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PERFUSION IMAGING: Pitfalls and Clinical Applications update

J.A. Guzmán-De-Villoria

Hospital General Universitario Gregorio Marañón, Madrid, Spain

jguzman.hgugm@salud.madrid.org

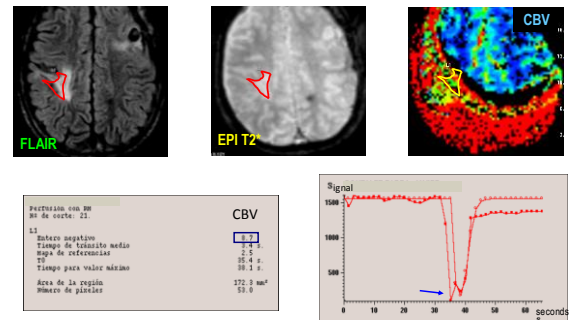
INTRODUCTION

- Perfusion MR techniques provides insights into dynamic processes not detectable during static conventional postGd sequences
- These additional data allow an adjunct knowledge of microvascular physiology of a wide variety of intracranial disease

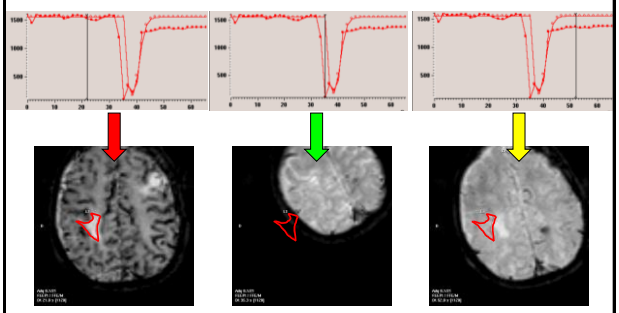
INTRODUCTION

- However, It is essential for a correct interpretation a prior knowledge of:
  - Technical issues related to MRI
    - Technique
    - Theorical model
    - Sequence
  - Sources of errors / Pitfalls
    - Leakage effects
    - Susceptibility artifacts
    - Movement artifacts

DYNAMIC SUSCEPTIBILITY-WEIGHTED MRI



ARTIFACT BY PATIENT MOVEMENT



MR Perfusion Techniques

- With exogenous contrast agent
  - T1-Weighted dynamic contrast-enhanced (DCE) MRI.
  - T2-Weighted dynamic susceptibility-weigthed contrast-enhnaced (DSC) MRI
- Without exogenous contrast agent
  - Arterial Spin Labeling (ASL)
  - Blood Oxigen Level Dependent (BOLD)
  - Intravoxel Incoherent Motion MRI (IVIM)

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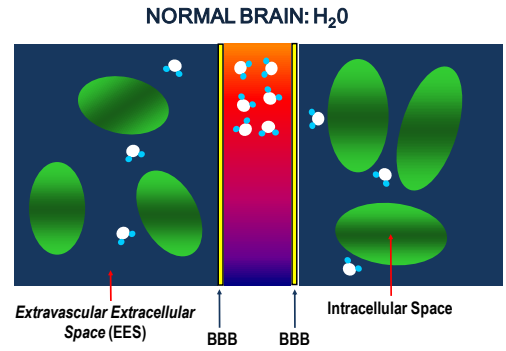
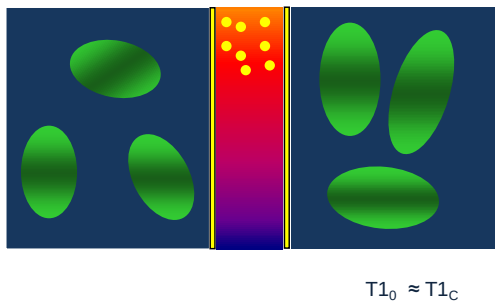
DCE MRI: Pharmacokinetic model

