The Effect of Groupwise Elastic Registration in Discrimination of Benign and Malignant Ovarian Cancers by Pharmacokinetic Parameters

Elaheh Kia[1,2], Anahita Fathi Kazerooni[1,2], Saeedeh Navaei Lavasani[1,2], Alireza Ahmadian[2], and Hamidreza Saligheh Rad[1,2]
[1]*Quantitative MR Imaging and Spectroscopy Group, Research Center for Molecular and Cellular Imaging, Tehran University of Medical Sciences, Tehran, Iran,*
[2]*Department of Medical Physics and Biomedical Engineering, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

Target Audience: Radiologists, physicists and surgeons with an interest in gynecological DCE-MR imaging

Purpose: Ovarian cancer is the common malignancy of the female in the developed world and is the primary indication for gynecological surgery **[1]**. Quantitative pharmacokinetic analysis of Dynamic Contrast Enhanced MRI (DCE-MRI) is a very useful clinical imaging modality to measure tumor angiogenesis, categorization and further assessment of ovarian lesions **[2]**. Pharmacokinetic modeling using a comprehensive two-compartmental model is a relevant tool for differentiating malignant from benign adnexal tumors and could potentially help oncologists with management decisions **[3]**. One of the major assumptions in quantification of DCE-MRI in abdominal organs is spatially-fixed region of interest over the time course of contrast agent passage. There are types of motion occurring in the image series, which could invalidate this assumption and thus the quantification outcome. Until now, in the quantitative analysis of this organ motion has been ignored. Proper registration of images that acquired in different time points produces a dataset without motion artifact. In this study we have implemented our previously proposed groupwise non-rigid registration method **[4]** on the ovarian dataset and investigated the effect of motion correction on quantitative analysis of DCE-MRI, using a pharmacokinetic model. The descriptive pharmacokinetic model was selected as the reference region model **[6]** to investigate the best quantitative parameters for differentiating benign and malignant tumors, and furthermore investigate the impact of registration on discrimination capability of the extracted parameters.

Material and Methods:

Data Acquisition: DCE-MR images of 26 patients (7 benign and 19 malignant patients with histological assessment) diagnosed with solid or solid/cystic ovarian masses were acquired on a 3T MR scanner (Siemens MAGNETOM Tim TRIO) using a surface phased-array coil, TE/TR = 1.74/5msec, flip angle = 60°, image matrix = 156×192, FOV =23×23cm2, slice thickness = 5mm, number of measurements = 52 at 6sec/volume, number of slices = 16. The acquisition was performed before and immediately after injection of 0.2mL/kg of Gadolinium (DOTAREM; Guerbet, Aulnay, France), followed by injection of 20cc normal saline solution with 3mL/min injection rate. Image registration: In our group-wise registration (GwReg) approach, at first, the pre-contrast image is taken as the reference and the consequent images are aligned with the reference image, and consequently, in order to improve the registration result all images are registered to the group mean image. We employed the elastic registration algorithm, in which the geometric transformation is a local affine model with a global smoothness constraint. Intensity variations are modeled with local changes in brightness and contrast. The mean squared error metric was applied to the intensity values to correct for nonlinear distortion. A least-squares technique was used to minimize the registration cost function. The evaluation of this method was presented in our previous work **[4]**. Pharmacokinetic modeling: Unfortunately DCE-MRI technique still has not been adopted in routine clinical practice due to its practical limitations such as: obtaining an accurate arterial input function (AIF), long scan time required for 3D data acquisition with high spatial resolution and a high signal-to-noise ratio (SNR) to estimate an accurate baseline T1(0). To overcome these difficulties we have used the reference region model in estimating pharmacokinetic parameters **[6]**. The model was applied to datasets to obtain k_{trans} and v_e biomarkers. The mean value of k_{trans} and v_e between benign and malignant groups was performed by student's t-test. A *P*-value of less than 0.05 was considered to be statistically significant.

