Dynamic susceptibility contrast (DSC) perfusion

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Basic Kinetic Modeling in Molecular Imaging

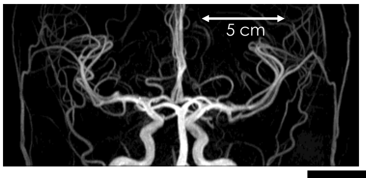
Dynamic susceptibility contrast (DSC) perfusion

Background:
- MR perfusion methods
- DSC perfusion physics
- DSC perfusion methodology

Applications:
- Stroke
- Brain tumors

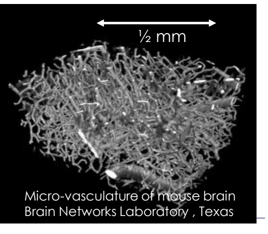
Caveats:
- Leakage
- Quantification

Perfusion: definitions



Macro-vasculature

Micro-vasculature

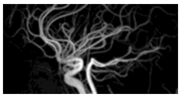


Blood flow: **tissue supply of blood**
- cerebral blood flow (CBF)
- ~ 20-80 ml/100g/minute in human brain

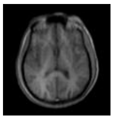
Blood volume: **proportion of blood in tissue**
- cerebral blood volume (CBV)
- ~ 2-5% in human brain

Checklist for MR perfusion

1. MR-visible contrast agent



2. MR imaging sequence (speed, coverage, image quality, sensitivity to tracer)



3. MR physics to get tracer concentration (MR signal equation, calibration scans)

$\Delta R_2^*(t) = -\ln[S(t)/S(\text{baseline})]/TE$

4. Tracer kinetic modeling to derive quantities of interest

$C_t(t) = CBF \cdot C_a(t) \otimes r(t)$

Some MR contrast agents

Exogenous CA
- Gd chelates
- Mn chelates
- Hyperpolarized gases
- Iron oxide

Endogenous CA
- Water protons
- Deoxyhemoglobin (BOLD effect)

Some MR perfusion metods

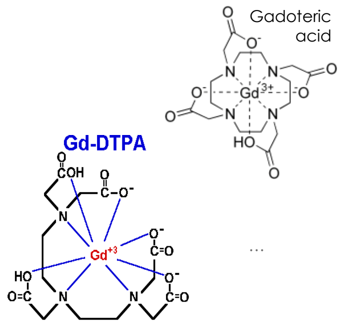
Dynamic susceptibility contrast (DSC)
CA: Gadolinium MR Imaging: T2*w

Arterial spin labelling (ASL)
CA: Water MR Imaging : 'T1w'

Dynamic contrast enhanced (DCE)
CA: Gadolinium MR Imaging : T1w

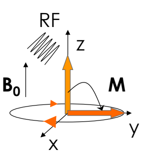
Contrast injection

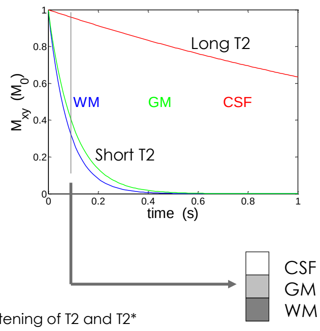
Paramagnetic Contrast, Gd chelates



- Decreases homogeneity in molecular environment
- Increases relaxation speed!
- Decreases both T_1 and T_2
- Intravascular in the brain

T2 weighting

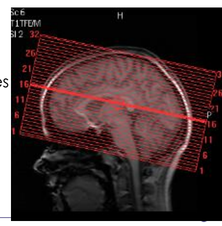




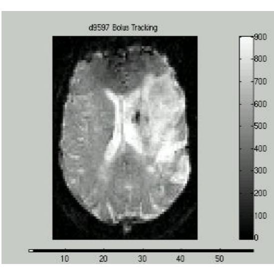
Effect of Gd: overall shortening of T2 and T2*