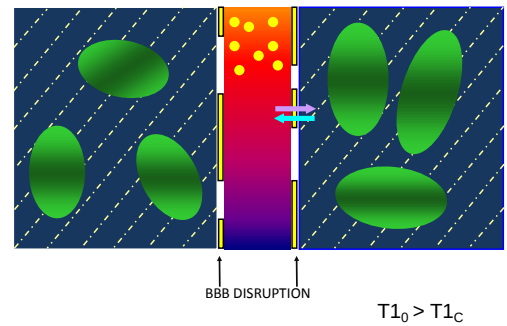


DCE MRI: Pharmacokinetic model



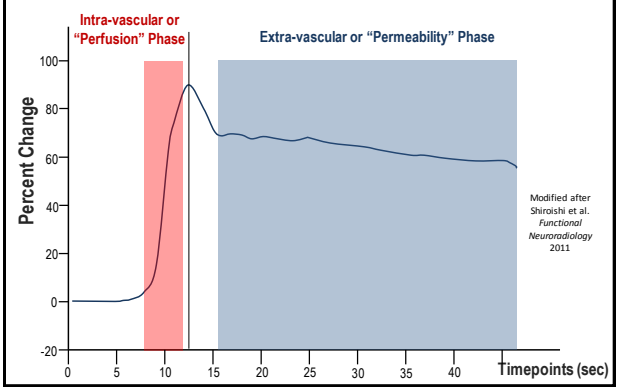
$T1_0 \approx T1_C$

DCE MRI: Pharmacokinetic model



$T1_0 > T1_C$

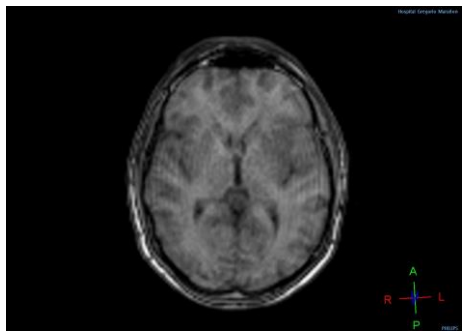
T1-DCE SIGNAL-INTENSITY CURVE



General DCE-Technique

PARAMETER	T1 (DCE)
Sequence	SPGR/FLASH/FFE 2D / 3D
Flip angle	~ 30º
TE	< 1.5 ms
TR	< 7 ms
Rate of Gd injection	2-5 cc/s
Dose of Gadolinum	0.1mmol/Kg

Dynamic scans of T1-DCE MRI



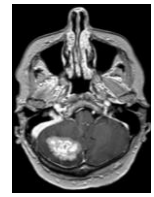
T1-DCE MRI: Variables

- K^{trans} *Tranfer constant*
  - Transfer coefficient from the plasma volume to the extravascular extracelullar volume
  - Reflect flow and permeability
  - Intact BBB → K_{trans} =0
  - Units: min^{-1}
- K^{ep} *Rate constant back*
  - Rate constant back to plasma space
  - Units: min^{-1}
- V_e *Volume of the extravascular extracellular space*
  - Depends on the structure of cerebral tissue (celullarity)
  - Units: mL/100g
- V_p *Blood Plasma Volume*
  - Related to Cerebral Blood Volume
  - Units: mL/100g

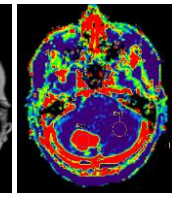
Limitations of T1-DCE MRI

- Complexity of quantification of perfusion parameters
- Calculation of baseline T1 values and arterial input function (AIF) are prone to errors
- User-friendly software is not widely available

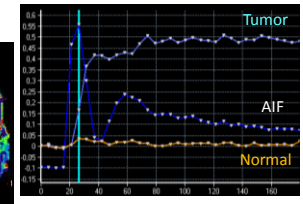
T1-DCE: Example



T1 + Gd



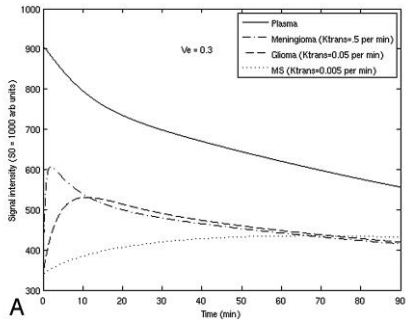
K^{trans} map



	Tumor	Normal
Ktrans (10^{-3}/min):	2038,24	0,00
Kep (10^{-3}/min):	937,91	0,00
Ve (10^{-3}):	2173,16	0,00
Vp (10^{-3}):	229,77	35,69
Area Under Curve	13,76	0,40

