Distinguishing Molecular Subtypes of Breast Cancer Based on Computer-aided Diagnosis of DCE-MRI

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Introduction: Previous studies [1,2] have suggested that genetic subtypes of breast cancer are associated with distinct imaging phenotypes on DCE-MRI. However, previous attempts to distinguish molecular subtypes of breast cancer are based on qualitative, visual examination of the tumors. In our previous work, we developed a computer aided diagnosis (CAD) system that exploited textural changes within the lesion as a function of contrast uptake (textural kinetics) to distinguish benign from malignant breast lesions [3]. In this study, we developed and evaluated a CAD system that uses dynamic texture for distinguishing triple negative (TN) tumors, which are estrogen receptor (ER) negative, from ER positive (ER+) tumors. We also evaluate the discriminability of textural kinetics with respect to static texture, dynamic contrast enhancement, pharmacokinetic, and morphological features for distinguishing different molecular breast cancer subtypes on DCE-MRI.

Methods: DCE-MRIs of 41 (20 TN, 21 ER+) histologically proven invasive ductal carcinomas were collected under IRB approval. Sagittal T1-weighted, spoiled gradient echo sequences with fat suppression consisting of one series before contrast injection of Gd-DTPA (precontrast) and 3-8 series after contrast injection (postcontrast) were acquired at either 1.5 Tesla or 3 Tesla (Siemens Magnetom or Trio, respectively). Single slice dimensions were 384x384, 512x512, or 896x896 pixels with a slice thickness of 3 mm. Temporal resolution between postcontrast acquisitions was a minimum of 90 seconds. An attending radiologist selected the 2D slice that was most representative of the lesion, and the radiologist manually delineated the boundary of the lesion. Thirteen co-occurrence texture features [4] were extracted at each time point pre- and postcontrast. Average signal intensity of the lesion as well as average lesion texture were calculated at each time point before and after contrast injection. On account of the variable number of post-contrast time points between lesions, a 3rd order polynomial was fit to each signal intensity vs. time and texture feature vs. time curve, and the resultant coefficient feature sets, intensity kinetics (IK) and textural kinetics (TK), respectively, were extracted. The pharmacokinetic (PK) parameters [5], k_{ep}, k_{trans}, and v_e, texture at the peak contrast enhancement (TP), and morphology features (M) were also extracted for comparison.

Results: M, IK, TP, PK, and TK features were compared in conjunction with a support vector machine (SVM) classifier for their ability to discriminate between TN and ER+ tumors on DCE-MRI via a randomized 10-fold cross validation scheme over 20 trials. Table 1 shows that textural kinetics were able to distinguish between TN and ER+ breast tumors more accurately than any other feature set considered here.

Feature Set	Accuracy (μ +/- σ)	Sensitivity (μ +/- σ)	Specificity (μ +/- σ)
M	0.60 +/- 0.06	0.57 +/- 0.08	0.64 +/- 0.10
IK	0.53 +/- 0.06	0.57 +/- 0.08	0.48 +/- 0.09
TP	0.53 +/- 0.05	0.73 +/- 0.05	0.32 +/- 0.08
PK	0.60+/- 0.04	0.62 +/- 0.08	0.58 +/- 0.06
TK	**0.68+/- 0.05**	**0.77 +/- 0.06**	**0.59 +/- 0.07**

Table 1: Classification accuracy, sensitivity, and specificity of feature sets using randomized 10-fold cross validation over 20 trials in a support vector machine classifier.

Concluding Remarks: In this study, we developed a CAD classifier that exploited textural dynamics for distinguishing TN from ER+ breast tumors. The top-performing feature set for differentiating between TN breast cancers and ER+ breast cancers was a second order dynamic texture feature. Pharmacokinetic parameters performed better than texture at a single time point and better than intensity kinetics. It is important to note that low temporal resolution is a limitation of the acquisition of the high spatial resolution images acquired in this study, which likely has an effect on any features that are time-dependent such as the PK parameters. However, we have also shown that heterogeneity of internal tumor enhancement as a function of time is a key dynamic tumor feature for discriminating molecular subtypes of breast cancer. Interestingly, textural kinetics outperformed attributes employed within the BIRADS classification system including lesion morphology and internal lesion enhancement at a single time point. The work presented here has significant translational implications for early identification of aggressive molecular subtypes of breast cancer, where rapid identification can expedite targeted tumor treatment.

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References

[1] T. Uematsu et al., "Triple negative Breast Cancer: Correlation between MR Imaging and Pathologic Findings," *Radiology*, (2009) vol. 250, no. 3.
[2] J.-H. Chen et al., "Triple negative breast cancer: MRI features in 29 patients," *Ann. Oncol.*, vol. 18, no. 12, pp 2042-2043 (2007).
[3] S.C. Agner et al., "Novel kinetic texture features for breast lesion classification on dynamic contrast enhanced (DCE) MRI", *SPIE Medical Imaging*, vol. 6915, 2008.
[4] R. M. Haralick et al., "Textural Features for Image Classificatiomn," *IEEE Trans. on Systems, Man, and Cybernetics*, (1973) **3**(6): 610-621.
[5] P.S. Tofts et al., "Quantitative Analysis of Dynamic Gd-DTPA Enhancement in Breast Tumors Using a Permeability Model," *Magn. Reson. Med.,* (1995) **33**: 564-568.