Standard DSC Perfusion Protocol

- Intravenous injection of Gd contrast agent
- Dose: 1-2 mmol/kg body weight
- Bolus injection: 3 – 5 ml/s
- Rapid imaging using GE-EPI (time resolution = 1-2 seconds)
- Voxel size ~ 2 mm x 2 mm, ~ 4 mm thick slices, 15 - 30 slices
- Total imaging time required: ~ 2 minutes



DSC time-series



E. Rostrup

Conversion of signal units to relaxation rate units

$$S(t) = S_0 \exp[-TE \cdot R_2^*(t)]$$

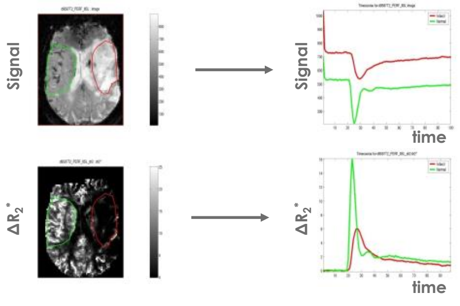
$$S(\text{baseline}) = S_0 \exp[-TE \cdot R_2^*(\text{baseline})]$$

$$S(t)/S(\text{baseline}) = \exp[-TE \cdot \{R_2^*(t) - R_2^*(\text{baseline})\}]$$

$$\Delta R_2^*(t) = R_2^*(t) - R_2^*(\text{baseline})$$

$$\Delta R_2^*(t) = -\ln[S(t)/S(\text{baseline})]/TE$$

Conversion of signal units to relaxation rate units



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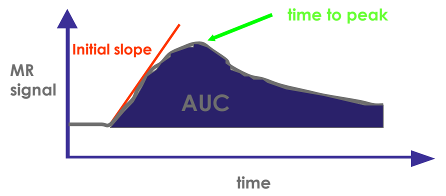
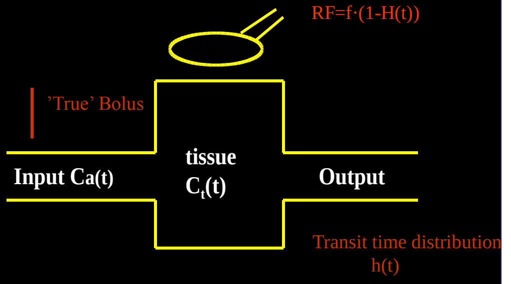
The tissue response

Qualitative parameters – used to obtain useful diagnostic contrast with a minimum of post processing

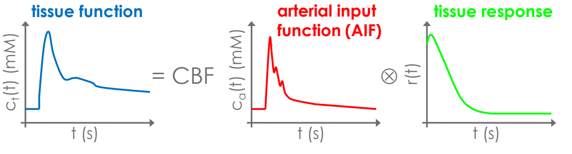


Single injection - residue detection



E. Rostrup

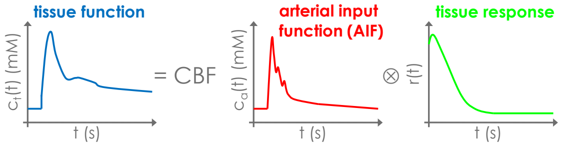
Tracer kinetic modeling



$$c_t(t) = CBF \cdot c_a(t) \otimes r(t) = CBF \cdot \int_0^t c_a(t')\, r(t-t')\, dt'$$

$$MTT = \int r(t)dt \qquad CBV = CBF \cdot MTT$$

Deconvolution



$$c_t(t) = CBF \cdot c_a(t) \otimes r(t) = CBF \cdot \int_0^t c_a(t')\, r(t-t')\, dt'$$

- Model-based: e.g. r(t) exponential
- Model-free: no model assumptions on r(t)