Portal IntelliSpace Philips

Signal intensity curves using DCE-MRI



Zaharchuk G AJNR Am J Neuroradiol 2007;28:1850-1858

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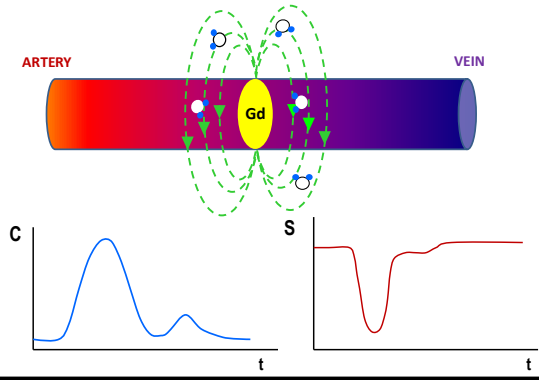
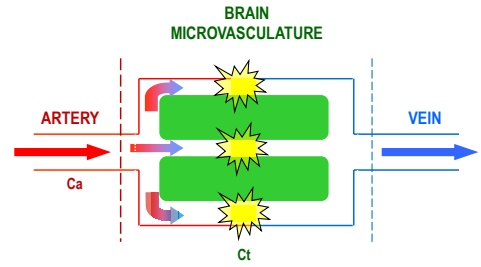
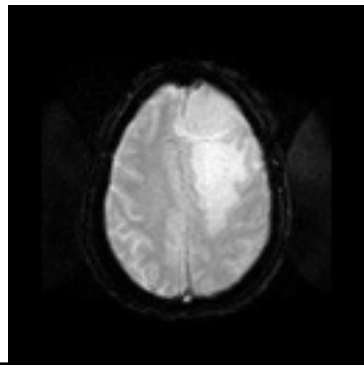
T2-DSC MRI: Principles



T2-DSC MRI: Pharmacokinetic model

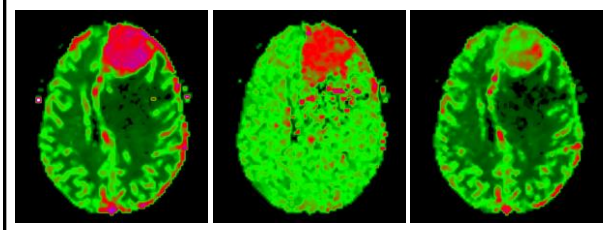


Dynamic scans of T2-DSC MRI



Parametric maps (Absolute quantifications)

Cerebral Blood Volume | Mean Transit Time | Cerebral Blood Flow

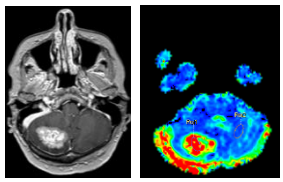


$$CBV = \frac{K_H}{\rho} \cdot \frac{\int C_m(t)dt}{\int AIF(t)dt}$$

$$MTT = \frac{\int C(t)dt}{C_{max}}$$

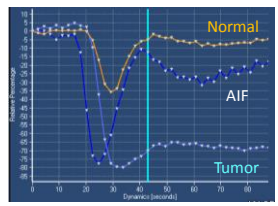
$$CBF = \frac{CBV}{MTT}$$

T2-DSC: Example



T1 + Gd

CBV map



	Tumor	Roi2
relCBF (ml/100g/min):	511.56	121.68
relCBV (ml/100g):	81.80	6.61
MTT(s):	9.59	3.26
TTP (s):	33.72	29.22
T0 (s) :	22.48	20.23
Delay(s) :	8.99	4.50
Roi Area (mm²) :	85.15	85.15

Portal IntelliSpace Philips

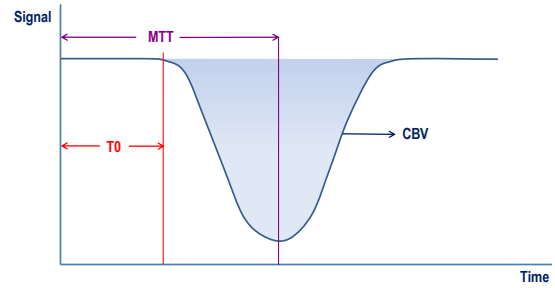
General DSC-Technique

PARAMETER	T2 (DSE)
Sequence	SE/GRE- EPI 2D Multislice
Flip angle	~ 30º
TR	~ 1000 ms
Rate of Gd injection	3-5 cc/s
Dose of Gadolinum	0.1mmol/Kg

