Perfusion Imaging in the Brain & Body

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Highlights:

- Perfusion can be assessed with time-resolved T1-weighted MRI measurements during administration of an extravascular contrast agent.
- The relation between the time-resolved contrast agent concentrations in the tissue and in the supplying artery can be used to determine the blood flow and the volume of distribution in the tissue.
- In most tissues, an extravascular contrast agent can access two regions, the intravascular volume and the interstitial volume. Mathematical modelling of these volumes and their interaction allows extracting further hemodynamic parameters of the tissue.
- Practical quantification: Hands-on example

Measuring perfusion with an extravascular tracer

Target audience: This course is aimed at basic research scientists and clinicians.

Objectives: To provide the audience with the fundamentals of measuring perfusion with extravascular tracers

The quantification of perfusion with an extravascular tracer relies on two key steps (1):

1. The tracer is administered intravenously, typically rapidly as a *bolus*, while the signal intensity in the tissue is monitored in a time-resolved manner. Often, perfusion-related information can be derived from examining these time-resolved signal intensities without any further post processing; for quantification, it is generally useful to derive the contrast agent concentrations from the signal intensities.
2. For the quantification of perfusion, the relation that links the tissue concentration with the concentration in a supplying blood vessel is required. If the system is linear and stationary, the tissue concentration can be described as the *convolution* of the arterial concentration with an as yet unknown *impulse response function* (IRF).

The entire information about the tissue hemodynamics is encompassed in this IRF. Deriving the IRF from the measured concentrations thus allows to determine a range of physiological parameters that characterize tissue perfusion.

Time-resolved measurement of contrast agent concentrations

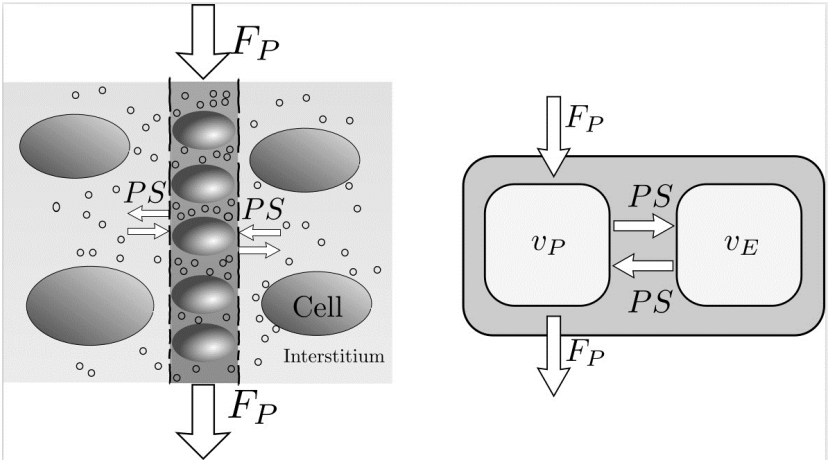
Prior to any quantification, time-resolved CA concentrations in tissue and artery have to be measured. In MRI, the most commonly used sequences for this purpose are heavily T1 weighted, so that the presence of contrast agent causes an increase in signal intensity -- hence the name dynamic

contrast-enhanced (DCE) MRI. We will provide an overview about commonly used pulse sequences and measurement strategies, and we will present the competing requirements on temporal resolution, spatial resolution and spatial coverage and contrast-to-noise ratio. Further challenges arise when the arterial concentration is to be measured.

Furthermore, the topic of deriving the contrast agent concentrations from measured signal intensities will be touched. This may include additional calibration measurements, in particular the measurement of precontrast relaxation rate $R_{1,0}$.

Quantification: Characterizing the impulse response function

The second part of this talk deals with the problem of determining the impulse response function, which is essential for the quantification perfusion or, more generally, the tissue hemodynamics. Several strategies exist for this purpose. A widely used technique is numerical *deconvolution*, which does not make any assumptions about the internal tissue function and allows determining the blood flow into the tissue, the *volume of distribution*, i.e. the volume that is accessible to contrast agent, and the mean transit time (2–4).



A tissue where the contrast agent can access the intravascular and the interstitial volume

Further insight into the tissue hemodynamics can be gained when the tissue regions and their interactions are modeled by means of tracer-kinetic theory (1,5,6) . In the context of DCE MRI, most tissues can be described in terms of two volumes that are accessible to the tracer (see figure): The contrast agent is carried into the capillary plasma volume v_p by the arterial plasma flow F_p. From there, it can extravasate into the interstitial (i.e. extravascular, extracellular) volumev_e, driven the permeability-surface area productPS. Eventually, the tracer will be washed out from v_e to v_p and leave the tissue with the venous outflow, which is equal to F_p.

A range of four-parameter models have been developed for this general two-region scenario, a topical overview can be found in (7). These models build on different assumptions, e.g. about the internal structure of the volumes v_p and v_e and will be presented briefly. Furthermore, we will present some three- and two-parameter limits, in particular the Tofts models and the compartment uptake model. These limits can be very helpful in the presence of measurement constraints, such as

low temporal resolution or short total acquisition time. Also, we will briefly touch the topic of data-driven model selection.

Practical model fitting

In the last part of the talk, we will demonstrate the application of all the above described principles to some actual, measured curves.

References

1. Ingrisch M, Sourbron S. Tracer-kinetic modeling of dynamic contrast-enhanced MRI and CT: a primer. Journal of Pharmacokinetics and Pharmacodynamics 2013;40:281–300. doi: 10.1007/s10928-013-9315-3.

2. Sourbron S, Dujardin M, Makkat S, Luypaert R. Pixel-by-pixel deconvolution of bolus-tracking data: optimization and implementation. Physics in Medicine and Biology 2007;52:429–447. doi: 10.1088/0031-9155/52/2/009.

3. Jerosch-Herold M, Swingen C, Seethamraju RT. Myocardial blood flow quantification with MRI by model-independent deconvolution. Medical Physics 2002;29:886–897.

4. Ostergaard L, Weisskoff RM, Chesler DA, Gyldensted C, Rosen BR. High resolution measurement of cerebral blood flow using intravascular tracer bolus passages. part i: Mathematical approach and statistical analysis. Magnetic Resonance in Medicine 1996;36:715–725.

5. Sourbron SP, Buckley DL. Classic models for dynamic contrast-enhanced MRI. NMR in Biomedicine 2013;26:1004–1027. doi: 10.1002/nbm.2940.

6. Koh TS, Bisdas S, Koh DM, Thng CH. Fundamentals of tracer kinetics for dynamic contrast-enhanced MRI. Journal of Magnetic Resonance Imaging 2011;34:1262–1276. doi: 10.1002/jmri.22795.

7. Sourbron SP, Buckley DL. Tracer kinetic modelling in MRI: estimating perfusion and capillary permeability. Physics in Medicine and Biology 2012;57:R1–R33. doi: 10.1088/0031-9155/57/2/R1.