

# Independent component analysis based identification and pharmaco-kinetic-modeling of prostate tumor DCE-MRI concentration data

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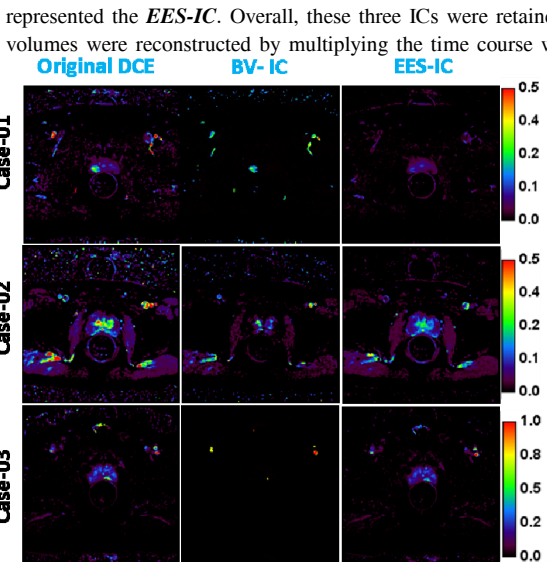
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**Introduction:** Dynamic contrast enhancement (DCE) imaging is used for studying tumor micro-vascular changes and evaluating efficacy of anti-angiogenic therapies. Pharmacokinetic (pK) modeling of DCE data is used to quantify tumor vascular properties in terms of: permeability and leakage coefficient ( $K^{trans}$ ), extra-vascular extracellular compartment (EES) fraction ( $v_e$ ) and plasma fraction ( $f_{pv}$ ) [1]. pK parameters depend on flow, endothelial surface area, permeability and blood volume. As such, pK model is over-simplified and cannot account for all these factors. Models attempting to account for all these factors can result in increased accuracy [2], albeit with unstable behavior due to noise. A method to separate these effects would be desirable for robust pK maps and clinical interpretation. Independent Component Analysis (ICA) allows blind separation of underlying sources from a mixture dataset. Previously, ICA has been used to remove artifacts in DCE images [3], improve tumor boundaries [4,5] and identify arterial input function [6,7]. Most of the previous work with ICA-DCE-MRI is however limited to using raw MRI signal data and interpretation of multiple components generated using ICA is not completely explained. Here, we describe ICA analysis on DCE-MRI concentration data in prostate and its utility in separating the blood volume and permeability components and removing artifacts, thereby improving fidelity of pK maps.

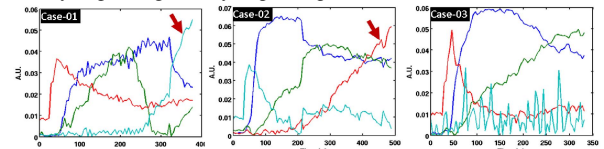
**Materials & Methods: Patient Data:** Data were acquired from seven prostate tumor patients.

An appropriate IRB approved the studies. **Imaging:** The datasets were obtained on a 1.5T GE Signa Genesis and 3.0T GE Signa HDx clinical scanners (GE Healthcare, Waukesha, WI). The protocol was: axial slices, 3D FSPGR, EIS TORSO coil, TE/TR = 1.3/3.8 ms, FA = 15°, TH = 6 mm, 256x256 matrix, 260 x 260 mm<sup>2</sup> FOV, 0.1 mmol/kg Gd-DTPA was injected intravenously at 0.3 cc/sec for 100 seconds, 50-65 bolus volumes (~4.5 s/ volume) in 3-5 mins. **DCE data**