T2-DSC MRI: Variables

- CBV- Cerebral Blood Volume
  - Total volume of blood traversing a given region of brain
  - Units: ml/100gr
- CBF- Cerebral Blood Flow
  - CBF is defined as the volume of blood traversing a given region of brain per unit time
  - Units ml/100gr/min
- MTT- Mean Transit Time
  - Average time that blood takes to pass from arterial inflow to venous outflow
  - Units: sec
- TP- Time-To-Peak
  - Time between the tracer injection and the maximum signal change
  - Units: sec

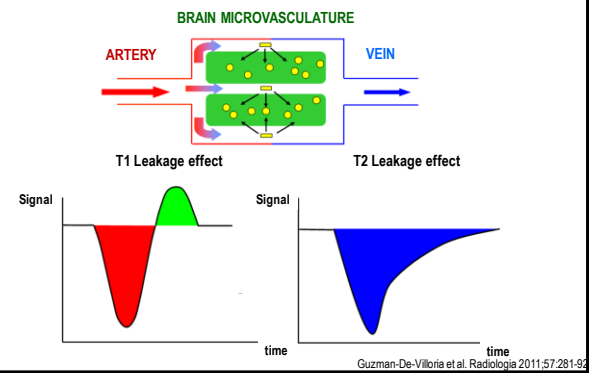
Signal-Time curve in DSC-T2* perfusion



Limitations of T2-DSC MRI

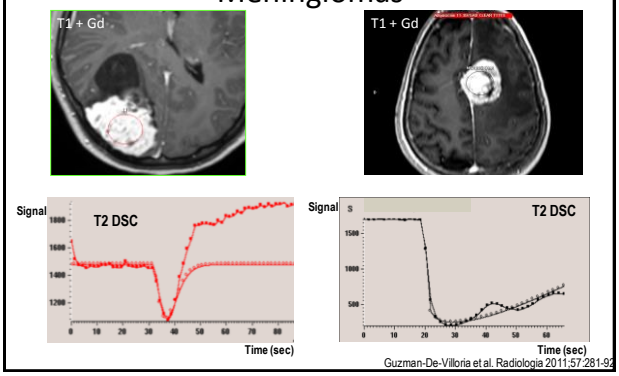
- Arterial Input Function (AIF) should be calculated to determine absolute quantification
  - Pitfalls related to:
    - Low cardiac input
    - Low injection rate (<3ml/s)
- Leakage due to increase BBB permeability
  - Pitalls related to:
    - T1 leakage effect
    - T2 leakage effect
- Prone to susceptibilty artifacts
  - Blood products, calcification, metal, air and bone

Pitfalls: Leakage effect



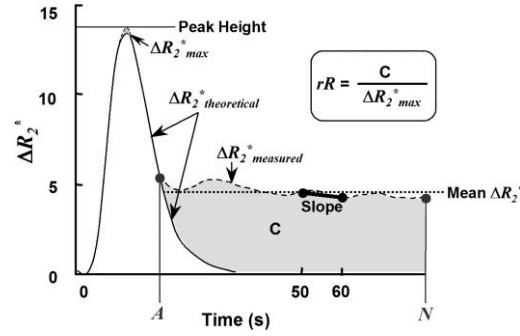
Guzman-De-Villoria et al. Radiologia 2011;57:281-92

Examples of leakage effects: Meningiomas



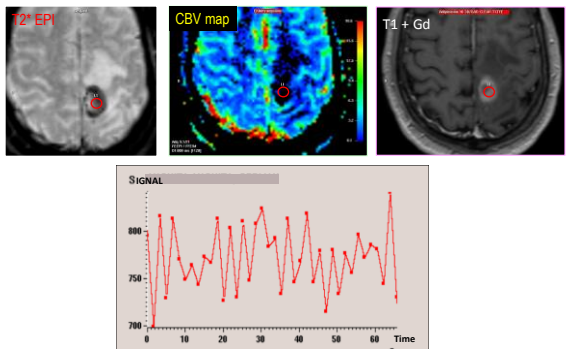
Guzman-De-Villoria et al. Radiologia 2011;57:281-92

