Determination of Arterial Input Function in Mouse-Model Using Clinical MRI

B. Keil[1], D. Theis[1], M. Fiebich[2], M. Behe[3], J. H. Figiel[1], K. J. Klose[1], and J. T. Heverhagen[1]

[1]Department of Diagnostic Radiology, Philipps University Marburg, Marburg, Germany, [2]Institute of Medical Physics and Radiation Protection, University of Applied Science, Giessen, Germany, [3]Department of Nuclear Medicine, Philipps University Marburg, Marburg, Germany

Purpose: The aim of this study was to implement a practicable method to estimate an arterial input function (AIF) in mice undergoing dynamic contrast enhanced magnetic resonance imaging (DCE-MRI). Furthermore, the examination of the inter-animal variability of AIF should result in a statement, if it is necessary to acquire an individual AIF for each mouse or if the use of general AIF-model is sufficient[1)].

Material and Methods: 11 serve combined immunodeficiency disease (SCID) mice were kept under anesthesia during the experiments using an intraperitoneal injection of xylazin and ketamine (0.1ml/l0g of solution containing 0.8 ml Rompun™, 1.2 ml Ketavet™, and 8 ml NaCl). A mouse tail vein was catheterized using a 20-gauge cannula. Subsequently the cannula was connected to a 30-cm-long polyethylene catheter. The distal end of the catheter was attached with a 1 ml tuberculin syringe. Catheter and syringe were filled with contrast agent gadolinium diethylenetriaminepentacetic acid (Gd-DTPA) (Magnevist™, Schering, Berlin, Germany), that was diluted in 0.9% saline to a final concentration of 0.06 M.

All images were acquired using a 1.5 T clinical whole body MR scanner (Sonata™, Siemens, Erlangen, Germany). For this system we built a dedicated small animal receive only coil to enhance the signal to noise ratio (SNR) and could therefore decreased acquisition time. The coil was constructed as a linear polarized modified saddle coil which consists of copper stripes supported on a tubular acrylic glass. The length of 10 cm and inner diameter of 4.2 cm allows to place the whole mouse inside the coil. A pixel wise native longitudinal relaxation time (T1) map was derived from a Saturation-Recovery-TrueFisp (SR-TRUFI) sequence[2)] (TR: 8000ms; TE: 5.33ms, FA: 50°, FoV: 67x50mm², matrix: 128x96, SL:1.5mm, voxel size: 0.52x0.52x1.5mm^3, NEX: 1). In addition we monitored the changes of signal intensity of contrast media bolus using a series of Saturation-Recovery-Gradient-Echo (SR-GRE) sequences (TR: 77ms, TE: 4.52ms, TS: 50ms, FA: 90°, FoV: 100x67mm², matrix: 128x96, SL: 1.5mm, voxel size: 0.78x0.71x1.5mm^3, NEX: 1). During the dynamic scan time of 2 minutes, 55 measurements were acquired. This yielded to a temporal resolution of 2 seconds per images. Bolus injection started immediately after 5 native images. All images were acquired in identically located single cardiac short-axis views. The AIF was estimated from the signal intensity changes in blood of the left ventricle (LV) according following formula:

$$C_P(t)=a_f \cdot exp\{-(t-t_0)m_f\} + a_s \cdot exp\{-(t-t_0)m_s\}$$

This double-exponential decay was firstly suggested by Tofts[3)] et al.

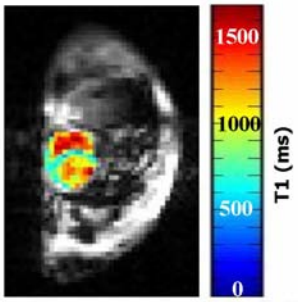

Figure 2: T1-map calculated from SR-TRUFI image series.

Results: The demonstrated method provides MR-images in sufficient qualities, from which an AIF can be estimated in a consistent and repetitive way. A T1-map is shown in Fig.2. The Signal-to-Noise (SNR) ratio and the resolution are adequate to resolve the left ventricle. The mean native T1 value for LV blood was 1.16±0.09 s (n=11). Mean signal intensity changes of the LV obtained from the dynamical SR-GRE series and T1-values were used to calculate the time dependent concentration of contrast agent (Fig.1). The inter-subject variability of three exemplary fitted curves is shown in Fig. 3.

Conclusion: This study has shown a practicable MR-imaging method for determination of AIF in mice. As the considerable inter-animal variability shows, a direct measurement of the AIF is mandatory to avoid significant errors.

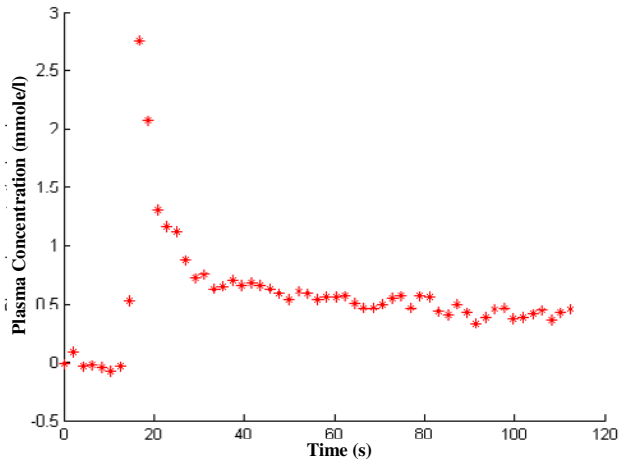

Figure 1: *top:* Time dependence of plasma concentration of Gd-DTPA acquired in the LV blood of mice. *bottom:* Series of dynamic imaging of contrast agent bolus in heart of a mouse.

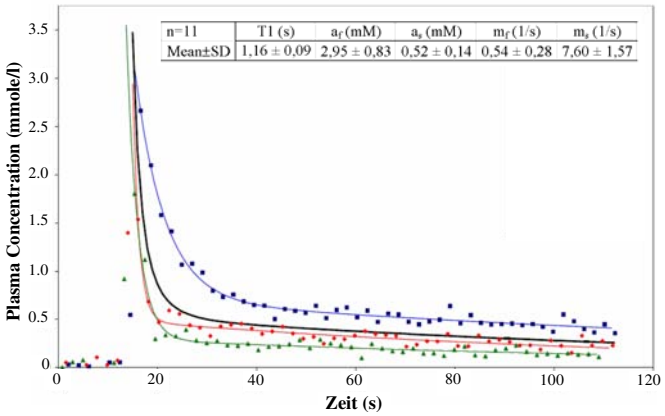

Figure 3: Three AIF examples fitted to a bi-exponential decay. The black solid line is the mean of all measured AIF. *Table:* averaged parameters from fitting procedure of the AIF and T1 measurements.

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