# Impact of Non-rigid Motion Correction on Pharmaco-kinetic Analysis for Breast Dynamic Contrast-Enhanced MRI

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**Target Audience**: Researchers and radiologists interested in non-rigid motion correction and pharmaco-kinetic modeling in breast dynamic contrast-enhanced MRI.

**Purpose**: Dynamic contrast-enhanced (DCE)-MRI is increasingly being used in understanding the pharmaco-kinetic (pK) characteristics of breast tumors. The $K^{trans}$ and $v_e$ estimates [1] used in tumor characterization depend on the DCE concentration time-courses. Cardiac pulsation, breathing and voluntary patient motion introduce rigid and non-rigid motion, which may corrupt the DCE analysis. Previous work demonstrated symmetric diffeomorphic normalization (SyN) [2, 3] to be more effective than b-splines [4] based approaches in correcting for motion in breast DCE MRI [5]. In this work we demonstrate the impact of SyN based non-rigid registration (NRR) on quantitative analysis of breast DCE-MRI using the $K^{trans}$ and $v_e$ estimates from the pK modelling of DCE data.

**Methods**: ***Imaging*:** Six breast cancer patients were scanned on 3T Discovery MR750 scanner (GE Healthcare, Waukesha, WI) using HD Breast coil. The DCE protocol consisted of: **a.** Volume imaging for breast assessment (VIBRANT) with time-resolved imaging of contrast kinetics (TRICKS) DCE MRI with echo-time (TE)/repetition-time (TR) = 3.7/7ms, flip-angle (FA)=12°, matrix size=512×512×112 (0.68mm×0.68mm×1.4mm resolution), axial orientation, 48 bolus phases with 9.3sec temporal resolution; **b**. Variable FA (VFA) data for longitudinal relaxation time ($T_1$) map estimation using 3D fast spoiled gradient echo (EFGRE) with: TE/TR=2.1/5.3ms, matrix size=256×256×112 (1.36mm×1.36mm×1.4mm resolution) and five FAs (2°, 3°, 5°, 10° and 15°). **c**. Bloch-Siegert [6] based $B_1$ map acquisition using a body receive coil with 2D Gradient echo and the following parameters: TE/TR = 13.5/30ms, FA = 20°, matrix size=128×128×22 (2.73mm×2.73mm×7mm resolution). All the studies were approved by an Institutional Review Board. ***NRR*:** 3D SyN based NRR [2, 3] was performed between the different 3D bolus volumes (phases) of the DCE signal data using the Advanced Normalization Tools (ANTs) software package [3]. The last-phase of the 4D data was used as the reference image volume. Mutual information was the similarity metric used. A multi-resolution framework with $M\times N\times P\times Q$ iterations was used ($M$ iterations at 8 times lower resolution, $N$ iterations at 4 times lower resolution, $P$ iterations at 2 times lower resolution and $Q$ iterations at the original data resolution; $M\times N\times P\times Q$ = 20×10×0×0). ***DCE data analysis*:** An in-house tool developed within the Insight Toolkit (ITK) framework was used for the DCE pK analysis. The Bloch Siegert based B1 data was processed to obtain the spatially varying scaling factor for flip angle correction. These FA scale maps were matched to VFA and DCE data resolution using a Lanczos sinc interpolation method available within ITK framework. For VFA data, FA was corrected at each voxel using $B_1$ scale maps. The corrected VFA data was processed to obtain the $T_1$ map. The $T_1$ map was matched to DCE resolution using the nearest neighborhood interpolation. No significant geometrical distortions were observed between $B_1$ map, VFA data and DCE data post NRR and hence only an identity transform was used for interpolation of $B_1/T_1$ data to DCE data. The $T_1$ map and $B_1$ FA scaling map were used to correct the signal to concentration mapping of DCE data [7]. The DCE concentration data was fit to two-parameter Toft's model using a population based AIF [8] to obtain $K^{trans}$ and $v_e$ estimates [1]. Only those voxels with coefficient of determination ($R^2$) > 0.5 for the pK model fit were retained for further analysis. The efficacy of SyN motion correction in improving the breast DCE-MRI pK analysis was evaluated using spatio-temporal slice characteristics, $K^{trans}$ and $v_e$ estimates before and after NRR.

**Results and Discussion**: Figures 1 and 2 demonstrate the efficacy of the SyN method in correcting the non-rigid motion in a case with significant motion deformation. Better alignment of the tumor and tissue boundaries and better spatio-temporal characteristics can be observed after NRR. Figure 3 shows that NRR methodology improves the temporal characteristics of the dynamic curves (needed to ensure fidelity of pK modeling). It can be observed that motion correction restored the shape characteristics of the dynamic curves in regions-of-interest (ROI) 1 and 2 where the dynamic enhancement was missing due to motion. Figure 4 shows improvement in the estimation of the $K^{trans}$ ($min^{-1}$) and $v_e$ maps after NRR, demonstrating the need of motion correction in breast DCE MRI.