Calculation of T2*-based permeability variables

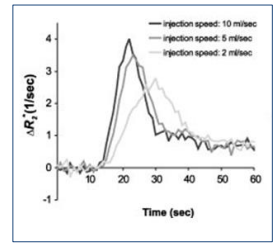


Thornhill R et al. AJNR Am J Neuroradiol 2010;31:1015-1022

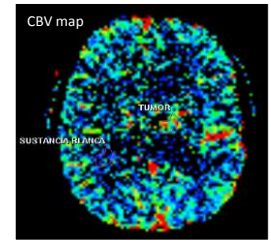
Susceptibility artifacts by blood products



Influence of injection rate on bolus shape



van Osch et al. Magn Reson Med 2003;50:614-622



Low signal-to-noise ratio due to inappropiate low injection rate

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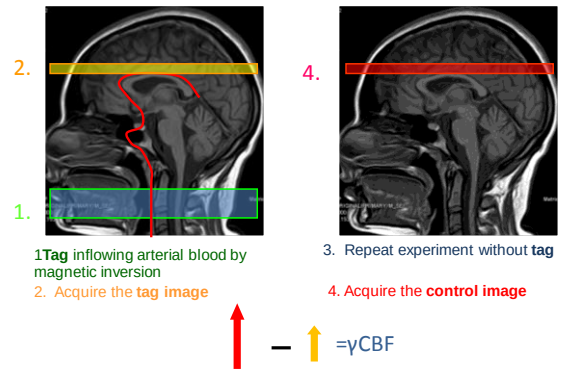
Basic principles of ASL



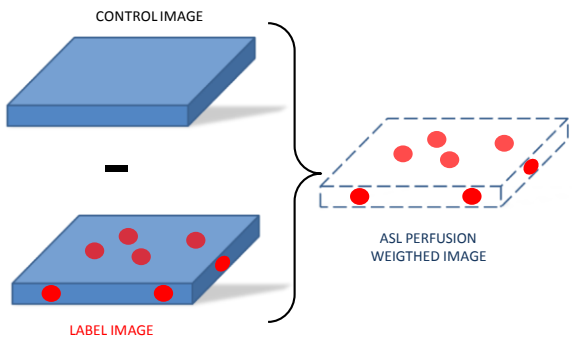
1**Tag** inflowing arterial blood by magnetic inversion

2. Acquire the **tag image**

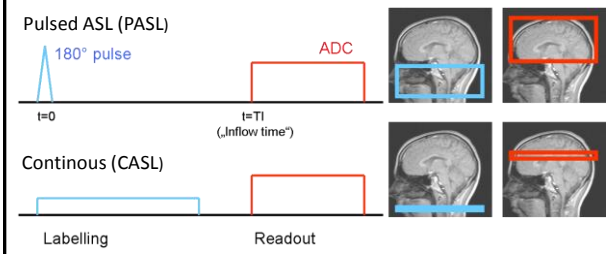
3. Repeat experiment without **tag**

4. Acquire the **control image**

ASL image: Image subtraction



Basic ASL Techniques



http://asl-network.org

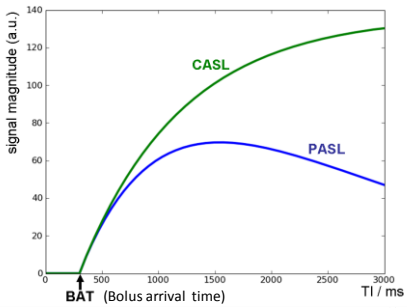
Continuous vs Pulsed ASL

- Continuous ASL (CASL)
  - Higher Signal-to-Noise Ratio
  - More hardware requirements
  - Higher specific absorption rate (SAR)
- Pulsed ASL (PASL)
  - Labelling efficiency is higher than in CASL
  - T1 signal decays when longer inflow times are chosen