L. Østergaard, Magnetic Resonance in Medicine 1996

Model-free deconvolution

$$c_t(t) = CBF \cdot \int c_a(t')\, r(t-t')\, dt'$$

Can be written as a matrix equation

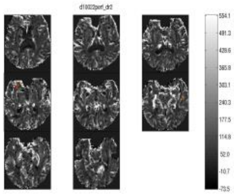
$$c_t = A \cdot R$$

There are numerical methods to solve by inverting A

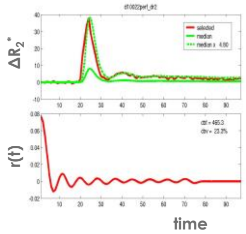
$$R = A^{-1} \cdot c_t$$

e.g. Singular Value Decomposition (SVD)
or Tikhonov regularization

Deconvolution



AIF from selected voxels



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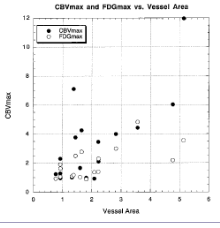
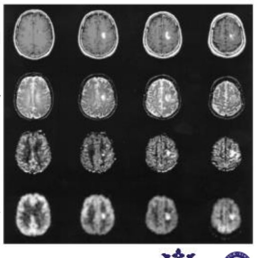
DSC perfusion and tumor angiogenesis

Vol. 6, 2189–2200, June 2000 Clinical Cancer Research 2189

High Microvascular Blood Volume Is Associated with High Glucose Uptake and Tumor Angiogenesis in Human Gliomas[1]

Hannu J. Aronen, Francisco S. Pardo, David N. Kennedy, John W. Belliveau, Scott D. Packard, Dora W. Hsu, Frederick H. Hochberg, Alan J. Fischman, and Bruce R. Rosen[2]





Multimodal MR imaging in acute stroke

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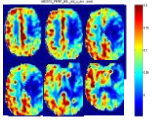
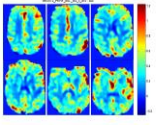
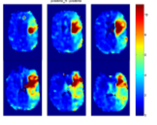
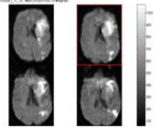








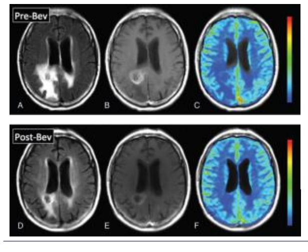
Review: e.g. Copen, Schaefer & Wu, Neuroimaging Clin N Am. 2011

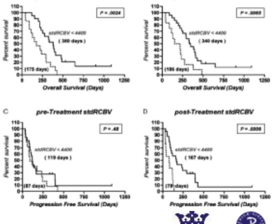
DSC and chemotherapy treatment response

Neuro-Oncology 2014; 0, 1–9, doi:10.1093/neuonc/not216

Dynamic-susceptibility contrast agent MRI measures of relative cerebral blood volume predict response to bevacizumab in recurrent high-grade glioma

Kathleen M. Schmainda, Melissa Prah, Jennifer Connelly, Scott D. Rand, Raymond G. Hoffman, Wade Mueller, and Mark G. Malkin





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Quantification?

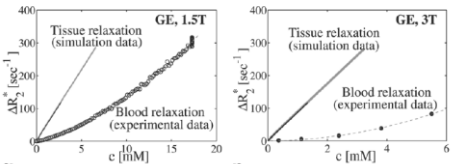
Theoretical Model of Intravascular Paramagnetic Tracers Effect on Tissue Relaxation

B.F. Kjølby, L. Østergaard, and V.G. Kiselev

See also, e.g., Kiselev, MRM (2001); van Osch, MRM (2003), Blockley, MRM (2009)

$\Delta R_2^*(t) = -\ln[S(t)/S(\text{baseline})]/TE$

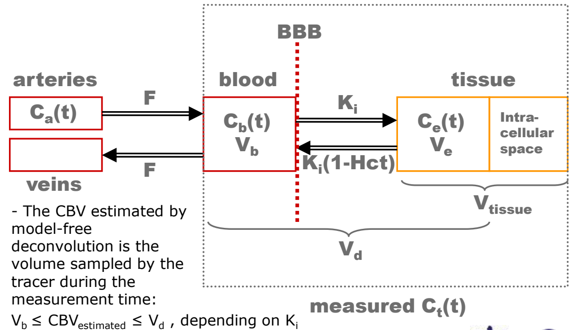
Relation beween $\Delta R_2^*(t)$ and c(t) ? $c(t) = \text{constant} \cdot \Delta R_2^*(t)$?



