A New Vascular Impulse Response Function for Modelling and Prediction with Measured Dynamic Contrast Enhanced Plasma Curves

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Introduction Dynamic contrast enhanced (DCE) imaging involves the injection of a contrast agent bolus, during which sequential images are acquired. The blood plasma curve shape is an important component of many modelling approaches for DCE imaging, and models of these curves can be used to produce functional parameter estimates. For predictions or comparisons to be made using plasma curve data obtained with different injection lengths or profiles it is necessary to include the effect of the injection profile on the plasma curve. In this abstract we present a methodology to estimate a vascular impulse response function (VIRF), which is independent of the injection profile, and can therefore be used to perform such predictions and comparisons.

Theory Assuming the distribution of contrast agent behaves as a linear system, the plasma curve is the convolution between the VIRF and the injection profile, typically a rectangle with given height and duration. To estimate the VIRF from noisy data it is necessary to deconvolve the injection profile from the data, but numerical deconvolution is known to be mathematically unstable. The approach taken here is to design a parametric model for the VIRF that can be analytically convolved with a rectangular injection profile giving a plasma curve that can be fitted to the acquired data by adjusting the VIRF parameters. The deconvolution is implicit and so avoids the stability issues of classic deconvolution algorithms. The estimated VIRF can be used to predict the plasma curve obtained with any injection profile, and VIRFs can be compared between data with different injection profiles.

Methods The VIRF is a model of the response of the whole vascular system to a notional impulse injection at the injection site, typically a peripheral vein. Empirically the VIRF requires components describing first pass, second pass and equilibration phases, as specified by

$$c_p(t) = c_B(t) \otimes R_M(t) + c_R(t - t_R) + c_R(t - t_R) \otimes R_E(t) \quad \textbf{(1)}$$

The first term describes the passage of the impulse through the cardio-pulmonary system – $c_B(t)$ models dispersion in the lungs, while $R_M(t)$ is an impulse response to model mixing through the heart. $c_R(t)$ describes the recirculation phase and includes a delay t_R, while $R_E(t)$ is an impulse response modelling reflux of contrast from the whole-body extra-vascular space. This reflux will start to appear in the region of interest at the same time as the second pass, so this equilibrium phase term is modelled as the convolution between $c_R(t)$ and $R_E(t)$. In principle there will also be further recirculation phases, but these have low amplitude and are rarely observed in in-vivo data. This model is an extension of that described in [1], and bears similarities with a heuristic model in [2]. $c_B(t)$ and $c_R(t)$ are modelled with raised-cosine functions [1] of the form $a(1 - \cos(\mu t))$ for $0<t<2\pi/\mu$. The mixing impulse response has unit area and is given by $R_M(t) = \mu_M \exp(-\mu_M t)$, while the equilibration phase has non-unit area, $R_E(t) = a_E \exp(-\mu_E t)$. The VIRF is thus defined by eight parameters: a_B, μ_B, μ_M (first-pass) a_R, μ_R, t_R (second pass), μ_E and a_E, and in principle these will be independent of the injection profile. To model image data from a suitable vessel the VIRF is convolved with the injection profile $I(t)$. If a power injector is used then the injection profile will be a rectangular function with known duration and amplitude. A key property of these model functions is that all the convolutions can be analytically calculated using only trigonometric and exponential functions. The data model is

$$d_n = f(c_p(t_n - t_0) \otimes I(t)) + \varepsilon_n \quad \textbf{(2)}$$

with t_n the imaging times, $f(\cdot)$ a function relating contrast concentration and image intensity changes, t_0 an estimated delay term, ε_n are noise terms and $I(t)$ is the injection profile. Parameters are estimated using least-squares fitting.

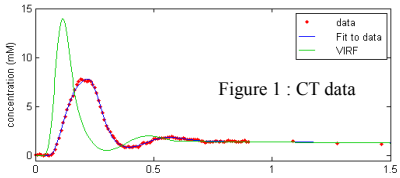

Figure 1 : CT data

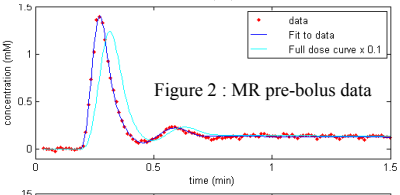

Figure 2 : MR pre-bolus data

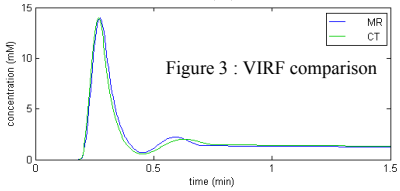

Figure 3 : VIRF comparison

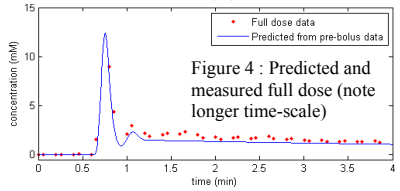

Figure 4 : Predicted and measured full dose (note longer time-scale)

