**Introduction:** Dynamic contrast enhanced MRI (DCE-MRI) has good sensitivity for malignant breast tumor detection, but, reported specificities vary widely. 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 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 index3 (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 (volume)\(^{2/3}\), and is a measure of the extent to which the shape deviates from spherical. 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 identified 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: \( S(t) = a \cdot t \cdot e^{-t/b} \) (\( t = 0,1,2, … 7 \)), 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 5\(^{th} \) to the 95\(^{th} \) 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 previously described for the first distribution over a range from the 5\(^{th} \) to the 95\(^{th} \) percentile (i.e., \( p^{th} \) percentile where \( p \) varies from 5 to 95). The 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.

**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 \( p \) (\( p = 5, 5^{th} \) percentile) was selected for further analysis. Figure 2 illustrates a plot of the \( 5^{th} \) percentile of TTP value vs. 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 \( 5^{th} \) percentile TTP and the SSI for classification of malignant versus benign tumors is 0.99 (\( 5^{th} \) percentile of TTP) – 0.10 (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 \( 5^{th} \) 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 \( 5^{th} \) percentile of TTP alone.

**Conclusion:** Combining SSI and \( 5^{th} \) percentile of TTP as quantitative predictors may provide better discrimination of malignant versus benign breast tumors than either predictor alone.

**References:**