Modeling the Arterial Input Function for Blood Pool Agents in DCE-MRI

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I. Introduction

Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) is a technique to measure the tracer concentration throughout a tissue of interest over time. In combination with pharmacokinetic modelling (PM) these data can provide the clinician with valuable information about tumour vasculature and tumour staging. The simplest pharmacokinetic model for tumour-blood vessel tracer exchange is the 2-compartmental Tofts model [1]:

$$C_t(t) = K^{trans} \cdot \int_0^t C_p(t') \exp\left(-\frac{K^{trans}}{\nu_e}(t-t')\right) dt'$$

The tissue tracer concentration C_t is described in terms of K^{trans}, the transfer constant between tumour and plasma compartment, and ν_e , the interstitial space fraction. Several studies show a strong positive correlation between K^{trans} and histological tumour grade after bolus injection of a blood pool agent (BPA). The arterial input function C_p (AIF) is the tracer concentration in a feeding artery. Though it is difficult to determine in vivo, the AIF is of primary importance for the accuracy of the PM. Until now, the aortic tracer concentration is often used as AIF. For P792 the aortic concentration is modelled as a sum of two degrading exponentials as it is a rapid clearance blood pool agent [2]. The aim of this project is to validate a model predicting the functional form of the AIF for the BPA P792 at different locations throughout the organisms blood stream.

II. Material & Methods

The proposed model subdivides the bloodstream into 3 compartments (Figure 1). The aortic compartment (AC) with volume V1 and concentration C1, depicts the heart and the aorta. The central vascular compartment (CVC, V2 & C2) contains the large branches of the blood stream that are in direct contact with the aortic compartment. Among these are the blood vessels in the principal excretion sites for P792, such as the kidney and the liver. Therefore a linear excretion flux of tracer with time constant K is included in this compartment. The peripheral vascular compartment (PVC, V3 & C3) represents the vasculature that shows a time delay in the supply of tracer (e.g. veins). Between compartments tracer is exchanged through a blood flow F.

To validate the model Wistar Albino Glaxo rats were used as test animals. Concentration-time curves were calculated from the signal intensity (SI) of a Turbo-Flash sequence. 2 rats were scanned in a slice through the renal artery, one after bolus injection, one after a continuous injection (30 s). The results were fitted to the CVC-concentration. 5 rats were scanned in a slice through the femoral artery after bolus injection. These results were fitted to the PVC-compartment. P792 was used as contrast agent . Tracer was injected through a jugular vein catheter into the right atrium (dose D). Furthermore the model impulse responses were examined and compared with literature.

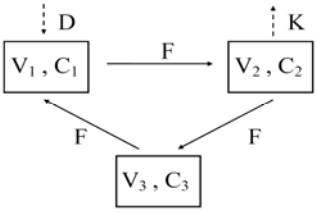

Figure 1: compartmental model of blood stream.

III. Results & discussion

Figure 2 shows measured concentration-time curves in the renal and femoral artery and the corresponding model fits. To validate the model the mathematical and physiological relevance of the fits was examined.

The goodness-of-fit parameter R^2 for all 7 fits is above 86%. The standard errors for the estimated model parameters are less than 25% of the fit values. Hence mathematically, the model is able to predict the concentration course over time. Fitted blood flow values (0.692-1.1 ml s^{-1}) and P792 clearance time constants ($0.591\ 10^{-3}$ – $0.995\ 10^{-3}\ s^{-1}$) are in good accordance with literature [2]. These values show the physiological relevance of the model.

The model impulse response for the AC can be approximated accurately by a sum of 2 degrading exponentials, in accordance with the literature [2]. However, the CVC- and PVC- impulse response is a sum of 3 degrading exponentials. This implies that employing the aortic concentration as AIF can introduce severe errors into the pharmacokinetic modeling.

IV. Conclusion

The model is physiologically relevant and able to predict the functional form of the AIF of P792 at different locations throughout the body.

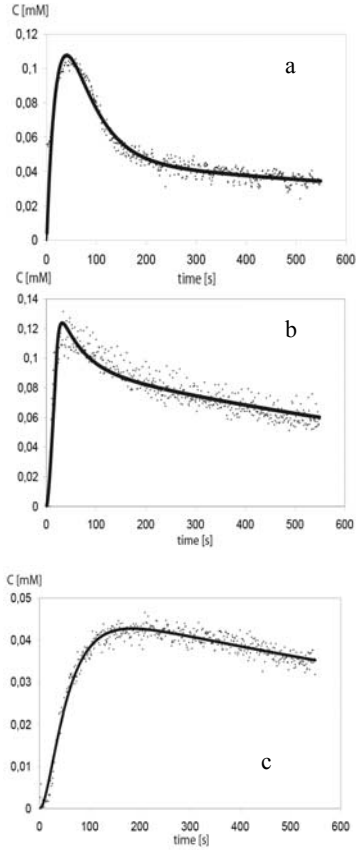

Figure 2: measured concentration-time curves and fits to the compartmental model (full line). a: in renal artery after bolus injection. b: in renal artery after continuous infusion. c: in femoral artery after bolus injection

References

[1] Tofts PS. Modeling Tracer Kinetics in Dynamic GD-DTPA MR Imaging. J Mag Reson Im 1997;7:91-101.

[2] Port M, Raynal I & Meyer D. P792 : a rapid clearance blood pool agents for magnetic resonance imaging : preliminary results.