Pseudocontinuous ASL

- Intermediate technique between CASL and PASL
- Uses a series of discrete RF pulses
- Combine the advantages of PASL and CASL
  - Less hardware demand
  - Higher tagging efficiency
  - Higher Signal-to-Noise ratio

PASL vs CASL: signal depending on the inflow time T1

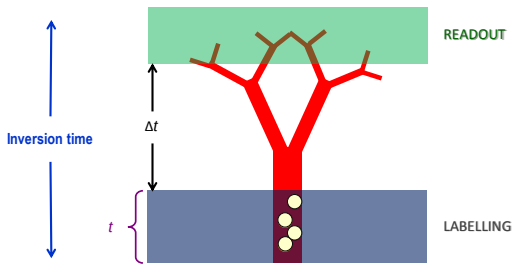


http://asl-network.org

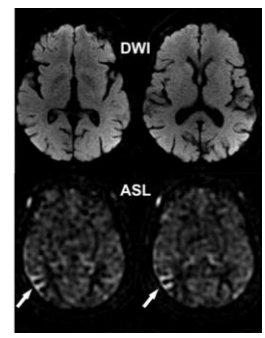
Limitations of ASL

- Low Signal-to-Noise ratio
  - Signal changes of 1-2%
- Low spatial resolution
  - Matrix size of 64 x 64 mm
- Prone to susceptibility artifacts
  - Much of the studies has employed EPI
- Motion artifacts
  - ASL is a subtraction technique, thus it is sensitive to subject movement
- Dependence of arterial transit time

ASL: Dependence of Arterial Transit Time

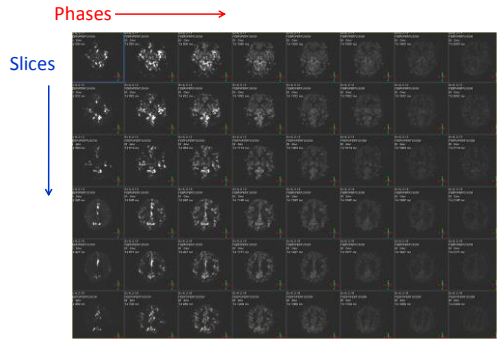


Patient with Transient Ischemic Attack: Arterial transit artifact in ASL

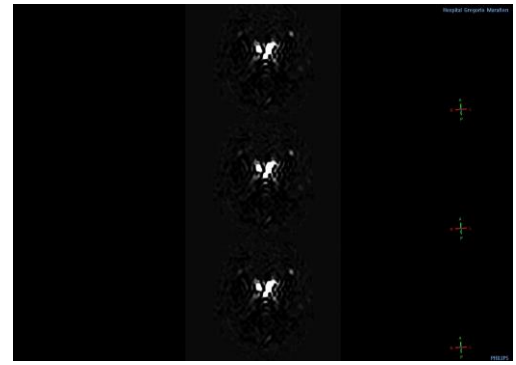


Kleinman J T et al. Stroke 2012;43:1556-1560

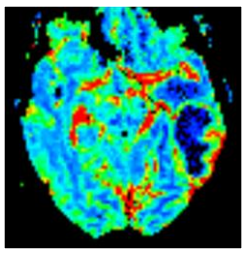
Multislice Multiphase ASL perfusion



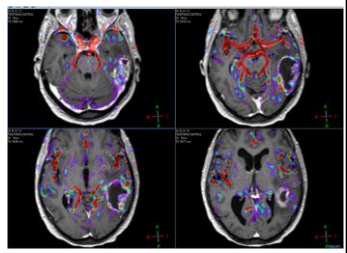
Multiphase ASL perfusion



Example: ASL vs DSC Perfusion in glioblastoma



DSC-T2* Perfusion



ASL Perfusion

Comparison between differents perfusion MR techniques

	T1-Weighted (DCE)	T2*-Weighted (DSC)	ASL
Temporal resolution	~3-6 s	~1-2 s	3-5 s
Acquisition time	3-5 min	2 min	3-5 min
Spatial resolution	1-mm-in-plane x 5 mm slices	2-mm-in-plane x 5 mm slices	3-mm-in-plane x 5 mm slices
Model parameters	K^{trans}, K^{ep}, V_p, V_e, AUC	CBV, CBF, MTT	CBF
Geometric artifacts	Low impact	Prone to problems at the skull base	Prone to problems at the skull base
Main advantages	Assessment of BBB Permeability	High experience	Contrast agent are not required
Sources of error	Calculation of T1 and AIF	Leakage effect	Low SNR

