The Time-to-peak Hot Spot Volume as an Indicator of Lesion Malignancy in Breast Dynamic Contrast Enhanced-MRI

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Introduction: Dynamic contrast enhanced-MRI (DCE-MRI) is utilized extensively for the diagnosis of breast lesions. Clinical DCE-MRI analysis typically involves visual inspection of the time evolution of the signal enhancement and morphology of the enhanced region. However, there is growing interest in the development and assessment of quantitative methods to provide objective and improved diagnostic indicators. Quantitative analysis applied to the time evolution (kinetics) of breast DCE-MRI includes several empirical measures. One very simple empirical parameter that has shown promise as a diagnostic indicator is the time-to-peak (T_{peak}) [1,2]. This is the time duration from the contrast agent injection to the maximal MRI signal for a given voxel. A nice feature of the T_{peak} is that, at least in theory, it should be independent of imaging timing parameters since the maximal signal is expected to occur at the time at which the shortest T1 for a given voxel occurs. The purpose of this work [3] is to investigate and optimize the diagnostic performance of a measure to be referred to as the T_{peak} hot spot volume, which is the volume of lesion tissue in which the T_{peak} values for the voxels are less than a threshold value. An investigation of the relation of hot spot volume to the lesion volume is also presented for both benign and malignant lesions.

Methods: DCE-MR images that had been acquired from 97 patients as part of clinical examinations between Jan. 1, 2005 and Jan. 1, 2007 were retrospectively analysed following approval from our Institutional Ethics Review Board. Lesions were classified as malignant (87) based on core biopsy results. Lesions were classified as benign (43) either based on core biopsy results (N = 25) or based on at least two-years of clinical and imaging follow-up indicating that the patient was free of breast cancer (N = 18). Image Acquisition: The DCE-MRI had been performed on a 1.5 T Siemens MRI system with a two-element breast coil (Siemens Avanto, Siemens, Erlangen, Germany). The 3D spoiled gradient echo sequence known as volume interpolated breath hold imaging (VIBE) was used with the following parameters: TR/TE = 4.5 ms/1.2 ms, flip angle = 20°, fat saturation with SPAIR. The image matrix size was 448 × 318 × 100, interpolated to 512 × 512 × 160 with a 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 (Gd-DTPA) (Magnevist, Bayer HealthCare Pharmaceuticals, USA) over 15 s to 20 s. The DCE acquisition consisted of 1 pre-contrast image and 7 post-contrast images with a temporal resolution of 1 min, with the middle of first post-contrast image occurring 1 min after the start of Gd-DTPA administration. 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 [4] 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 [5]: $S(t) = a \cdot t \cdot e^{-t^c/b}$ $(t = 0,1,2,\ldots 7)$, 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 T_{peak} hot spot volume was calculated as a function of T_{peak} threshold. This hot spot volume was defined as the volume of tissue corresponding to lesion voxels with T_{peak} less than the threshold. Statistical Analysis: The dependence of the hot spot volume on threshold value was determined for all lesions using threshold values in the range from 1 min to 7 min. The hot spot volume was expressed as an absolute volume and as a fraction of the lesion volume (fractional volume). Receiver operating characteristic (ROC) analysis was employed to assess the hot spot volumes as indicators for differentiating benign versus malignant lesions. The area under ROC curve (AUC), which is a measure of diagnostic performance, was determined (SPSS 17.0, SPSS Inc., USA) as a function of T_{peak} threshold. In addition, linear regression analysis was performed to investigate the relationship between hot spot volume and lesion volume for both benign and malignant lesions.

Results and Discussion: As shown in Figure 1, benign lesions tend to have smaller hot spot volumes than those of malignant lesions at any T_{peak} threshold. However, the overlap between benign and malignant lesions is largest at the highest and lowest thresholds. This is demonstrated and quantified by the relationships of AUC versus T_{peak} threshold (Figure 2) which indicates the maximal AUC value of (0.944 ± 0.019) at approximately 3 min. A similar plot for the fractional hot spot volume (not shown) also demonstrates a maximal AUC (0.913 ± 0.024) at a threshold of approximately 3 min. A further investigation of the absolute hot spot volume at the optimal threshold (3 min) revealed that the rate of increase in hot spot volume with lesion volume is much greater for malignant compared to benign lesions. This is illustrated in Figure 3 as well as by the slopes of the linear regressions in Table 1. Note that although Figure 3 is a log-log plot, the parameters in Table 1 correspond to the relationship prior to log transformation. In contrast to the changes in absolute hot spot volume with lesion volume, no significant correlation was found between fractional hot spot volume (at a threshold of 3 min) and lesion volume for either benign or malignant lesions.