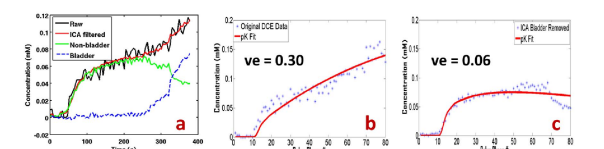
**analysis:** Analysis was performed using automated in-house tool developed for pK modeling using ITK. Signal data was converted into concentration units using the baseline images and fixed tissue specific  $T_1$  values (1317ms at 1.5T, 1597ms at 3.0T). Concentration data was fit to two-parameter ( $K^{trans}$ ,  $v_e$ ) and three-parameter ( $K^{trans}$ ,  $v_e$ ,  $f_{pv}$ ) Tofts model using a population based AIF [8]. **ICA:** JADE-ICA [9, 10] was applied to concentration data to obtain spatially independent components (sources). To ensure that spurious spikes did not affect the ICA separation, we removed voxels with maximum concentration exceeding 1mM. Previously 6 to 10 components have been used for DCE-MRI ICA [5, 6]. We initially hypothesized that DCE data primarily consists of blood volume component (BV-IC) and permeability/EES component (EES-IC) along with noise, and so started with 3 components for ICA. However, we observed that four ICs were needed in most cases, so that a late recirculation IC could be separated well. After the late recirculation IC and BV-IC sources were identified, the remaining two ICs were added and represented the EES-IC. Overall, these three ICs were retained. Each IC comprised of a time course and a spatial distribution map. Individual IC component 4D



**Figure 3.**  $K^{trans}$  (min<sup>-1</sup>) maps for ICs in different cases. BV-IC clearly highlights the elevated  $K^{trans}$  regions as observed in original  $K^{trans}$  maps.



**Figure 1.** The four IC time-courses in three cases. In cases (01 and 02) with significant bladder slices, a recirculation IC is noticed at ~200s from earliest contrast arrival (see arrows).



**Figure 2.** (a) Concentration curve in vicinity of bladder is corrupted due to partial volume. ICA separation allows this to be rectified. The fit to both the voxel (b) before and (c) after ICA based filtering

volumes were reconstructed by multiplying the time course with the spatial map. pK modeling as described above was performed for the BV-IC and EES-IC 4D volumes. **Results and Discussion:** Fig 1 shows the ICs in three representative cases. Notice that the curve intensities have arbitrary units and need to be scaled by spatial maps to obtain concentration curves for each IC. We observed that BV-IC rises first, followed by EES-IC (~ 15-20 s after BV-IC). Except for one case (Case-03, Fig.1), we observed a characteristic recirculation IC at ~ 200s post BV-IC. Further investigation revealed the source of this curve to be the contrast filling in the bladder and was confirmed by correlating with bolus arrival signal in bladder. We observed that voxels in the vicinity of the bladder were corrupted by this delayed circulation due to partial volume effects (Fig 2a). ICA was able to reliably separate the bladder recirculation from true pK dynamics (Fig 2b,c). In Case-03, only a single slice of bladder was present and hence no recirculation peak was observed (Fig 1). Fig 3 shows the  $K^{trans}$  map obtained in a regular data set with two parameter model with no ICA performed (left column) and using BV-IC (middle column) and EES-IC components (right column). We noticed that ICA performs very good delineation of high blood volume compartment.  $f_{pv}$  map was also elevated in regions of BV-IC, almost zero in EES-IC. Appropriate model selection (2-param or 3-param) for a given tissue voxel has been considered as way to obtain reliable quantification with DCE-MRI data. The BV-IC can provide a spatial map of regions where the 3-parameter pK model can be used to describe the data without compromising on fitting accuracy or increasing noise susceptibility. In cases where pK model parameters are used to study the progression of a tumor, IC maps can be used to understand which component of tumor vasculature responds to treatment. This can enable better differentiation of patient/tumor population. **Conclusions:** We have demonstrated the utility of ICA for removing artifacts, obtaining improved pK model parameters as well as distinction of elevated blood-volume regions in prostate tumor DCE data. The method can also be used for appropriate pK model selection and gain a better understanding of tumor response to therapy.

**References:** [1]. Tofts PS, 1997, JMRI, 7(1), 91-101. [2]. Lawrence ST et al., J. Cereb Blood Flow Metab 18:1365-77. [3]. Martel AL, et al., 2008, MRM, 59(4), 874-884. [4]. Wu XY, et al., 2007, Medical Image Analysis, 11(3), 254-265. [5]. Koh TS, et al., 2008, JMRI, 28(1), 271-277. [6]. Mehrabian H, et al., 2013, IEEE Trans Med Imag, 32(4), 699-710. [7]. Mehrabian H, et al., 2013, IEEE ISBI. [8]. Morgan et al., Br. J Cancer 2006;94:1420-1427; [9]. Cardoso J-F, et al., 1993, IEE Proceedings F, 140(6). [10]. <http://perso.telecom-paristech.fr/~cardoso/Algo/Jade/jadeR.m>