Tracer-kinetic analysis of Gd-EOB-DTPA in the liver with a dual-inlet two-compartment uptake model

S. Sourbron[1], W. Sommer[2], C. Zech[2], M. Reiser[2], and K. Herrmann[2]
[1]Ludwig-Maximilian-University Munich, Munich, Bavaria, Germany, [2]Ludwig-Maximilian-University Munich

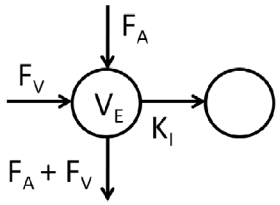

Figure 1. A diagram of the dual-inlet two-compartment uptake model for Gd-EOB-DTPA in the liver. The compartments model the extra-cellular (left circle) and intra-cellular (right circle) space. The model is defined by 4 free parameters: the arterial (F_A) and venous (F_V) blood flow, the extracellular volume (V_E) and the intracellular uptake rate (K_I).

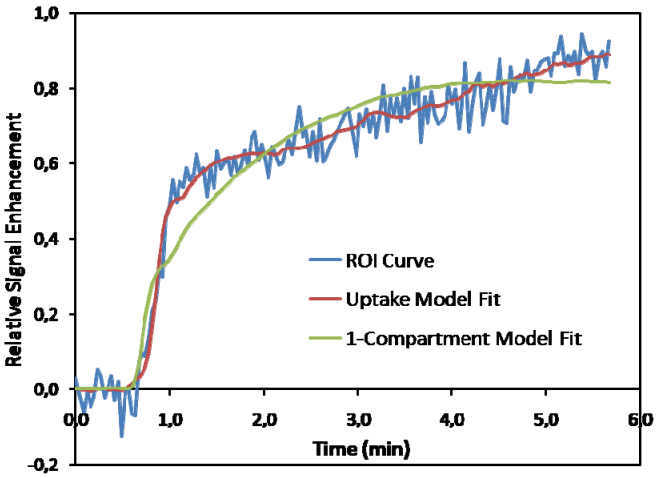

Figure 2. A typical example of a ROI curve in normal appearing liver tissue (blue), a fit to a dual-inlet 1-compartment model (green) and to the dual-inlet 2-compartment uptake model (red). The curve shows a typical bi-phasic behaviour: a rapid early rise corresponding to Gd-EOB-DTPA uptake in the extracellular space, and a slower increase corresponding to the intracellular uptake.

Normal Appearing Liver Tissue	Mean	Sdev
Blood Flow (ml/100ml/min)	110	35
Arterial Flow Fraction (%)	29	14
Extracellular MTT (sec)	12	3.8
Extracellular Volume (ml/100ml)	11	3.6
Uptake Fraction (%)	3.0	1.2
Uptake Rate (10^{-2}/min)	1.7	0.7

Table 1. Means and standard deviations of all parameters, calculated with the dual-inlet two-compartment uptake model for Gd-EOB-DTPA. The intracellular *uptake rate* is a new parameter produced by the uptake model. The intracellular *uptake fraction* is the ratio of intracellular uptake rate to total washout rate out of the extracellular space.

PURPOSE: Liver perfusion can be quantified from bolus-tracking MRI with an extracellular tracer and a dual-inlet one-compartment model [1]. The liver-specific contrast agent Gd-EOB-DTPA is taken up in the hepatocytes, and therefore has the potential to provide an additional and more direct measure of liver function [2,3]. The aim of this study is to develop and validate a tracer-kinetic model for bolus-tracking MRI with Gd-EOB-DTPA. In this first step, the model is evaluated in normal appearing liver tissue.

MATERIALS AND METHODS: A *dual-inlet two-compartment uptake model* was designed, by modifying the single-inlet uptake model used in the brain [4] (figure 1). The result is a direct generalization of the dual-inlet one-compartment model for the liver [1], providing one new parameter: the intracellular uptake rate K_I (min^{-1}). Arterial- and venous delay times were fitted as additional parameters. DCE-MRI data were acquired at 3T (Siemens Verio) in 25 patients using the 3D gradient-echo sequence TWIST (48 coronal slices, 4mm thickness, 192x192 matrix, 2.1sec temporal resolution, 5min acquisition). A standard dose of Gd-EOB-DTPA (Primovist, Bayer) was injected 10 sec after the start of the acquisition at 2ml/s. Patients were breathing freely throughout the acquisition. Data were post-processed using the software PMI 0.4 [4]. Tracer concentration was approximated by relative signal enhancement S/S_0-1. ROIs were drawn on parametric maps of descriptive indices in the abdominal aorta and the portal vein to measure arterial- and venous input functions. In each patient, 5 circular ROIs were drawn on different slices in normal-appearing liver tissue.

RESULTS: All enhancement curves showed the typical bi-phasic pattern illustrated in figure 2. The one-compartment model did not provide a good fit to any of the data, and produced unphysical values for the total blood flow and the arterial flow fraction. The uptake model fitted all data accurately (figure 2), and provided values in the expected range for all known parameters (table 1). After correction for the difference in relaxivity between intra- and extracellular spaces [4], the average value for the new parameter K_I was 1.7 x 10^{-2} min^{-1}, with a relatively narrow range of normality (standard deviation 0.7).

CONCLUSION: These first data indicate that the addition of exactly one new intracellular compartment is both necessary and sufficient to model Gd-EOB-DTPA kinetics in the liver. The method may present a new and practical paradigm in functional liver MRI, producing quantitative measures of both perfusion and hepatobiliary function.

REFERENCES: [1] Hagiwara (2008) *Radiology* **246**: 926-34 [2] Ryeom (2004) *Kor. J Radiol* **5**: 231-9 [3] Nilsson (2009) *JMRI* **29**: 1323-31 [4] Sourbron (2009) *MRM* **62**: 205-17.