Diagnosis of Breast Lesions utilizing an Integrated Model-Free and Model-Based Analysis of DCE-MRI

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Introduction: A wide range of dynamic contrast-enhanced (DCE) sequences and protocols, image processing methods, and interpretation criteria were developed and evaluated in the last twenty years. Special attempts were made to better understand the origin of the contrast observed in breast lesions using physiological models that take into account the vascular and tissue-specific features that influence tracer perfusion. In addition, model-free algorithms to decompose enhancement patterns in order to segment and classify different breast tissue types have been developed, including a preliminary study using principal component analysis (PCA) (1). The purpose of this work is to evaluate a new method that integrates PCA with the three time point (3TP) model based analysis in order to improve breast cancer diagnosis.

Methods: All cases were analyzed retrospectively using a data base obtained as described elsewhere (2,3). Overall we analyzed 69 lesions, 38 benign and 31 malignant (including 10 DCIS) lesions.

DCE-MRI images were loaded into Matlab (version 7.0.1) workspace and the lesion was delineated based on previous histological confirmation. Principle component analysis (PCA) (4) was calculated per case on raw data or enhancement images of a central lesion slice using entire breast ROIs. Projection coefficient maps that measure the spatial distribution of the eigen-vectors were then calculated and displayed. Using the similarity of eigen-vector shapes among all malignant cases, we calculated a representative median eigen-base and projected all malignant and benign cases on it. This process insured standardization and enabled us to compare between cases. In addition, the data was loaded into an in-house, three time points (3TP) tool described in detail elsewhere (5,6) that was configured to process the specific MRI and examination protocol. The 3TP analysis produces color-coded parametric maps accompanied by a calibration scheme that relates color hue and color intensity to the physiological parameters: the influx transcapillary transfer constant and extracellular volume fraction that is assumed to be equal to the transcapillary influx transfer constant divided by the transcapillary efflux transfer constant.

The Integration of the PCA decomposition with the 3TP method to differentiate between benign and malignant lesions was evaluated by plotting the 3TP labels for all cases vs. the projection coefficient values of the two relevant eigen-vectors. The statistical relevance of PCA products was evaluated using receiver operating characteristic (ROC) curves.

Results: The analysis of each case yielded seven principal eigen-vectors. A typical example of the main three eigen-vectors and the corresponding projection coefficients maps obtained by projecting the data on the eigen-vectors is shown in Figure 1A-C, for a breast with a malignant lesion. The eigen-value magnitudes of the other 4 eigen-vectors were significantly lower than those of the first three eigen-vectors (Figure 1D) and their projection-coefficient maps indicated that they are mainly reflecting random noise contributions. This observation can be easily translated for applications of noise filtration and data compression.

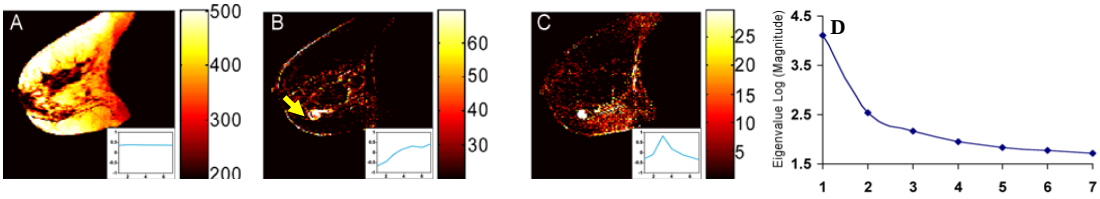

Figure 1. Principal component analysis of DCE images of a breast with IDC. Projection coefficient maps of the 1st 2nd and 3rd eigen vectors in a breast slice (A to C respectively) with the eigen-vectors sorted according to their eigen-values shown in (D). The inserts in A to C are graphical representation of each eigen-vector, plotting the eigen-vector coordinates at the specific seven time points. The arrow in B indicates the lesion position