Complicated relation between $\Delta R_2^*(t)$ and c(t), very different for tissue (c_t) and blood (c_a).

- Perfusion quantification will be biased

2-Compartment model of tissue



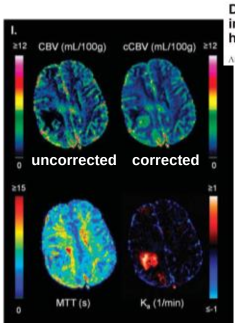
- The CBV estimated by model-free deconvolution is the volume sampled by the tracer during the measurement time:

$V_b \leq CBV_{estimated} \leq V_d$, depending on K_i

measured $C_t(t)$

- The physics of the relaxation due to Gd changes when the contrast agent is extra-vasated

Correction for leakage in brain tumors



T_1- and T_2^*-dominant extravasation correction in DSC-MRI: Part I—theoretical considerations and implications for assessment of tumor hemodynamic properties

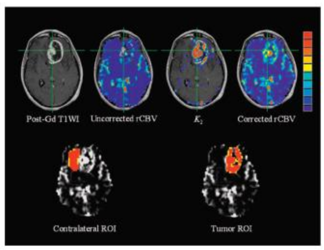
Atle Bjørnerud, A Gregory Sorensen, Kim Mouridsen and Kyrre E Emblem

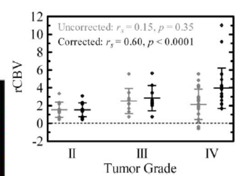
- Extravasation of contrast agent will bias DSC derived parameters
- Correction schemes exist and give measures of blood brain barrier permeability

Influence of leakage correction on tumor grading

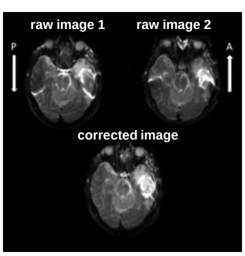
Relative Cerebral Blood Volume Maps Corrected for Contrast Agent Extravasation Significantly Correlate with Glioma Tumor Grade, Whereas Uncorrected Maps Do Not

Boxerman et al., AJNR (2006)





Distortions of dynamic images

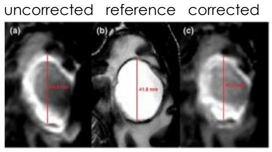


Technical Note

Correction of B0-Distortions in Echo-Planar-Imaging–Based Perfusion-Weighted MRI

Jonas Vardal, Raimo A. Salo, MS, Christopher Larsson, Anders M. Dale, PhD, Dominic Holland, PhD, Inge Rasmus Groote, PhD, and Atle Bjørnerud, PhD

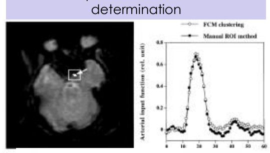
uncorrected reference corrected



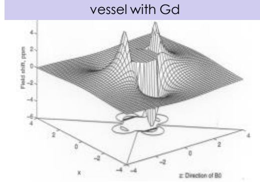
- EPI images usually employed for bolus tracking are prone to distortions

Determination of arterial input function

Example of automated AIF determination



Simulation of field distribution around vessel with Gd



- The AIF is difficult to determine due to the low quality of EPI images
- An AIF outside a large vessel is often preferable
- Many methods in the literature for automated AIF determination

Murase, JMRI (2001)
Duhamel, MRM (2006)
Bjørnerud, JCBFM (2010)
...

Dynamic susceptibility contrast (DSC) perfusion

- MR method for measuring brain perfusion
- Dynamic imaging during Gd bolus injection
- CBF, CBV, MTT can be quantified using model-free deconvolution
- Applications in acute stroke and neuro-oncology
- Beware of methodological issues!