Essig M et al. AJR 2013;200:24-34 (Modified)

PERFUSION IMAGING: Pitfalls and Clinical Applications update

Perfusion in Multiple Sclerosis: Physiopathology

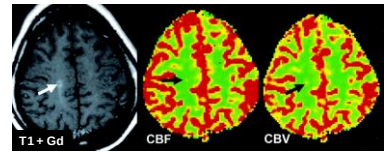
Immunopathological studies suggests that vascular factor may contribute to the pathogenesis of MS

- Perivenular lymphocytic cuffing and intravascular fibrin deposition may induce venous obliteration
- Cytotoxic T cells may activate endotelial cells and activate a clotting cascade
- Inflammatory edema may impair microcirculation

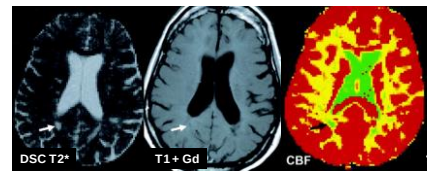
Perfusion in Multiple Sclerosis: Findings

- Perfusion parameters are decreased in:
  - Normal appearing white matter (NAWM)
  - Normal appearing grey matter (NAGM)
    - Basal ganglia, thalamus
  - Hypointense T1 plaques
- Hiperperfusion is demonstrated in:
  - Enhancing lesions
    - Elevation of perfusion may precede the BBB breakdown

Perfusion in Multiple Sclerosis Type of plaque



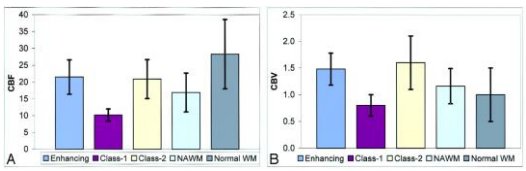
Example of increased perfusion in enhancing lesion



Example of decreased perfusion in a nonenhancing plaque

Ge Y et al. AJNR Am J Neuroradiol 2005;26:1539-1547

Perfusion in MS: Type of plaque

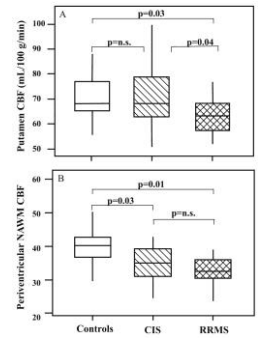


Class-1: Non-enhancing lesions with perfusion characteristics markedly dissimilar to enhancing lesions.

Class-2: Non-enhancing lesions with perfusion characteristics similar to enhancing lesions.

Ge Y et al. AJNR Am J Neuroradiol 2005;26:1539-1547

Perfusion in Multiple Sclerosis Clinical evolution



Varga A et al. J Neurol Sci 2009;282:28-33

Prediction of hemorrhage in ischemic stroke

- Acute ischemic stroke is treated with mechanical clot-retrieval devices and/or phramaceutical recanalization therapies (tPA)
- A succeful recanalization of the vessels improves the chances of recovery
- However critical complications such hemorrhagic transformation may result

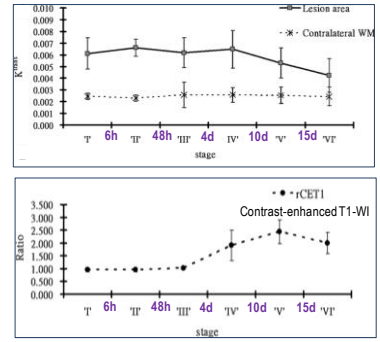
Prediction of hemorrhage in ischemic stroke

- Clinical and radiologic findings have associated with higher risk of HT
  - Early contrast-enhancement on T1-WI
  - Volume of severe diffusion abnormality
  - Volume of severe perfusion abnormality
  - Leukoaraiosis
  - Prior cerebral microbleeds
- However, it remains difficult to identify patients at high risk of HT