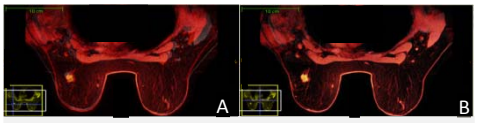


*Figure 1: Comparison of overlay between two phases of the 4D DCE data before (a) and after NRR (b).*

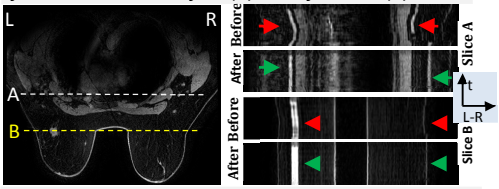


***Figure 2:** NRR efficacy demonstrated using spatio-temporal profile at A and B before and after NRR.*

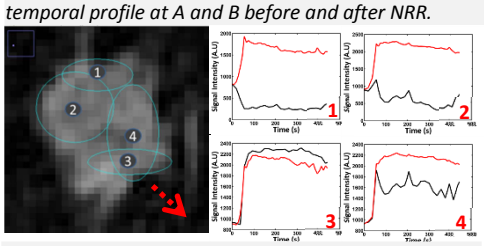


***Figure 3:** Average DCE-MRI signal time-course before (black) and after (red) NRR in 4 ROIs within the tumor. The direction of tumor motion is shown by red arrow.*

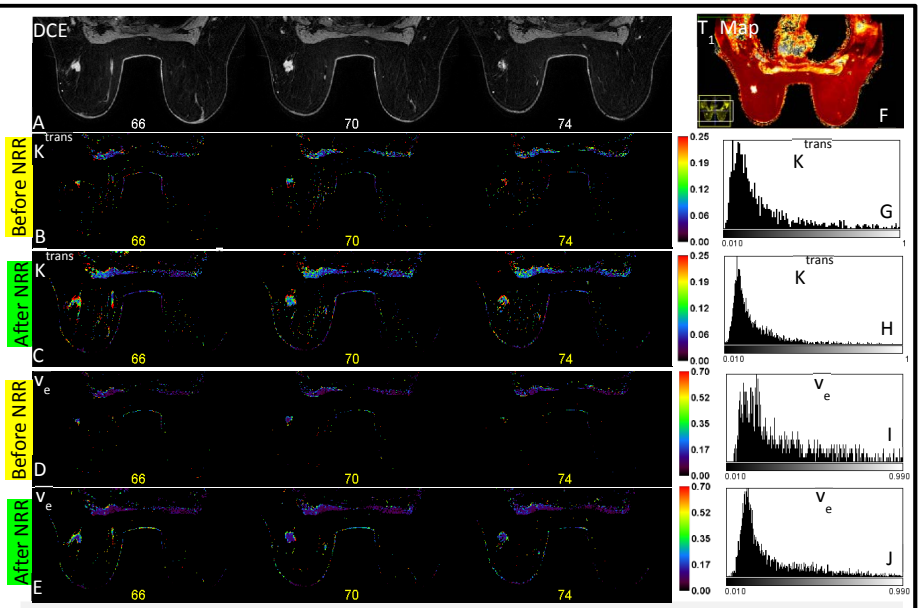


***Figure 4:** Comparison of Ktrans (b, c) and ve (d, e) before and after NRR of 4D DCE data (a). T1 map used in the pK analysis is shown overlaid on the DCE data for a representative slice (f). The histogram of the Ktrans (g, h) and ve (i, j) values within the tumor are also shown. Better pK results are observed after NRR because the curves in the tumor exhibit "characteristic" DCE behavior (see Figure 3).*

**Conclusion:** SyN based non-rigid registration corrected breast motion and recovered DCE data characteristics, resulting in the enhancement of $K^{trans}$ and $v_e$ estimates. NRR has potential for improving the robustness of pK analysis.

**References**: [1] Tofts PS et al, JMRI. 1999;10(3):223-32. [2] Klein A et al, Neuroimage 2009;46(3):786–802. [3] Avants B et al, Penn Img Comp and Sci Lab. 2009. [4] Modat M et al, Comp Meth Prog Biom. 2010;98(3): 278–84. [5] Chebrolu V et al, ISMRM 2014: p 1051. Klein S et al, IEEE Trans on Med Img 2010;29(1):196–205. [6] Sacolick LI et al, MRM. 2010;63(5):1315-22. [7] Chang MC et al, ISMRM 2013: p 2199. [8] Morgan B et al, Br J Cancer. 2006;94(10):1420-7.