A comparison between arterial input function approaches for high temporal resolution pharmacokinetic analysis of prostate cancer at 3.0T

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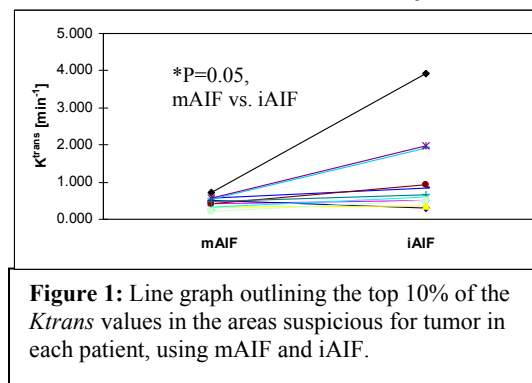
Introduction: Pharmacokinetic (PK) analysis allows for quantification of dynamic contrast enhanced (DCE) MRI data, as a method of detecting and quantifying underlying abnormal tumor vascular physiology. The two-compartment model most commonly used is based on the principles of Kety, where low-molecular-weight contrast is thought to diffuse from the vascular space into the extravascular extracellular space, and then slowly leak back into the vascular space. The archetype of the two-compartment model is the Generalized Tofts Model. This requires knowledge of the Arterial Input Function (AIF), the temporal contrast agent concentration in the feeding artery (femoral artery for the prostate). Accurate individualized AIF (i-AIF) taken in the femoral artery yields more patient specific PK parameters, but suffers from inter- and intra-observer variability, in-flow effects, and B1 inhomogeneities. A model-based AIF (*1) has been used in DCE analysis of ovarian cancer (*2), and also in prostate cancer at a limited temporal resolution (*3). In this work, we present the results using both i-AIF and model-based population averaged AIFs (m-AIF) for high temporal resolution DCE MRI analysis at 3T. The objective of this work is to determine the variability in PK analysis using m-AIF and i-AIF by comparing their performance in areas suspicious for prostate cancer on endorectal prostate MR at 3.0T.

Material and Methods: PK analysis was performed using both i-AIF and m-AIF in 13 patients who were enrolled in a prospective study approved by the institutional review board. All patients had elevated PSA (mean ± SD=14.22 ±15.6 ng/ml) and underwent endorectal prostate MR at 3.0T. At the time of prostate MR imaging, 4 patients had recent biopsy proven cancer. 9 patients were clinically suspected of having prostate cancer, and subsequent to the MR they had an MR-directed prostate biopsy (7 patients) or a radical prostatectomy (2 patients), the pathology results of which were also available at the time of this analysis.
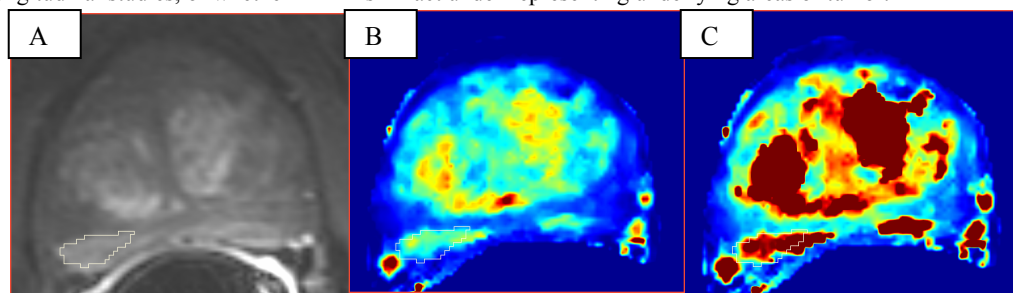
DCE was performed with 3D-Fast spoiled gradient (FSPGR) using: 26 cm FOV; 6mm slice thickness; 256x160 Matrix; contrast (Gadolinium gadopentetate (Gd)) injection rate of 3ml/sec; slab thickness 16-20 slices, 5 sec/slab, 60 temporal phases, with a total scan time of 5 minutes. i-AIFs were individually measured from voxels in the femoral artery on the slice of interest, and m-AIF PK maps were also obtained using a population averaged bi-exponential AIF. Analyses of the slices of interest were performed using both i-AIF and m-AIF using Cinetool (GE Global Research), and transported into 3D Slicer (www.slicer.org). An ROI suspicious for tumor was contoured on raw DCE images using 3D Slicer, after review of all multiparametric image sequences (including T2 and Diffusion) and of the tumor location on pathology. For each outlined ROI, the mean prostate T_1 was assumed to be 1597 msec (*4) and the mean signal intensity changes from the DCE images were used to calculate the estimated Gd concentration as a function of time. The mean of the top 10% ("hot spot") PK values of K^{trans} (forward value transfer constant) and the K_{ep} (reverse reflux rate constant between extracellular space and plasma) within the ROI were obtained.

Results: Suspicious areas with pathological correlates were contoured by one radiologist in 13 patients. 2 patients were excluded due to significant prostate motion during the DCE acquisition. Prostate cancer was confirmed by pathology in 7/11 patients (4 by biopsy, 3 by radical prostatectomy), and 4/11 false positive cases were identified with no cancer at biopsy. Mean prostate K^{trans} values obtained were significantly different using m-AIF and i-AIF, with a mean ±SD of 0.462±.12 min^{-1} vs. 1.136±1.09 min^{-1} respectively (P=0.046, 2-tailed paired t test). Mean K_{ep} using m-AIF were 1.84±.88 min^{-1}, and 2.39±1.28 min^{-1} using i-AIF.

Figure 1: Line graph outlining the top 10% of the *Ktrans* values in the areas suspicious for tumor in each patient, using mAIF and iAIF.

Conclusion: Explicit AIF measurement from patient femoral arteries yields different derived PK results to mAIF, likely due to B1 inhomogeneity in i-AIF analyses (known to be more problematic at 3T), and flow-induced signal artifacts, prominent in the axial imaging plane which is standard for visualization of the prostate anatomy. Even though m-AIF does not account for patient specific uptake differences in flow and cardiac output, it yields less variable PK analysis results. Further studies are required to determine if mAIF will allow for more robust comparisons in longitudinal studies, or whether mAIF is in fact under-representing underlying areas of tumor.

Figure 2: (A) Early phase DCE image depicting enhancement in the right peripheral zone of the prostate. This ROI is outlined using 3D Slicer. The corresponding K^{trans} maps of the ROI using mAIF (B) and iAIF (C). The highest 10% K^{trans} values ("hot spot") in these ROIs were calculated.

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*3. Meng et al. Acad Radiol. 2010 Apr;17(4):520-5. *4. de Bazelaire et al. Radiology 2004; 230(3): 652-9.