Prediction of HT using permeability imaging

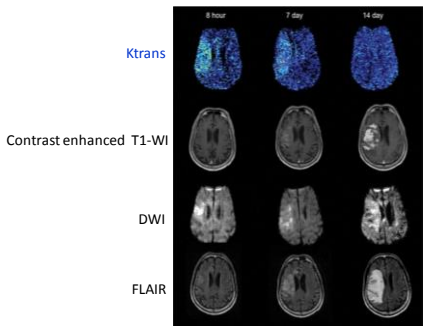
- Permeability variables have been described as predictors of HT in acute ischemic stroke
- Disruption of the BBB is a necessary, albeit not sufficient condition for HT
- Permeability in ischemic stroke patients is related to:
  - Clinical variables
  - Thrombolytic treatment
  - Time course

Dynamic changes in permeability and contrast-enhanced T1 after ischemia



Liu H et al. Stroke 2013;44:1872-1877

Case: 61-year-old with right middle artery infartion

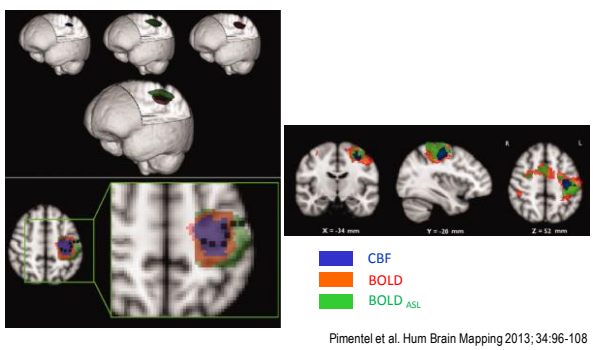


Liu H et al. Stroke 2013;44:1872-1877 (Modified)

Functional MRI based on perfusion methods

- The most common method used for activation studies is based on the blood oxygen level-dependent (BOLD) contrast
- The location of BOLD signal change may not reflect the localitation of neuronal activity
- Better spatial location is found by CBF measurements

Localization of the hand motor area by ASL and BOLD fMRI



Pimentel et al. Hum Brain Mapping 2013; 34:96-108

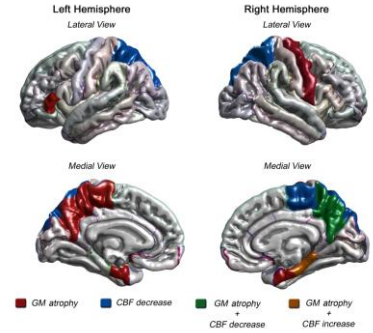
MR perfusion in Alzheimer Disease

- The hallmark of AD on MRI is cortical atrophy, particulary in the medial temporal and parietal lobes
- In AD, biomarkers is necessary given the paucity of clinical or cognitive measures sensitive of changes in these early stages
- Several previous studies have used perfusion MR techniques in order to describe biomarkers of AD

Patterns of perfusion in AD

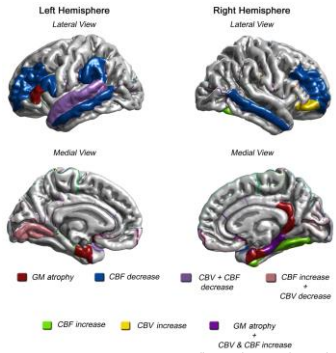
- Hypoperfusion pattern has been described in parietotemporal association areas for AD and as a biomarker of rapid conversion to AD.
- However, results for the temporal lobes are inconsistent in early states of AD:
  - Hypoperfusion (*Binnewijzend MA, Radiology 2013*)
  - Hyperperfusion (*Alsop, Neuroimage 2008*)

Differences in perfusion and cerebral volume between patients with MCI and controls



Lacalle-Aurioles M et al. J Cerebr Blood Flow Metab (in press)

Differences in perfusion and cerebral volume between patients with EA and controls



Lacalle-Aurioles M et al. J Cerebr Blood Flow Metab (in press)

CONCLUSIONS

- Different MRI techniques are currently available for cerebral perfusion measurements
- Prior kwnoledge of basic principles of each of these techniques helps to the neuroradiologist to identity pifalls
- Perfusion MR is now routinely used in daily routine and in research centers and universities