

Chemistry of Contrast Media

Basic Considerations about Suitable Modalities and Probes

Basics in pharmacokinetics: Low molecular weight MR probes

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Learning Objectives:

- To know which methods are used to measure the effects of low molecular weight contrast on the T1 and T2* relaxation of water spins
- To know the main pharmacokinetic model to assess the T1 effect of low molecular weight contrast
- To understand the meaning of the parameters derived from this kinetic modeling and limitations in measuring their values
- To know some examples of the use of kinetic modeling to assess tumor vascularity.

A unique property of Magnetic Resonance is the broad range of options to monitor and image dynamic processes in the body. To derive physiologic or metabolic relevant parameters from the measured variables it is common to apply kinetic models to the data. This lecture will focus on the basics of one of the most widespread dynamic MR measurements in oncologic research: dynamic contrast MRI (DCE-MRI) to assess abnormal tumor vascularity. In this MR approach the uptake of an extracellular low molecular weight MR contrast agent (mostly Gd-DTPA) is measured by its effect on the T1 relaxation of the proton spins of water. This effect potentially can be influenced by a number of factors including physiological relevant ones, in particular blood flow, vessel permeability and the size of the extracellular compartment. In another approach called “dynamic susceptibility contrast” MRI the effect of the contrast agent on T2* relaxation is measured. This method is mostly applied to the brain and kinetic models can provide blood volume as one of its useful parameters. These methods are used for diagnostic purposes, but also to assess the effect of drugs, mostly anti-angiogenic drugs on tumor vascularity. In these applications it is important to apply some kind of calibration to eliminate as much as possible systemic and other non-relevant variations. It is possible to interpret the data of effects on water relaxation without a physiological model, but a more advanced analysis applies a physiological pharmacokinetic model to extract relevant parameter values. Numerous variations and refinements of one or two compartment models for DCE-MRI have been proposed [1,2]. The most critical element in these analyses is the determination of the so-called arterial input function, which describes the blood supply by the tumor feeding arteries and allows to derive absolute parameter values. In principle this would calibrate the model output to values that are comparable among different sites, but differences in the MR methods and data analysis, as used in practice, hamper such a comparison. In the evaluation of drugs by DCE-MRI it is important to assess the reproducibility of the applied method.

Relevant Publications:

1. Dynamic Contrast-Enhanced Magnetic Resonance Imaging in Oncology. Springer 2005. Editors A. Jackson, DL. Buckley, GJM. Parker.
2. Sourbron SP, Buckley DL. Classic models for dynamic contrast-enhanced MRI. NMR Biomed. 2013 May 15.

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