Physiologically Based Multiple Reference Tissue Method (PB-MRTM) for Arterial Input Function (AIF) Estimation

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Introduction: We previously proposed a multiple referent issue method (**MRTM**) (1-2) which uses an iterative curve fitting approach to simultaneously calculate kinetic parameters and an AIF in 2 or more reference tissues by assuming that their AIFs have the same shape with a possible difference in the bolus arrival time. Normal tissues and/or tumor sub-regions segmented from tumor ROI can be used as reference tissues (2). The previously presented MRTM uses a blind identification method (2-3) to reconstruct the AIF, where no functional form is assumed for the AIF. This leads to less satisfying performance in data with low SNR and temporal resolution (2). We now incorporate a physiologically based AIF reconstruction method into the MRTM (**PB-MRTM**).

Materials and Methods: Distribution of contrast agents used in DCE-MRI or other imaging modalities is similar to small drug distribution, for which previous pharmacokinetic models predicting the AIF from the injection profile and physiologic parameters such as the cardiac output (**CO**) have been described (4). PB-MRTM combines the MRTM concept with those pharmacokinetic models; the AIF is estimated by iteratively searching for the set of physiologic parameters whose corresponding AIF gives the best fit to the measured reference tissue data, and the final set of physiologic parameters estimated are then used to construct the final AIF.

We apply the PB-MRTM to CT and MRI data acquired on the same day from the pelvic regions of 20 cervix cancer patients. Two axial slices of CT images were scanned at the rate of 1/s for 120s and then 1/15s for 120s after injection of iohexol 300 (1.5ml/kg, 4ml/s). Six axial slices of MRI images were scanned on a GE 1.5T MR scanner using 3D GRASS at the rate of 1/7.5s for 450s after injection of gadodiamide (0.1mmol/kg, 2ml/s). In both CT and MRI data, the AIF was estimated by the PB-MRTM using muscle and tumor sub-regions and compared to the AIF measured directly from the signal in the external iliac artery (EIA). With an AIF, we can infer the CO since the area under the first pass of the AIF is proportional to the amount of contrast agent injected, and inversely proportional to the CO (4).

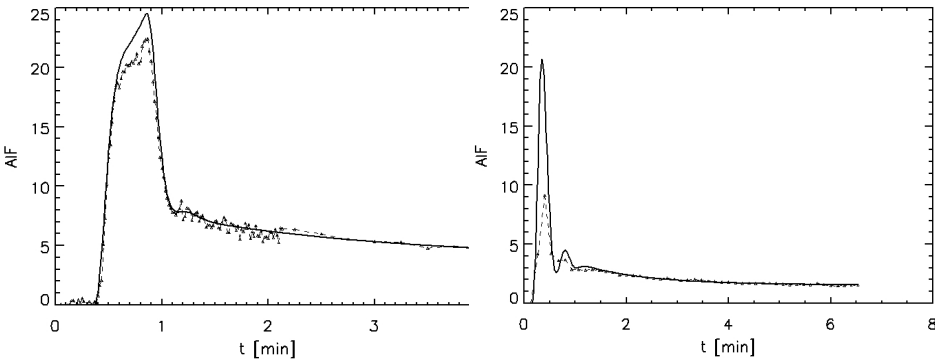

Figure 1. The AIF estimated by PB-MRTM (solid lines) compared with the AIF measured from arteries (dashed lines). (**a**) CT data (**b**) MRI data from a representative patient. The cardiac output (CO) estimated from the CT AIF was 5.7 l/min. In MRI data, the CO calculated from the AIF directly measured in arteries was 10.6 l/min; while the CO calculated from the AIF estimated by the PB-MRTM was 5.5 l/min, close to the CO calculated from CT AIF.

Results: In CT data, the difference between the local AIF estimated by the PB-MRTM method and the remote AIF directly measured from the EIA was generally small (Fig. 1a). In MRI data, the AIF estimated by the PB-MRTM matched well with the AIF directly measured from the EIA in the washout phase, but had much higher first pass peaks (Fig. 1b). Using the pharmacokinetic models (4), we fit CO from the EIA measured AIF in MRI data and observed that they were unrealistically large, generally exceeding 10 l/min; meanwhile, the CO simultaneously estimated by the PB-MRTM were very close to the typical CO for patients at rest, generally in the range of 5-7 l/min. In addition, the CO estimated by the PB-MRTM from the MRI and CT data of the same patients were very close to each other (Figure 1).

Conclusions and Discussions: The good match between the AIF estimated by the PB-MRTM and the AIF directly measured from the EIA in CT data, as well as that the CO estimated by the PB-MRTM from CT and MRI data were both realistic and close to each other suggest PB-MRTM can give an accurate estimate of the AIF. The AIF directly measured from arteries in MRI might be inaccurate, indicated by that the inferred CO was unrealistically large, this is likely due to the under-estimation of the first pass due to artifacts including T2* effect, in-flow effects in DCE-MRI.

References: 1. Yang C *et al*, MRM 2004; 52: 1110-1117. 2. Yang C *et al*, MRM 2007; early view. 3. Riabkov DY and Di Bella EV, IEEE Trans Biomed Eng 2002; 49:1318. 4. Krejcie TC *et al*, J Pharmacol Exp Ther 1996;278:1050-1057.