Results and Conclusions: **Fig. 1** illustrates the box-and-whisker plots for k_{trans} and v_e in both benign and malignant tumors. It can be observed the registration effectively improves the discrimination of benignity from malignancy. It can also be observed by using the student t-tests. The difference between the mean values of each imaging markers in the two groups was tested using the student t-tests. **Table 1** depicts the *P*-value for the k_{trans} and v_e parameters before and after the registration. A significant difference was found between benign and malignant groups using k_{trans} parameter. After the registration based on the achieved results the k_{trans} parameter seems to be a more reliable parameter than v_e in categorizing benign and malignant ovarian lesions. In conclusion, the proposed registration method could improve the estimation of perfusion kinetic parameters. It was also shown that k_{trans} and v_e parameters could conveniently be used for distinguishing malignant from benign complex ovarian tumors using quantitative DCE-MRI.

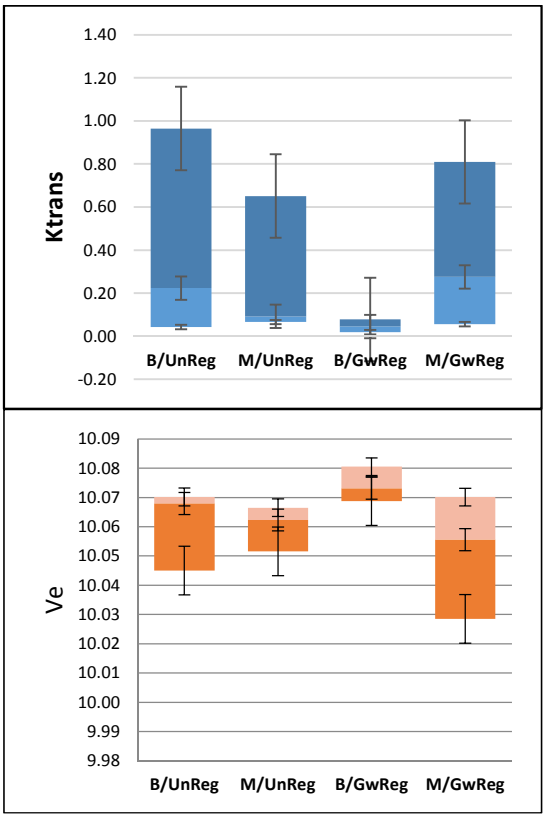

Fig 1. Box-and-whisker plots for K_{trans} and v_e in both benign and malignant cases.

Table 1. Approximate t-test for K_{trans} and v_e parameters in both registered and unregistered datasets

	GwRegistered	UnRegistered
K_{trans}	0.00112	0.23298
v_e	0.15636	0.16502

References: [1] Bernardin L., et al. Effectiveness of semi-quantitative multiphase dynamic contrast-enhanced MRI as a predictor of malignancy in complex adnexal masses: radiological and pathological correlation. *Eur Radiol* 2012, 22(4), 880-890, [2] Priest A.N. et al. Dynamic contrast-enhanced MRI in ovarian cancer: Initial experience at 3 tesla in primary and metastatic disease. Magnetic Resonance in Medicine, 2010, 63(4), 1044-1049. [3] Thomassin-Naggara, I. et al. Epithelial ovarian tumors: value of dynamic contrast-enhanced MR imaging and correlation with tumor angiogenesis. *Radiology*, 2008, 248(1), 148-159. [4] Kia E, et al. A Groupwise Non-Rigid Registration Approach for Accurate Quantification of DCE-MRI in Characterizing Ovarian Cancers. *Proc. Intl. Soc. Mag. Reson. Med.* 22 (2014), [6] Yankeelov, T. E., et al. Quantitative pharmacokinetic analysis of DCE-MRI data without an arterial input function: a reference region model. *Magn Reson Imaging*, 2005, 23(4), 519-529.