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MRI May Be Noninvasive Method to Measure Breast Cancer Prognosis

- MRI is valuable in assessing the extent of breast cancer and monitoring treatment response.
- Diffusion-weighted MRI and dynamic contrast-enhanced MRI reflect tumor cellularity and vascularity.
- Both correlated with histopathological markers and prognostic factors.

SAN ANTONIO — Quantitative magnetic resonance imaging measures were associated with prognostic tumor markers, demonstrating the potential of magnetic resonance imaging for prediction of disease prognosis and stratification of patients to appropriate therapies, according to preliminary data presented at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium, held Dec. 6-10, 2011.

“Breast cancers are heterogeneous, and different subtypes of breast cancer will respond differently to therapy,” said Sana Parsian, M.D., a research assistant in the department of radiology at the University of Washington in Seattle. “Every patient with breast cancer must undergo biopsy to be evaluated for the type of breast cancer they have. Based on that, adjuvant medical therapies are prescribed for them.”

Parsian and her colleagues hypothesized that some quantitative magnetic resonance imaging (MRI) measures, such as diffusion-weighted MRI (DWI) and dynamic contrast-enhanced MRI (DCE), would correlate with histopathological markers by enabling the researchers to measure the tumor’s cellularity and vascularity.

In DWI, the diffusion of fluids along a field gradient reduces the MRI signal, so it can determine cellularity of the tumor by measuring the degree of water mobility. DCE enables viewers to see more information about tumor vascularity. A malignant cell group needs a blood supply to grow, and those vascular changes cause tumors to appear differently on DCE compared with normal tissue, Parsian said. The enhancement pattern seen on an MRI is called kinetics.

Researchers evaluated correlations between DWI and DCE kinetics and histopathologic markers of breast cancer determined from biopsy, such as estrogen receptor (ER), progesterone receptor, HER2, p53 and the ki67 proliferation marker, in 41 invasive cancers among 36 patients. They found statistically significant correlations between MRI measures and all markers, except ER, which was only marginally associated with one of the DCE measures. Each of the DCE kinetics parameters significantly discriminated grade III tumors from grades I and II and luminal A from luminal B and basal-like intrinsic subtypes.

“When we looked at these measures, we realized there was a correlation with biomarkers,” Parsian said.

Although these are preliminary data, she hopes that someday MRI might provide valuable noninvasive information about tumor biology for selecting and guiding targeted therapies.

Parsian said larger prospective studies are needed to confirm these results and that MRI may complement biopsy to sample the whole tumor and reflect tumor heterogeneity.

“I think the final goal of radiology is to get more information while doing the least amount of intervention possible for the patient,” she said. “It would be great if we could improve our understanding of breast cancer biology and predict response to different therapies with imaging. Our study suggests MRI may play a valuable role in this process.”

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The mission of the CTRC-AACR San Antonio Breast Cancer Symposium is to produce a unique and comprehensive scientific meeting that encompasses the full spectrum of breast cancer research, facilitating the rapid translation of new knowledge into better care for patients with breast cancer. The Cancer Therapy & Research Center (CTRC) at The University of Texas Health Science Center at San Antonio, the American Association for Cancer Research (AACR) and Baylor College of Medicine are joint sponsors of the San Antonio Breast Cancer Symposium. This collaboration utilizes the clinical strengths of the CTRC and Baylor and the AACR’s scientific prestige in basic, translational and clinical cancer research to expedite the delivery of the latest scientific advances to the clinic. The 34th annual symposium is expected to draw nearly 8,000 participants from more than 90 countries.

Presenter: Sana Parsian, M.D.

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Title: Quantitative MRI for Noninvasive Prediction of Prognostic Markers in Breast Cancer.

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Background: Magnetic resonance imaging (MRI) is a valuable tool for assessing extent of breast cancer and monitoring treatment response. Quantitative measures by diffusion-weighted MRI (DWI) and dynamic contrast-enhanced (DCE) MRI reflect tumor cellularity and vascularity. Tumor grade and some histopathological markers, such as ER, PR, HER-2, Ki67 and P53, are prognostic factors that can also be associated with tumor cellularity and vascularity. DWI and DCE measures may therefore provide a noninvasive means for predicting disease prognosis and stratifying patients to appropriate therapies. The purpose of this study was to investigate the correlation between quantitative MRI features and prognostic pathological factors in patients with invasive breast cancer.

Methods: This IRB-approved retrospective study included patients with biopsy-proven invasive cancer who underwent 1.5T breast MRI (including DCE and DWI) from October 2005 to May 2006 prior to treatment. Pathology data was obtained from pre-treatment biopsy and intrinsic subtype classification was approximated by standard immunohistochemistry characteristics. After excluding cases with missing MRI or pathology data, the final study cohort included 41 invasive cancers (36 ductal and 5 lobular carcinomas) in 36 patients. MRI measures included lesion DCE kinetic features: peak initial enhancement (PE), percent rapid enhancement (RE), and percent washout (WO), and DWI normalized apparent diffusion coefficient values (nADC). Associations between imaging features and pathology markers, cancer grades and intrinsic subtypes were evaluated by Mann-Whitney U test and multivariate logistic regression.

Results: Results of univariate comparisons are summarized in Table 1. One or more DCE-MRI kinetic parameters were significantly predictive ($p < 0.05$) of each of the histopathological markers with the exception of ER, which was marginally associated with WO ($p = 0.05$). Each of the DCE kinetics parameters significantly discriminated grade III tumors from grades I and II and luminal A from luminal B and basal-like intrinsic subtypes. In multivariate regression, both PE and WO were significant independent predictors of tumor grade ($p = 0.0094$, $p = 0.0005$, respectively). WO and nADC were significant independent predictors of PR status ($p = 0.0054$, $p = 0.0027$), while PE was the only significant independent predictor of both Ki67 ($p = 0.014$) and intrinsic subtype ($p = 0.015$).

Conclusion: This preliminary study suggests that quantitative MRI measures are associated with prognostic tumor markers and may provide valuable noninvasive characterization of tumor biology. Larger prospective studies are needed to validate our findings.

Table 1. Imaging features versus prognostic pathological factors in 41 invasive breast tumors (p

values given)

| | n +/- | PE | RE | WO | nADC |
|---------|--|--------|--------|--------|--------|
| ER | 31+/ 10- | 0.145 | 0.457 | 0.051 | 0.121 |
| PR | 25+/ 16- | 0.015* | 0.095 | 0.015* | 0.028* |
| HER2 | 5+/ 36- | 0.297 | 0.036* | 0.484 | 0.577 |
| Ki-67 | 27 high/ 14 low | 0.020* | 0.069 | 0.017* | 0.891 |
| P53 | 9+/ 30- | 0.460 | 0.325 | 0.048* | 0.841 |
| Grade | 12 I/ 14 II/ 15 III | 0.004* | 0.036* | 0.004* | 0.908 |
| Subtype | 17 Luminal A/ 15 Luminal B / 9 Basal | 0.009* | 0.027* | 0.021* | 0.096 |

* Significant correlation ($p < 0.05$)