Beyond Histopathologic Prognostication: Can DCE-MRI improve Breast Cancer Recurrence Risk Prediction?

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Target Audience: Clinicians and scientists interested in the role of DCE-MRI in breast cancer recurrence risk assessment.

Purpose and Background: In the era of personalized medicine, it is now becoming increasingly important to have access to prognostic markers able of informing treatment decisions by providing information on the long-term clinical outcome of patients[1-2]. To date, pathologic evaluation of tumor tissue remains the gold standard for this purpose. Emerging studies have suggested that imaging features have the potential to capture information about underlying tumor biology that could complement standard pathologic assessment[3-5]. However, studies on the role of DCE-MRI in improving breast cancer prognostication are still limited. Towards this end, the goal of this study was to investigate the complementary value of morphologic breast DCE-MRI tumor characteristics as prognostic markers for breast cancer recurrence risk assessment.

Materials and Methods: DCE-MRI images were retrospectively analyzed from 57 women diagnosed with estrogen receptor (ER)-positive, node-negative invasive breast cancer. The women had previously undergone Oncotype DX profiling[6] of their tumor. Two experienced radiologists assessed 7 tumor features. The features consisted of disease multifocality, lesion size, lesion shape, margin morphology, enhancement amount, enhancement morphology and associated non-mass enhancement (NME). The Oncotype DX score was used as a surrogate marker for breast cancer recurrence probability. Oncotype DX is a widely-used clinical gene expression assay that generates a prognostic score predicting breast cancer recurrence ten years after treatment, using a continuous score stratified into 3 risk categories (risk: low $\leq$17, medium=18-30, high $\geq$ 31)[6]. Multivariate three-class linear discriminant analysis (LDA) was performed to determine joint associations between the DCE-MRI tumor features and the Oncotype DX recurrence risk category. We then compared the performance of an LDA model that includes only standard pathologic features with an LDA model that includes a combination of the MRI features and pathologic features. Performance of the LDA models was assessed using Receiver Operating Characteristic (ROC) curve analysis. Histopathologic features consisted of histologic subtype, grade (mBR score), pathologic tumor margin, PR- and HER2-receptor status.

Results and Discussion: LDA analysis yielded two MRI features (Table 1), multifocality and lesion size, as significant in predicting the recurrence risk categories ($p<0.05$). A three-class LDA model that included the assessed MRI features had significant agreement with the Oncotype DX recurrence risk categories (Fig.1, kappa=0.41, p=0.01). When only pathologic features were considered in an LDA model, ROC analysis revealed some discriminant capacity in distinguishing between recurrence risk categories (AUC=0.59 for low vs. intermediate risk, 0.50 for intermediate vs. high risk and 0.78 for low vs. high risk). A model combining MRI and pathologic features had higher discriminatory capacity (Fig.2, AUC=0.78 for low vs. intermediate risk, 0.74 for intermediate vs. high risk and 0.81 for low vs. high risk). Overall, our results suggest that the DCE-MRI can complement histopathologic factors in predicting breast cancer recurrence risk. Imaging features can potentially improve prognostic risk assessment by adding global multi-parametric tumor feature information that may not be currently captured by the standard histopathologic markers.

Conclusion: Our results indicate that integrating DCE-MRI tumor features with standard histopathologic markers can potentially improve prognostic assessment for women diagnosed with breast cancer. A model that incorporates imaging features in prognostic assessment may have significant implications on the management of breast cancer patients.

References: (1)Paik et al., J Clin Oncol (2006). (2)Albain et al., Lancet Oncol (2010), (3)Loiselle et al., JMRI (2011), (4)Bathen et al., Breast Can Res Treat (2007). (5) Szabo et al, Eur Rad, 2003, (6) Paik et al., NEJM. (2004)

Tumor Feature	Coefficient	p-value
Intercept 1	0.179	0.934
Intercept 2	2.127	0.332
Mu tifocality	2.136	0.014
Size	-1.176	0.041
Enhancement Shape	-0.201	0.570
Enhancement Margin	0.334	0.465
Enhancement Amount	0.155	0.802
Enhancement Morphology	0.093	0.908
Enhancement Kinetics	0.091	0.848
Associated Non-mass Enhancement	0.610	0.482

Table 1: Three-class LDA model assessing joint associations between DCE-MRI tumor features and Oncotype DX recurrence risk categories. Reported are LDA partial regression coefficients and associated Wald test p-values.

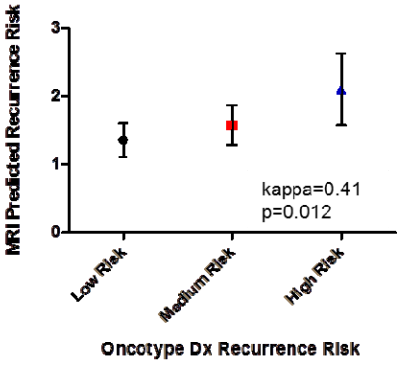

Fig.1: Distribution and agreement between the MRI-predicted recurrence risk scores and the recurrence scores as determined by the Oncotype DX gene expression assay.

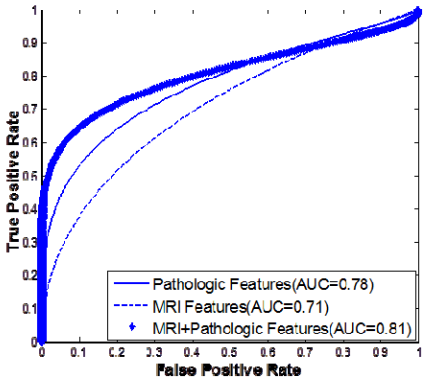

Fig.2: Receiver operating characteristic curves assessing performance of pathologic features, MRI tumor features and their combination in classifying high Oncotype DX recurrence risk.