Spatial Information based DCE-MRI Data Reconstruction and analysis using PCA

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Introduction: Dynamic and 4D MRI have been used to understand the functional and metabolic aspects of disease and its progression. Examples include dynamic contrast enhancement (DCE) for micro-vasculature of tumors and MR spectroscopic imaging (MRSI) for tissue bio-chemistry. The post-processing strategy for most of these protocols consists of obtaining parametric maps using ***voxel-by-voxel*** estimation of the model parameters describing the data (e.g. pharmaco-kinetic (pK) model for DCE data [1]). The problem with this approach is that model fits are poor due to noise from variety of sources: *patient motion, systemic noise and fluctuations.* Ultimately, this results in "pixelated" maps even within a homogenous tissue. Smoothening with simple one-dimensional filter changes the shape of enhancement curves and is not desirable. Recently there has been an increased interest in using spatial prior data and overlapping information for processing of dynamic MRI data, thereby improving the confidence in quantification [2, 3, 4]. Previously, a principal component analysis (PCA) based method was described for SNR improvement in DCE data, which considered entire ensemble of dynamic 4D data [5]. However, spatial data fidelity is being increasingly recognized as critical for accuracy of information derived from DCE data [4]. Therefore, in this work we investigated a block-wise PCA based approach to reconstruct the DCE-MRI data using the neighborhood information, to separate noise from true contrast enhancement while preserving the tissue heterogeneity in reconstructed maps. We demonstrate marked improvement in data fitting fidelity and improved lesion conspicuity using this approach. The results are presented in DCE phantom as well as prostate cancer cases. **Methods and Materials: Phantom**: The DCE-phantom as described in [3] was used for evaluation errors introduced due to the reconstruction strategy being adopted in the study. **Patient Data:** Data for our study were acquired from two patients with prostate tumor patients. An appropriate IRB approved the study. **Imaging**: The datasets were obtained on a 1.5T GE Signa clinical scanner. The protocol was: Axial slices, 3D FSPGR sequence with EIS TORSO coil, TE = 1.3 ms, TR = 3.8 ms, FA = 15°, TH = 6 mm, matrix size = 256 x256 , FOV = 260 x 260 mm2, 0.1 mmol/kg Gd-DTPA was injected i.v at 0.3 cc/sec for 100 seconds, 30-80 bolus volumes (~4.5 s/ volume), in 3-5 mins. **DCE data analysis**: The entire analysis was performed using completely automated in-house tool developed for DCE analysis within the ITK framework [6]. The DCE signal data was converted into concentration units using the baseline images and fixed tissue T_1 = 1317 ms. The concentration curves were then analyzed on voxel-by-voxel basis to obtain the semi-quantitative (e.g. **Bolus arrival time (BAT), Max-slope**) parameters. Next the DCE concentration data was fit to two-parameter Toft model using non-linear Levenberg-Marquardt procedure to obtain $\mathbf{K_{trans}}$ and $\mathbf{V_e}$ estimates [1]. The R^2 value of the fit was also recorded to measure the fidelity of the fitting procedure. **Single Voxel analysis (SVA):** The data analyzed as above for each curve on voxel-by-voxel basis was termed as single voxel analysis (SVA). **PCA-Reconstruction**: In this work we used a block based approach to obtain a reconstructed curve using PCA at any given voxel location. The methodology was as follows: Given a voxel at location V(x, y, z), we sweep the entire 3D neighborhood of this voxel till all the neighborhoods have visited the given voxel at least once [Fig.1]. At each sweep, the curves are stacked in a matrix. For a 3x3x3 neighborhood used in our study, each sweep results in 27 curves. Next, PCA is performed on the set of these 27 curves and first two components with largest variance are selected for reconstruction. This number was arrived, based on visual inspection of reconstructed curves with different variance components, though a more sophisticated cut-off can be used [5]. The PCA reconstructed curve per sweep is stored. Post all sweeps per voxel, the resulting curve for that voxel is computed as the median of the stacked PCA reconstructed curves. The PCA based offline reconstruction was performed in MATLAB. The parameters from the resultant curve per voxel were obtained as described in ***DCE data analysis*** section. **Statistical analysis:** The semi-quantitative and pK model parameters were tested for statistical significance between SVA and PCA-based methodologies. Analysis was performed using ANOVA tool provided in MedCalc software. We separated the curves with poor SVA fit ($R^2 < 0.8$) to see if the PCA based recon improves the fit.

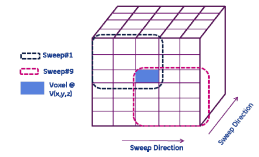

Figure 1. A cuboidal neighborhood mapped during each sweep at given voxel (blue)

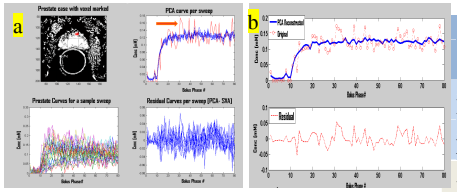

Figure 2. The curves at a given voxel location are stacked to provide a reliable PCA-recon. The red curve shown by bold red arrow in (a) indicates the noisy curve at given voxel.

