

Tissue estimated vascular input functions improve DCE-MRI model fitting

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Introduction

Dynamic contrast enhanced (DCE) imaging allows for the characterization of vascular tissue properties, such as K^{Trans} and extra cellular volume. To model the pharmacokinetic (PK) behaviour of the injected contrast agent, it is necessary to estimate or measure the arterial input function (AIF) of the imaged region. To reduce the variability in a measured AIF, a population AIF is often used, where the AIF is derived from multiple measurements within a group of patients [1]. Using prostate DCE-MRI data we compared the performance of a published population (*PP*) input function [2] against tissue extracted input functions obtained using methods previously outlined [3]. Both patient specific tissue extracted (*PST*) AIFs and a derived tissue cohort (*DTC*) AIF were used as a comparison. The pharmacokinetic behaviour was modelled using the extended Kety model [4] and the results compared with histological slides.

Methods and Materials

Data from twelve prostate cancer patients were studied. Following prostatectomy a tissue slicer was used to slice the whole prostate gland, base to apex, into equally spaced cross-sections of 4mm perpendicular to the posterior surface of the gland. After processing, tumour within the gland was outlined by an experienced histopathologist. MR data were acquired from an endorectal coil on a 1.5 Tesla Philips Intera scanner. Dynamic images were acquired with a double dose bolus of Gd (0.2 mmol/kg) using the following parameters: TR 4.1ms, TE 1.77ms, flip angle 30°, 90 timepoints, 8x5mm contiguous slices, temporal resolution 3.52s. Dynamic slices containing histologically identified tumour were analysed using the in-house software tool MRIW, in which the acquired data are first transformed to give estimates of the tracer concentration using established methods [5]. The data modelling makes use of a cosine modelled AIF function based on 4 parameters [6]. A cosine form of Parker's [2] population input function was used, and patient specific tissue AIFs derived from the prostate tissue were obtained from ROI's containing the whole prostate. A stratified optimisation procedure was used to simultaneously estimate tissue parameters and AIF parameters [3]. The AIF amplitude was determined by scaling the estimated curve to match the plasma concentration measured by Parker [2] 4 minutes post onset. The median of the individual AIFs was taken to define a cohort AIF. Prostate tissue AIFs were successfully extracted in 10 of the 12 cases examined. In two cases the analysis failed to converge on a solution. Kinetic parameter maps (K^{Trans} , v_e , v_p and kep) were estimated by fitting the tissue data with the extended Kety model [4], driven by the three input functions. An efficient analytic implementation of the convolution was used in the curve-fitting procedure to ensure rapid, accurate parameter estimates.

Results

All three input functions fit the data well with a small residual sum of squares. The resulting K^{Trans} parameter maps show good visual agreement with histological slices, see figure 1 for an example. All *PST* AIFs were more dispersed in the first pass section compared to the *PP* AIF, and had significantly reduced fitting residuals (-10%, $p < 0.05$). Consequently the *DTC* AIF is also more dispersed than *PP* AIF, see figure 2. The use of *PP* input function frequently produced lower estimates of V_p when compared to both the *PST* and *DTC* input functions, see figure 3. The tissue derived input functions resulted in more similar estimates of K^{Trans} across patients, using both the *PST* and *DTC* AIFs. The standard deviation of the K^{Trans} measurements was 0.1, 0.05 and 0.06 min^{-1} for the *PP*, *PST* and *DTC* AIFs respectively.

Discussion and Conclusions

In all cases the *PST* AIFs extracted from the prostate gave a reduced residual sum of squares compared to the *PP* approach. The additional dispersion of the first pass of the tissue extracted input functions (*PST* and *DTC*) appears to result in better estimates of V_p and a more consistent estimate of K^{Trans} . Our findings suggest that the performance of PK modelling can be enhanced by using tissue derived AIFs on a per patient basis. The reduced variability in K^{Trans} estimates could prove particularly important in a clinical trials setting where reproducibility of measurements is key.

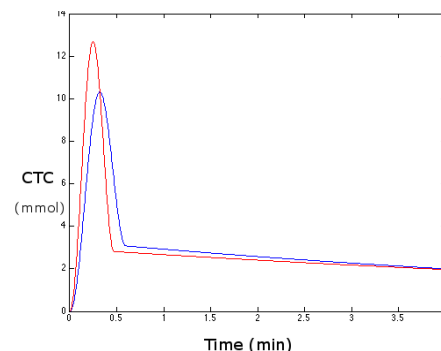


Figure 2. Cosine form of AIFs. Published population (*PP*) AIF (red) and derived tissue cohort (*DTC*) AIF (blue).

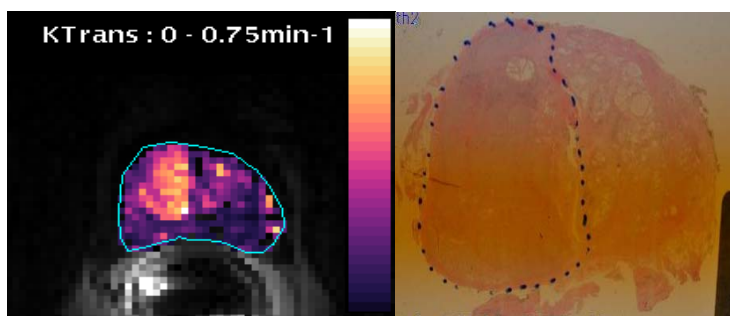


Figure 1. Parameter map and histology slice from an example patient, using a patient specific (tissue) AIF. Increased K^{Trans} is highly correlated with the tumour region.

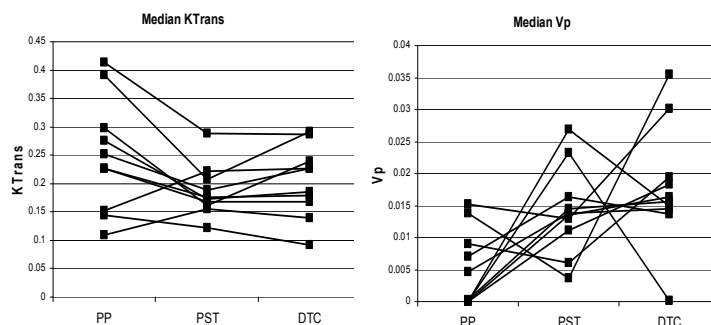


Figure 3. Median K^{Trans} and V_p parameters obtained from 10 prostate datasets using three alternative AIFs: published population (*PP*), patient specific tissue (*PST*) and derived tissue cohort (*DTC*)

References

[1] Wang Y, et al. Magn. Reson. Med. 59(5), 1183-9 (2008), [2] Parker GJ, et al. Magn Reson Med 2006, 56:993-1000, [3] Orton M, et al. In. Proc. ISMRM 3498 (2007), [4] Tofts P 1997 J. Magn. Reson. Imaging 7 91-101. [5] Dynamic Contrast Enhanced MRI in Oncology, A. Jackson, et al. Springer, 2005, [6] Orton MR et al 2008 Phys. Med. Biol. 53 1225-1239 We acknowledge the support received from the CRUK and EPSRC Cancer Imaging Centre in association with the MRC and Department of Health (England) grant C1060/A10334, also NHS funding to the NIHR Biomedical Research Centre