Quantitative perfusion measurements of liver metastasis from DCE-MRI using Inversion Recovery TrueFISP

R. Strecker[1], K. Scheffler[2], J. Hennig[3]

[1]MRDAC, Section of Medical Physics, University Hospital, Freiburg, BW, Germany, [2]MR Physics, Dept. of Radiology, University Hospital, Basel, Basel, Switzerland, [3]Section of Medical Physics, University Hospital, Freiburg, BW, Germany

Introduction

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has been widely used to evaluate anti-angiogenic and anti-vascular agents in clinical trials [1]. Data acquisition in DCE-MRI is mostly based on the application of FLASH protocols either as multi-slice 2D or 3D with long repetition times. However, tumors of the liver (or lung) on the one hand show fast Gd uptake kinetics with a time to peak enhancement phase in some cases in the order of ~10-15s, while on the other hand are affected by spatial variation due to patient breathing motion.

We developed a DCE-MRI protocol using an Inversion Recovery trueFisp (IR trueFISP) sequence for DCE-MRI of liver metastasis. The approach is based on the application of an inversion pulse followed by the acquisition of a single 2D slice with a fast repeated data acquisition period to freeze breathing motion. The increased image contrast with a high contrast-to-noise ratio (CNR) between tumor and surrounding healthy tissue allows an accurate tracking of the tumor during breathing. Moreover, T1 quantitation allows direct determination of contrast agent concentration values.

Materials and Methods

Data acquisition: The IR trueFISP sequence was implemented on a clinical 1.5T scanner with a high-speed gradient system (Sonata, Siemens, Erlangen) [2]. The hyperbolic secant inversion pulse covering a thick slab is followed by an arbitrary number of trueFISP image readouts. TE/TR could be optimized to 1.25/2.5ms with fully balanced gradients on all three axes. For a quick transition into the driven equilibrium state an adjustable number of preparation pulses with an linear increasing flip angle increment is used.

To ensure proper sampling of contrast uptake in liver tumors we use a high temporal resolution of 3s and up to 10 images at inversion times between 50 and 1850ms are acquired. Slice thickness is 10mm and inplane resolution is 3.1mm. Collection of 110 time points results in a total acquisition time of 5,5min. A single dose of Gd-DTPA with injection rates between 2-3 ml/s is typically administered using an power injector.

Data analysis: Data analysis is performed using a custom-built software package developed under Matlab 13. The data processing consists of several steps for the accurate determination of concentration values and physiologic parameters:

1. A ROI spanning the metastasis is defined in a precontrast frame for all inversion images and then semi-automatically tracked using a correlation analysis-based algorithm. To minimize through-plane movement during breathing the 2D slice is acquired in a mainly coronal oriented view.

2. T1 quantitation is performed by an external Levenberg-Marquardt (LM) routine written in C using the analytic expression as published [3]. Concentration values are calculated according to $C(t) = (1/T_1 - 1/T_{10})/k_t$, with k_t the relaxivity of Gd-DTPA taken from literature (4.3mmol/ml*s).

3. Pharmacokinetic modeling is done using the multicompartment model of Tofts [4]. Deconvolution is performed with a vascular input function either taken from aortic signal or a template function. The initial area under curve (iAUC) is additionally calculated as a data-driven parameter [5].

4. The pixelwise analysis is performed offline without further user interaction running a matlab script.

Results

An example from an antiangiogenic clinical phase I trial using the IR trueFisp DCE-MRI protocol is shown in Fig. 1 and 2. Color-coded K^{trans} maps as a result from pixelwise analysis are shown in Fig. 1(A-C) pre-treatment, day 2 (d2) and day 28 (d28) after treatment. The corresponding concentration curves averaged over the whole ROI are display in Fig. 2 demonstrating a significant reduction of iAUC at d2 and d28 after treatment. The lower concentration values are concordantly reflected in significantly lowered values for median K^{trans} (0,37 at d28 vs. 0,99 at d0 [1/min]); median iAUC (6,31 at d28 vs 13,1 at d0 for initial 60s [mmol/l*s]).

Discussion

The results demonstrate that the proposed DCE-MRI technique allows the assessment of the effects of therapeutic agents on microvasculature in liver metastasis. The technique using a IR trueFISP sequence offers a high CNR between tumor and surrounding tissue. The custom-built analysis software utilizes a tracking algorithm and needs little user interaction enabling robust tracking of the metastasis even in image series with non-uniform breathing patterns. Gd concentration values are determined from T1 quantitation with a temporal resolution of 3s to provide robust modeling of transfer constant K^{trans} and extravascular extracellular volume fraction Ve.

Further evaluation of the protocol has to be undertaken in comparative studies of IR trueFISP vs. i.e. FLASH.

References

(1) Morgan B, et. al. *J Clin Oncol.* 2003 Nov;21(21): 3955-64.
(2) Scheffler K. *Magn Reson Med.* 2001 Apr; 45(4): 720-3.
(3) Scheffler K. *Magn Reson Med.* 2003 Apr; 49(4): 781-3.
(4) Tofts PS, et. al. *J Magn Reson Imaging.* 1999 Sep;10(3): 223-32.
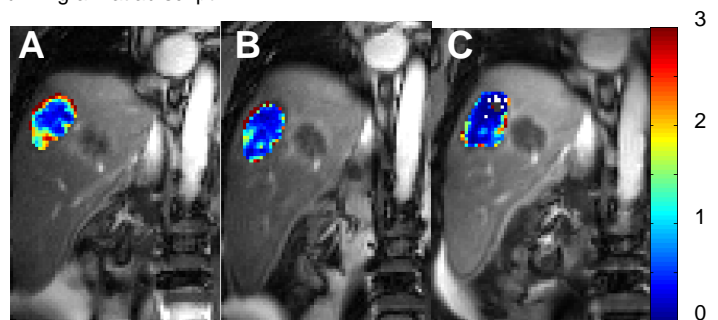(5) Evelhoch JL. *J Magn Reson Imaging.* 1999 Sep; 10(3): 254-9.

Figure 1: K^{trans} maps from a patient with liver metastasis registered to original trueFISP images. A) pre-treatment, B) day 2 and C) day 28 after treatment.
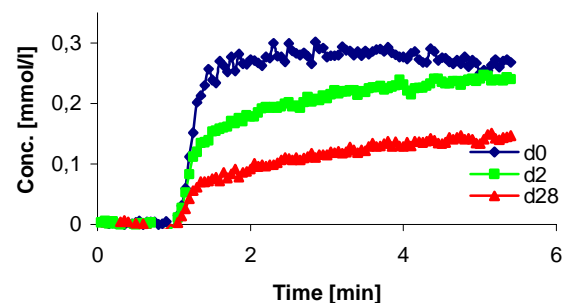

Figure 2: Concentration curves from the same patient averaged over the whole ROI. A strong reduction of contrast agent uptake (iAUC) in the metastasis at d2 and d28 is observed.