Data Acquisition Dynamic data sets containing plasma curves were obtained from patients using CT imaging followed two hours later by MR imaging. Axial CT data (GE lightspeed 16) were acquired using a breath-hold protocol consisting of a 55 second breath-hold during which 4 slices were acquired every 0.5 seconds, followed by 12 images acquired every 11.2 seconds under sequential breath-hold, total acquisition time = 3.5 min. A power injector was used to deliver 0.5 ml/kg of Omnipaque contrast agent at 4 ml/sec. Data taken from an ROI inside the aorta are shown in figure 1, and for this example 38 ml was delivered in 9.5 sec – note the figure shows the first 1.5 min only. Two dynamic data sets were acquired during the MR imaging (Seimens Avanto, 1.5T), the first a pre-bolus measurement designed to measure the aortic plasma curve using a small contrast injection, the second a standard dynamic acquisition to measure the tissue response. The pre-bolus data used a single coronal slice positioned over the descending aorta and a GE sequence with 0.7 sec temporal resolution, TR/TE/FA = 5.5ms/1.21ms/20°. Data were acquired for 4 mins, and at the start 0.02 ml/kg ($1/10^{th}$ the standard dose) of Gd-DTPA contrast agent was delivered with a power injector at 3 ml/sec. To enable concentration quantification, pre-contrast images were acquired with the same TR/TE and FA = 3°, NSA = 60. Data taken from an ROI in the aorta are shown in figure 2, and for this example 1.5 ml was delivered in 0.5 sec. Approximately 10 minutes after these data were obtained a second dynamic data set was obtained with 14 slices using a 3D GE sequence TR/TE/FA = 3.05ms/0.88ms/16°, during which 0.2 ml/kg of Gd-DTPA was delivered at 3 ml/sec – in this case 15.2 ml in 5.1 sec. A sequential breath-hold scheme was used [3] where two image volumes were acquired during a 6 second breath-hold followed by a 6 second breathing interval, data are shown in figure 4. Breath-hold pre-contrast quantification images were also acquired with FA = 3°, NSA = 4.

Results The figures show results of applying the proposed modelling approach to CT and MR data acquired from one patient. Figure 1 shows the dynamic CT data and the curve fitted using equation (2). The green curve is the corresponding VIRF, and as expected this is narrower and taller than the measured curve. It is clear that the proposed model has an appropriate complexity to describe all salient features in this data. Figure 2 shows the pre-bolus MR data, and since the injection only lasts 0.5 sec the VIRF shape is virtually indistinguishable from the data fit curve, so we omit this from the figure (the scaling is indicated in fig. 3). The light blue curve shows the predicted full-dose curve, scaled by a factor of 0.1 to enable easy comparison, and as expected this curve is wider than the pre-bolus curve. Given the different injection durations it is clearly not appropriate to compare the acquired data directly, and this is obvious from the figures. Instead we can compare the VIRFs obtained in each case, and this is shown in figure 3, where a good correspondence is clear. The main difference is in the recirculation, which may be because the effective SNR for this part of the curve is worst, or may be due to physiological differences (e.g. different heart-rate) between the two acquisitions. Finally in figure 4 the full-dose curve predicted using the pre-bolus data is compared with a measured curve obtained using the full dose injection – the predicted curve has been manually shifted in time to best match the data. In this case the temporal resolution is insufficient to confidently capture the peak concentration, and the predicted curve suggests that the peak falls between data points. The overall amplitude of the data is higher than the predicted curve, and this is probably due to acquisition effects, such as flip-angle errors, flow effects or signal saturation due to large concentrations (this sequence was designed to give a linear response for typical tissue conc., i.e. < 2mM).

Conclusions We have presented a model and methodology for estimating a vascular impulse response function that can be used for comparison and prediction of plasma curve shapes under different injection conditions. This has been demonstrated on an example comparing two MR and one CT measurements. Our intention is to compare the qualities of the two imaging methods for measuring plasma curves using the whole study, for which the methodology presented will be essential.

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[1] Orton MR, et. al., *Phys Med Biol.* 2008; **53**(5):1225-39. [2] Parker GJ, et. al., *Magn Reson Med.* 2006; **56**(5):993-1000. [3] Orton MR, et. al., *Phys Med Biol.* 2009; **54**(5):2197-2215.