INTRODUCTION

• Perfusion MR techniques provide 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 priori knowledge of:
  – Technical issues related to MRI
    • Technique
    • Theoretical model
    • Sequence
  – Sources of errors / Pitfalls
    • Leakage effects
    • Susceptibility artifacts
    • Movement artifacts

DYNAMIC SUSCEPTIBILITY-WEIGHTED MRI

MR Perfusion Techniques

• With exogenous contrast agent
  – T1-Weighted dynamic contrast-enhanced (DCE) MRI.
  – T2-Weighted dynamic susceptibility-weighted contrast-enhanced (DSC) MRI
• Without exogenous contrast agent
  – Arterial Spin Labeling (ASL)
  – Blood Oxygen Level Dependent (BOLD)
  – Intravoxel Incoherent Motion MRI (IVIM)
MR Perfusion Techniques

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DCE MRI: Pharmacokinetic model

General DCE-Technique

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>T1 (DCE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequence</td>
<td>SPGR/FLASH/FFE</td>
</tr>
<tr>
<td>Flip angle</td>
<td>~ 30°</td>
</tr>
<tr>
<td>TE</td>
<td>&lt; 1.5 ms</td>
</tr>
<tr>
<td>TR</td>
<td>&lt; 7 ms</td>
</tr>
<tr>
<td>Rate of Gd injection</td>
<td>2-5 cc/s</td>
</tr>
<tr>
<td>Dose of Gadolinum</td>
<td>0.1mmol/Kg</td>
</tr>
</tbody>
</table>
Dynamic scans of T1-DCE MRI

T1-DCE MRI: Variables

- $K^{trans}$ Transfer constant
  - Transfer coefficient from the plasma volume to the extravascular extracellular volume
  - Reflect flow and permeability
  - Intact BBB $\rightarrow K_{trans} \rightarrow 0$
  - Units: min$^{-1}$
- $K^0$ Rate constant back
  - Rate constant back to plasma space
  - Units: min$^{-1}$
- $V_v$ Volume of the extravascular extracellular space
  - Depends on the structure of cerebral tissue (cellularity)
  - 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

Signal intensity curves using DCE-MRI

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1. EL AGENTE PERTURBA EL CAMPO MAGNÉTICO

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 \( \frac{\kappa_0}{p} \int \frac{C(t)dt}{AIF(t)} \)

MTT \( \int_{-\infty}^{\infty} C(t)dt \)

CBF \( \frac{MTT}{CBV} \)

T2-DSC: Example

T2-DSC: Example

T2-DSC: Example

General DSC-Technique

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

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
  - Pitfalls related to:
    • T1 leakage effect
    • T2 leakage effect
- Prone to susceptibility artifacts
  - Blood products, calcification, metal, air and bone

Examples of leakage effects: Meningiomas

Calculation of T2*-based permeability variables

Signal-Time curve in DSC-T2* perfusion

Signal

MTT

T0

CBV

Time

Signal

T1 Leakage effect

T2 Leakage effect

Signal

Time

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

Susceptibility artifacts by blood products

Influence of injection rate on bolus shape

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Basic principles of ASL

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

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

Patient with Transient Ischemic Attack: Arterial transit artifact in ASL
Phases
Slices

Multislice Multiphase ASL perfusion

Example: ASL vs DSC Perfusion in glioblastoma

DSC-T2* Perfusion
ASL Perfusion

Comparison between different perfusion MR techniques

<table>
<thead>
<tr>
<th></th>
<th>T1-Weighted (DCE)</th>
<th>T2*-Weighted (DSC)</th>
<th>ASL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal resolution</td>
<td>~3-6 s</td>
<td>~1-2 s</td>
<td>3-5 s</td>
</tr>
<tr>
<td>Acquisition time</td>
<td>3.5 min</td>
<td>2 min</td>
<td>3-5 min</td>
</tr>
<tr>
<td>Spatial resolution</td>
<td>1-mm-in-plane x 5 mm slices</td>
<td>2-mm-in-plane x 5 mm slices</td>
<td>3-mm-in-plane x 5 mm slices</td>
</tr>
<tr>
<td>Model parameters</td>
<td>Ktrans, Kep, Vp, AUC</td>
<td>CBV, CBF, MTT</td>
<td>CBF</td>
</tr>
<tr>
<td>Geometric artifacts</td>
<td>Low Impact</td>
<td>Prone to problems at the skull base</td>
<td>Prone to problems at the skull base</td>
</tr>
<tr>
<td>Main advantages</td>
<td>Assessment of BBB Permeability</td>
<td>High experience</td>
<td>Contrast agent are not required</td>
</tr>
<tr>
<td>Sources of error</td>
<td>Calculation of T1 and AIF</td>
<td>Leakage effect</td>
<td>Low SNR</td>
</tr>
</tbody>
</table>

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

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

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.

Prediction of hemorrhage in ischemic stroke

- Acute ischemic stroke is treated with mechanical clot-retrieval devices and/or phramaceutical recanalization therapies (tPA)
- A successful 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

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

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 localization of neuronal activity
- Better spatial location is found by CBF measurements

Localization of the hand motor area by ASL and BOLD fMRI

MR perfusion in Alzheimer Disease

- The hallmark of AD on MRI is cortical atrophy, particularly 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

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

CONCLUSIONS

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