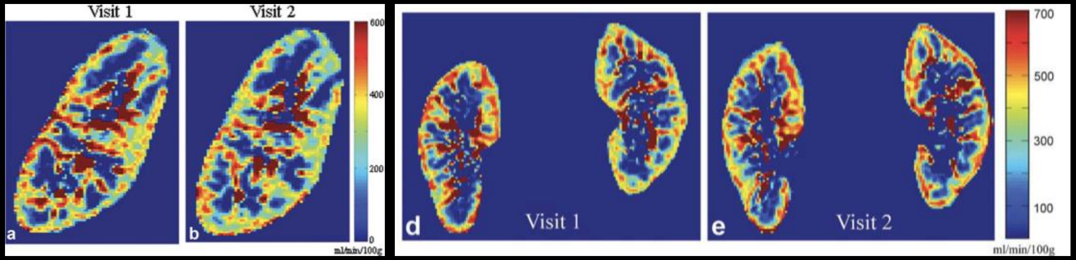
Nathan S. Artz, MS, Andrew L. Wentland, BS,* Elizabeth A. Sadowski, MD,† Arjang Djamali, MS, MD,‡ Thomas M. Grist, MD,*† Songwon Seo, MS,§ and Sean B. Fain, PhD*†*

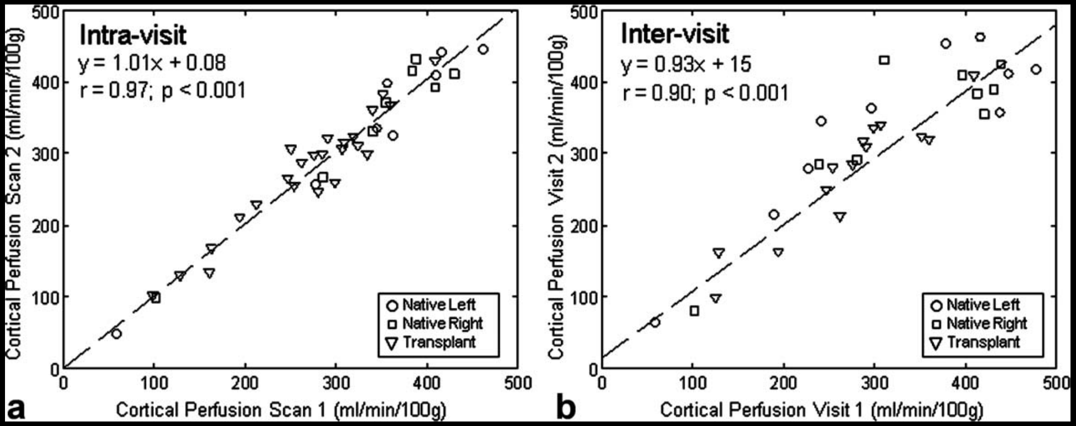


- Comparison of ASL (FAIR-bSSFP) with microspheres counting in a swine model
- Assessment of response to different challenges / anesthetic agents
- Good correlation between microspheres/ASL


Reproducibility of Renal Perfusion MR Imaging in Native and Transplanted Kidneys Using Non-Contrast Arterial Spin Labeling

Nathan S. Artz, PhD,[1] Elizabeth A. Sadowski, MD,[2] Andrew L. Wentland, MS,[1] Arjang Djamali, MS, MD,[3] Thomas M. Grist, MD,[1,2] Songwon Seo, MS,[4] and Sean B. Fain, PhD[1*]





- ASL measures reproducibly cortical BF in native and transplanted kidneys

Perspectives for renal ASL: towards technical consensus

- How to promote the use of ASL and make it easier for non-expert investigators?
- There is a wide-range of ASL techniques and parameters to optimize

  FAIR-QUIPSS II SE-EPI, PICORE Q2TIPS GRASE, Background-suppressed PCASL FSE ?
  PLD, TI_1, vascular crushers?
  Free, paced breathing, navigators, realignment?
  Single-compartment, $T_{1,b}$, two-compartments, labeling efficiency?

- A consensus approach by ASL technical experts has been proved successful in the brain

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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

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Table 1
Recommended Labeling Parameters

Parameter	Value
PCASL labeling duration	1800 ms
PCASL PLD: neonates	2000 ms
PCASL PLD: children	1500 ms
PCASL PLD: healthy subjects $<$70 y	1800 ms
PCASL PLD: healthy subjects $>$70 y	2000 ms
PCASL PLD: adult clinical patients	2000 ms
PCASL: average labeling gradient	1 mT/m
PCASL: slice-selective labeling gradient	10 mT/m
PCASL: average B_1	1.5 µT
PASL TI_1	800 ms
PASL TI	Use PCASL PLD (from above)
PASL labeling slab thickness	15–20 cm

Table 2
Recommended Imaging Parameters

Parameter	Value
Spatial resolution	3–4 mm in-plane, 4–8 mm through-plane
3D RARE stack of spiral or 3D GRASE	4–15 ms readouts, turbo-factor of 8–12, echo train of up to 300 ms
2D EPI or spiral	Single shot, minimum echo time
Scan time	4 min for acute cases, 2 min with lower spatial resolution
Field strength	Use 3T when available; for 1.5T, use lower spatial resolution
Vascular crushing gradients	Not recommended under most circumstances; when applicable, use VENC = 4 cm/s in the Z-direction

➔ Parenchima WG1 and panel led by María Fernández-Seara & Fábio Nery

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Take-home messages

- Arterial Spin Labeling is a non-invasive technique for measuring tissue perfusion
- It is fully quantitative, and reproducible at will due to the absence of contrast agent
- The past 10 years have seen a lot of developments to overcome challenges specific to renal imaging (motion, spatial coverage …)
- Clinical applications show great potential especially in CKD and renal transplantation
- There are strong efforts through international collaboration to establish ASL as a standard go-to technique

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