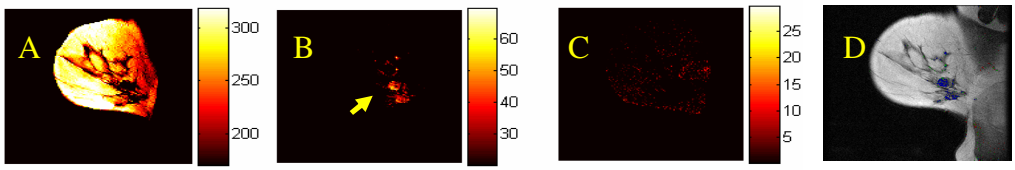

Figure 2. Principal component analysis of DCE images of a breast with hamartoma (benign). Projection coefficient maps of the 1st 2nd and 3rd eigen vectors in a breast slice (A to C respectively). The corresponding 3TP color coded map is shown on D. The arrow in B indicates the lesion position

Repeating the PCA transformation for all lesions showed that the 1st eigen-vector is almost identical in all the lesions, benign and malignant and is constant over time. The first and dominant eigen-vector appeared constant in time and hence was not related to the dynamics of contrast enhancement. High projection coefficient values of this eigen-vector were predominantly in the fat tissue presumably due to sequence effects. Thus, most of the variability in the time dependent changes in the intensity can be explained by using only two eigen-vectors, the 2nd and 3rd one. A high identity of the 2nd eigen-vector was also found among all lesions. However, a disparity was observed for the 3rd eigen vector; most malignant lesions exhibited a wash-out like pattern of the 3rd eigen vector with appreciable projection coefficient values in the ROI of the lesion whereas most benign lesions exhibited as a 3rd eigen vector a noise like pattern and distribution with a null projection coefficient values in the ROI of the lesion (Figure 2). Correlation of the 2nd and 3rd eigen values with the 3TP labeling (Figure 3) showed for all cases that a rotation of the eigen vector coordinates by ~70.7 degrees clockwise leads to a congruence between the 3TP wash-in labeling (reflecting the transcapillary influx transfer constant) and the 2nd eigen-vector as well as between the 3TP wash-out labeling (reflecting the transcapillary efflux transfer constant) and the 3rd eigen vector. Projection coefficient maps of the rotated eigen-vectors provided PCA derived maps that reflected the physiological dynamic process determined by the two transcapillary transfer constants.

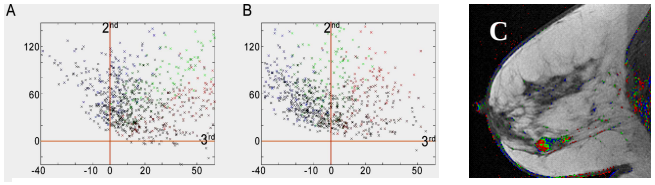

Figure 3. Correlation of PCA derived 2nd and 3rd eigen-vectors and the parameters derived from the 3TP method in a single patient for breast tissue with cancer. A. before rotation, B. after rotation and C. 3TP of the lesion (same lesion as in Figure 1)

ROC analysis applied in order to evaluate the diagnostic significance of each rotated eigen vector, based on the histopathological findings showed that the projection maps of the 3rd rotated eigen vector (or the 2nd enhancement eigen vector) yields a much higher AUC as compared to the 2nd eigen vector demonstrating the importance of the wash-out pattern in the differentiation between benign and malignant lesions.

Summary: the model-free method based on principal component analysis uses all the time points, and provides a means to separate experimental and noise distortions from those related to the physiological relevant information embedded in DCE-MRI. This study shows that specific PCA eigen-vectors can be transformed to reflect physiological behavior in a standard manner and lead to the construction of diagnostically significant projection coefficient maps of rotated eigen-vectors. The reproducibility of the patterns (for a standardized protocol) and the fast image processing makes it an attractive choice for CAD.

Further studies are underway to demonstrate the capacity of this method to improve the accuracy of a prospective breast DCE-MRI study.

References: **1.** Twellmann, T. *et al.* Biomed Eng Online, 3: 35, 2004. **2.** Kelcz, F.. *et al.* Am. J. Roentgenol., 179: 1485-1492, 2002. **3.** Furman-Haran, E. *et al.* Cancer, 104: 708-718, 2005. **4**. Jolliffe, I. T. Principal Component Analysis. Springer-Verlag, 1989. **5.** Degani, H. *et al.* Nature Med., 3: 780-782, 1997. **6.** Furman-Haran, E. and Degani, H. J. Comput. Assist. Tomogr., 26: 376-386, 2002.