Time-to-Peak and Spherical Shape Index from Dynamic Contrast Enhanced MRI as Combined Predictors of Tumor Malignancy

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Introduction: Dynamic contrast enhanced MRI (DCE-MRI) has good sensitivity for malignant breast tumor detection, but, reported specificities vary widely[1]. Further development of quantitative image assessment methods should help to provide increased and more consistent specificity. Although, there are a huge number of reports involving quantitative analysis of signal time evolution and several reports on morphological analysis, very little work in which signal evolution and morphology are combined as quantitative predictors has been done. One previous study[2] incorporated two-dimensional (2D) morphological features with signal evolution features describing the evolution of the mean signal from a region of interest within the tumors. Images with lower spatial resolution (5 mm thick slices), but higher time resolution (10s to 20s) than typical in present clinical protocols were analyzed in this earlier work. To obtain a diagnostic accuracy > 90%, seven features including patient age were required as predictors.

In the present study, a signal evolution feature (time to peak (TTP)) and a 3D morphological feature (spherical shape index[3] (SSI)), both obtained from tumor regions segmented automatically with K-means clustering, are investigated as independent and combined predictors of malignancy. The TTP is the time from the contrast agent injection to peak signal. The SSI is the ratio of the tumor surface area to its $(\text{volume})^{2/3}$, and is a measure of the extent to which the shape deviates from spherical[3]. Our analysis also takes advantage of tumor heterogeneity by assessing the distribution of TTP values within the tumor.

Methods: Analysis was performed on DCE magnetic resonance images from 31 patients that had been acquired in clinical examinations between Jan. 1, 2005 and Jan. 1, 2007. A total of 18 benign and 29 malignant biopsy indentified lesions were studied. Image Acquisition: Using a 1.5T Siemens MRI system with a two-element breast coil, one pre-contrast and 7 post-contrast images (time resolution=1min) were acquired for each patient with a 3D VIBE sequence (TR/TE = 4.5ms/1.2ms, flip angle = 20°, fat saturation with SPAIR). The matrix size was 448 × 318 × 100, interpolated to 512 × 512 × 144, with field of view ranging from 300 mm × 300 mm × 176 mm to 350 mm × 350 mm ×176 mm. Contrast agent administration involved manual injection of a 20 ml dose of gadopentetate dimeglumine over 15 s to 20 s. Lesion Segmentation: A 3D rectangular box enclosing the lesion was positioned by a radiologist (O.S.) on the first post-contrast image. Voxels inside the box were classified into two clusters by K-means clustering applied to the images obtained by subtracting the pre-contrast image from each post-contrast image. The cluster with the higher signal enhancement on the first post-contrast image averaged across all voxels was considered as the lesion. Time to Peak: Voxel-by-voxel curve-fitting was applied within the lesion using an empirical model[4]: $S(t) = a \cdot t \cdot e^{-t^c/b}$ $(t = 0,1,2,\ldots 7)$, where a, b, c are adjustable parameters, t is the time, and S is the signal enhancement. For this model the TTP is given by $(b/c)^{1/c}$. The distribution of TTP values within each lesion was characterized by determining percentile values of this distribution over a range from the 5th to the 95th percentile (i.e., p^{th} percentile where p varies from 5 to 95). Spherical Shape Index: For each lesion, the SSI was calculated from the surface area and volume. The continuous surface area was estimated with a voxel-based weight method[5] previously described for dealing with surface representation in digital images. Differentiation of Lesions: First, linear discriminant analysis (LDA, Matlab R2009a Statistics Toolbox 7.1) was applied to determine the optimal linear combination of TTP and SSI values for classification of benign versus malignant tumors. Then the TTP, the SSI and the combined predictor were tested as predictors of lesion diagnosis (malignant versus benign) using both t tests and receiver operating characteristic (ROC) analysis.

Results and Discussion: Figure 1 illustrates a plot of the p^{th} percentile values of the TTP versus p for each lesion, where p varies from 5 to 95. The overlap between TTP percentile values for benign and malignant lesions increases with increasing value of p. Thus, a low value of p (p = 5, 5th percentile) was selected for further analysis. Figure 2 illustrates a plot of the 5th percentile of TTP value versus SSI for all lesions. Higher SSI indicates greater deviation from spherical shape (SSI of sphere = 4.8). Based on the LDA, the optimal linear combination of the 5th percentile TTP and the SSI for classification of malignant versus benign tumors is $0.99 \cdot (5^{\text{th}}$ percentile of TTP$) - 0.10 \cdot$ (SSI), with TTP in minutes. The solid line represents the boundary which is perpendicular to the axis of this predictor and is mid way between the means of the combined predictor values for malignant and benign lesions. Table 1 provides the results of the t test and ROC analysis for the 5th percentile of TTP, the SSI and the combined predictor. Although the combined predictor did not provide a larger area under the ROC curve than one of the original predictors (SSI) alone, the combined predictor did result in the highest t value. This suggests that the combined predictor may be a stronger discriminator of malignant versus benign lesions compared to either the SSI or 5th percentile of TTP alone.

Conclusion: Combining SSI and 5th percentile of TTP as quantitative predictors may provide better discrimination of malignant versus benign breast tumors than either predictor alone.

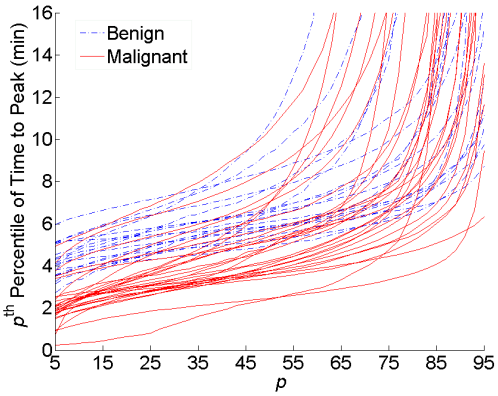

Fig. 1. Plot of p vs. p^{th} percentile of TTP for all lesions. Overlap between TTP percentile values for benign and malignant lesions increases with increasing value of p.

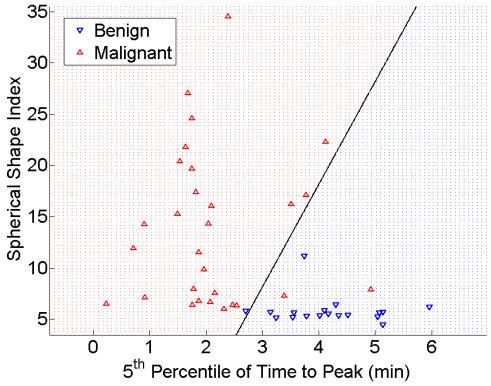

Fig.2. Linear discriminant analysis for classification of benign versus malignant lesions using the 5th percentile of TTP and the SSI. The solid line is perpendicular to the axis of the combined predictor and is mid way between the means of the combined predictor values for malignant and benign lesions.

Feature	t test		AUC ± SD
	t value	P value	
5th perc. TTP	7.3	4×10^{-9}	0.93 ± 0.04
SSI	4.4	6×10^{-5}	0.97 ± 0.02
Combination	8.6	5×10^{-11}	0.97 ± 0.02

Table 1. Results of t test and ROC analysis for predicting lesion diagnosis (malignant versus benign). Predictors include 5th percentile of TTP, SSI and the optimal linear combination of 5th percentile of TTP and SSI obtained from LDA. AUC represents area under the ROC curve.

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