Heterogeneity of Vascular Permeability in Breast Lesions with Dynamic Contrast Enhanced MRI

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Introduction

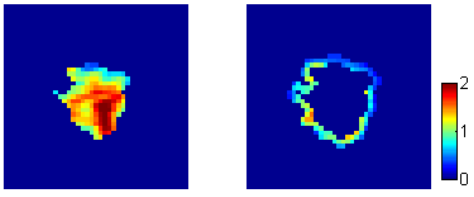
Dynamic contrast enhanced (DCE) MRI is being increasingly used to characterize abnormalities of the breast. Features of the contrast uptake and washout demonstrate high negative predictive value for identifying and characterizing breast lesions. We performed compartment modeling using the Tofts' model [1]. Mean vascular permeability over tumor volume has been generally used to characterize tumors. However, tumors are known to be heterogeneous for many characteristics such as growth rate, metastatic potential, biochemical properties, sensitivity to chemotherapeutic agents and radio-sensitivity [2,3,4]. Therefore, it is desired to investigate spatial characteristics of kinetic parameters. In this study we utilized spatial statistics and an iterative erosion method to characterize segmented lesions based on the arrival time of contrast agent.

Method

Nine patients with 8 benign and 6 malignant breast lesions were examined with DCE-MRI after intravenous injection of 0.1 mmol/kg Gd-DTPA. MR images were obtained using a spoiled gradient echo sequence with temporal resolution of 30 s. Before compartment modeling, acquired images were co-registered to the first time series of images and lesions were segmented based on the arrival time of contrast agent [5]. Spatial statistics were used to assess heterogeneity within the lesions. Global Moran's I statistics with inverse distance weighting were used to estimate overall degree of spatial autocorrelation, which is a weighted sum of covariances between a particular voxel's value and its neighboring voxels' values:

$$I = \frac{\sum_{i}^{n}\sum_{j\neq i}^{n} w_{ij}(v_i - \bar{v})(v_j - \bar{v})}{S^2 \sum_{i}^{n}\sum_{j\neq i}^{n} w_{ij}} \qquad (1)$$

where w_{ij} is an inverse distance weight, v is voxel value, and S^2 is the variance [6]. Positive I means clustering of similar values and negative I means that neighboring values are more dissimilar than random (I=0). Secondly, we investigated disparity between the interior and the periphery in permeability by eroding a 3D tumor mask as illustrated in Figure 1. We continued the erosion procedure until no interior volume remained. Mean difference (Δk_{ep}) over all possible erosions in permeability between the interior and the periphery was calculated. Standard deviation of vascular permeability (k_{ep}^{std}) was also computed.



(a) (b)

Figure 1. Permeability maps demonstrated the interior (a) and the periphery (b) after two iterations of erosion for a malignant lesion. Permeability was higher.in the interior than in the periphery.

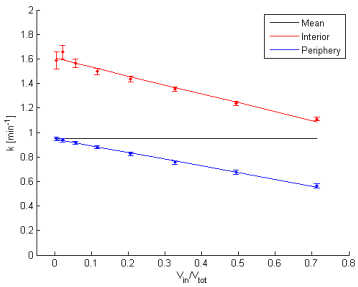
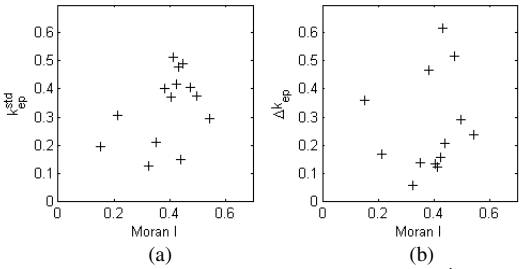


Figure 2. Permeability in the interior (red) and the periphery (blue) was compared to mean permeability (black) for a typical lesion. Difference in permeability (Δk_{ep}) is nearly constant no matter what fractional volume was chosen.

Results

Compartment modeling was performed on each voxel within segmented lesions. Vascular permeability (k_{ep}) was found to be lower in the periphery than in the interior. Figure 1 shows k_{ep} maps in the interior (left) and the periphery (right) after two iterations of erosion. Figure 2 shows mean permeability in the interior and the periphery as a function of fractional interior volume. Difference in permeability between the interior and the periphery was nearly constant no matter what fractional volume was chosen in this case. It was found that mean difference (Δk_{ep}) was 0.21 ± 0.15 min^{-1} for benign and 0.41 ± 0.22 min^{-1} for malignant lesions. For both benign and malignant lesions, k_{ep} is higher in the interior than in the periphery, and the difference was larger in malignant lesions than in benign lesions. There was no statistically significant difference between the two groups (p=0.067). Moran's I was calculated and used as a measure of kinetic heterogeneity. Moran's I was found to be 0.35 ± 0.11 for benign and 0.45 ± 0.06 for malignant lesions (p=0.057). Malignant lesions were more heterogeneous than benign lesions. The values of k_{ep}^{std} were 0.28 ± 0.14 for benign and 0.41 ± 0.07 for malignant lesions (p=0.065). As shown in Figure 3, there was no strong correlation between Moran's I and either Δk_{ep} or k_{ep}^{std}. This indicates that neither Δk_{ep} nor k_{ep}^{std} fully represents spatial heterogeneity. This was true because they used only partial or no spatial information. Finally we found that all the metrics we examined performed better than mean k_{ep} (p=0.20) in differentiating benign from malignant lesions.



(a) (b)

Figure 3. There was a correlation of 0.42 between k_{ep}^{std} and Moran's I (a) and 0.20 between Δk_{ep} and Moran's I (b).

Conclusion

We investigated spatial characteristics of breast lesions. Results showed that vascular permeability was higher in the interior than in the periphery and the difference in permeability was larger in benign than in malignant lesions. It was also found that malignant lesions were more heterogeneous than benign lesions. The classification performance of the metrics such as Δk_{ep}, k_{ep}^{std} and Moran's I was found to be better than that of mean permeability over lesions. Further study with increased number of patients is necessary to draw definitive conclusions on classification performance.

References

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