Table 1. Parameters from two patient studies

Parameter	BAT	Max-slope	K_{trans}	V_e	R^2
Mean_SVA	49.22	0.0117	0.073	0.15	0.77
Mean_PCA	43.99	0.0063	0.068	0.15	0.91
Mean_SVA	41.21	0.0115	0.126	0.32	0.89
Mean_PCA	38.81	0.0095	0.123	0.32	0.93

Results: PCA based reconstruction did not introduce any errors [residual error due to reconstruction = 0] for a uniform voxel placed in the phantom. As seen in Fig.2 a and b, PCA based reconstruction of the dynamic curve at a given voxel is smooth, with most of the noisy fluctuations in the residual. The smoothening of the data using PCA based reconstruction results in improved estimation of the bolus arrival time (BAT) parameter [Fig 3], especially in the peripheral regions where signal is corrupted due to motion. Overall, the fidelity of non-linear fitting is improved for PCA recon-data as manifested in increase in R^2 value (Table 1), especially when pixels with $R^2 < 0.8$ with SVA were considered (Fig. 4): For Patient#1, from 0.6 for SVA to 0.85 for PCA based recon. For Patient#2: from 0.66 for SVA to 0.86 for PCA based recon. Since BAT estimation is crucial for accuracy of other maps such Max-slope and pK model fitting, these parameters show very less pixilation effects in "PCA" based spatial recon DCE data, compared to SVA based parametric maps (Fig. 5 and 6). The effect is more pronounced for semi-quantitative maps, since lack of fitting procedure implies they are easily susceptible to noise fluctuations [Fig. 5]. Statistically significant differences were observed between two approaches for BAT, TTP, Max-slope and K_{trans} parameters [Table 1]. **Discussion:** We have introduced a methodology for incorporating spatial information using PCA to remove any systemic variations in the dynamic DCE data. There is concomitant improvement in fidelity of data fitting to pK-model, thereby improving the confidence in quantification with DCE MRI. While PCA gave satisfactory results in our analysis, other data separation methods such as independent component analysis or total variation filter [7] based noise cleanup can be used for separation of noisy variations from true dynamic trend in the data. Since DCE analysis is primarily ROI driven, the computational cost of this methodology should not be of much concern. In current analysis, we have not performed any tissue classification and used a general cuboidal neighborhood. For specific anatomy (e.g. head), we can restrict the neighborhood to be within a particular tissue type (such as grey matter / white matter) and further improve the reconstruction fidelity. **Conclusions:** PCA based reconstruction of dynamic DCE data using spatial information helps to produce smooth parametric maps, while preserving the lesion conspicuity. This will improve the accuracy of DCE-MRI quantification and enhance the sensitivity of the method in clinical scenario.

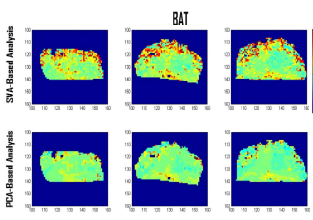

Figure 3. Bolus arrival time (BAT) map is more consistent with PCA based recon (bottom row) compared to SVA

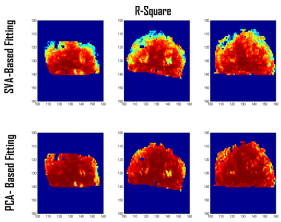

Figure 4. Use of PCA based recon (bottom row) results in improved fidelity of pK-model fitting to the DCE data.

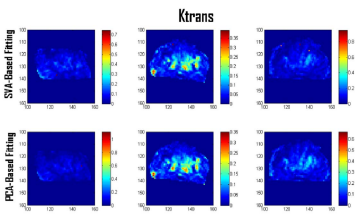

Figure 5. Elevated K_{trans} map shows focal lesions. While the visual conspicuity is retained, the quantitative numbers are different for PCA and SVA analysis.

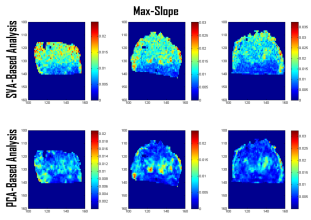

Figure 6. Max slope with PCA-recon shows conspicuous lesion, similar to fig. 4, compared to SVA-recon.

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References: [1]. Tofts et.al. JMRI 1999;10(3):223-232. **[2].** Croitor Sava et.al. , NMR Biomed 2011; 24:824-835. **[3].** Kelm et.al. IEEE Trans. Med. Img. 28(10), 2009 **[4].**Gal Y., IEEE Trans. Med. Img. 29(2), p. 302, 2010. **[5].** Balvay D. et.al. Radiology, ;258(2):435-45, 2010. **[6].** http://www.itk.org. **[7].** Louchet C, et.al. , SIAM J. on Img. Sci. 2011, Vol. 4, No. 2, pp. 651-694