Conclusion: Quantitative analysis of the T_{peak} hot spot volume can be optimized for diagnostic performance providing indicators for differentiating benign versus malignant breast lesions.

References:

1. Ikeda, O., et al., Acta Radiol 1999
2. Chen, W., et al., Med Phys 2006
3. Submitted to Academic Radiology for publication
4. Lee, S.H., et al., IEEE Eng Med Biol Soc 2007
5. Gal, Y., et al., IEEE Eng Med Biol Soc 2007

	Coefficient		*F* Statistics
	Slope	Intercept (mm^3)	*p* value
Benign	0.04 ± 0.004	-26 ± 24	< 0.001
Malignant	0.25 ± 0.018	43 ± 437	< 0.001

Table 1. Linear Regression Analysis for absolute hot spot volume at a threshold of 3 min versus lesion volume.

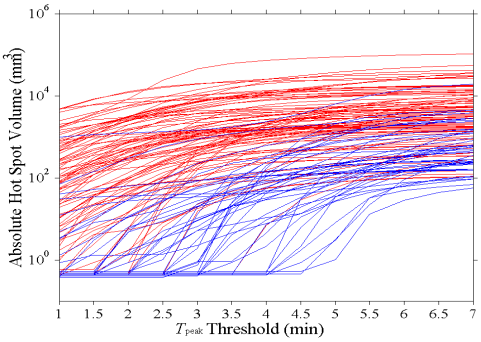

Figure 1. Absolute hot spot volumes for all lesions. Each red line represents a plot of the absolute hot spot volume versus T_{peak} threshold for one malignant lesion and each blue line represents this plot for one benign lesion. Note the log scale of the vertical axis in the figure.

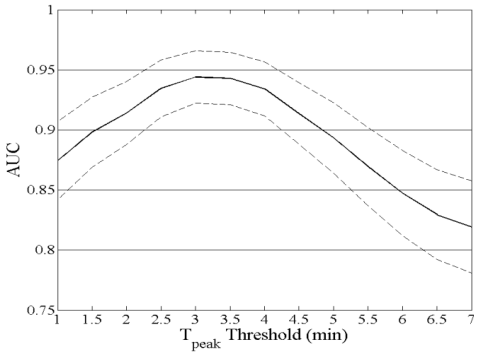

Figure 2. The AUC value as a function of T_{peak} threshold for absolute hot spot volume. The AUC value is shown with solid line. Two dashed lines above and below the solid line are the AUC plus and minus one standard error, respectively. The maximal AUC is achieved at the threshold of 3 min.

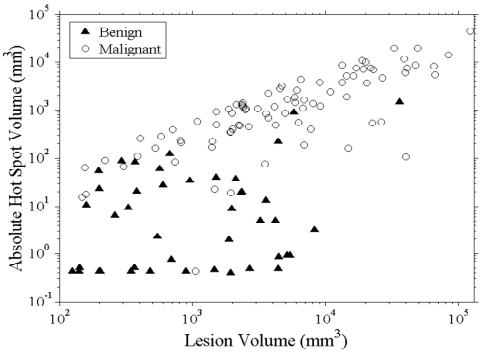

Figure 3. Relationship between absolute hot spot volume (T_{peak} threshold of 3 min) and lesion volume for benign (triangles) and malignant (circles) lesions. Note the log scale on both axes. Benign lesions tend to have smaller absolute hot spot volumes than those of the malignant lesions. Both benign and malignant lesions showed a significant linear correlation between absolute hot spot volume and lesion volume, although the slope of the regression line is larger for malignant lesions (Table 1).