Novel Blood Based Circulating Tumor Cell Biomarker For Breast Cancer Detection

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BACKGROUND AND PURPOSE

The goal of mammogram screening (and other breast-cancer screening tests) is to detect breast cancer earlier than it would otherwise manifest clinically, when it is more likely to be localized. Data clearly show that detection of breast cancers at smaller sizes and earlier stages is associated with better patient outcomes, lower morbidity, and reduced breast cancer death.1

There is an unmet need for a blood test to detect breast cancer in women with dense breast tissue or clinically aggressive subtypes that may be missed by mammograms. Cell-free DNA in blood has shown 15-58% sensitivity for breast cancer.2 In this study, we evaluated the performance of a circulating tumor cell (CTC) assay as a complimentary biomarker for detecting breast cancer in an Asian population, which has high incidence of dense breast tissue.

METHODS AND STUDY DESIGN

A single-center, IRB-approved, prospective and blinded clinical study was conducted on 114 Taiwanese females with biopsy-confirmed breast cancer, and 50 healthy controls confirmed by ultrasound or mammogram. A single-center, IRB-approved, prospective and blinded clinical study was conducted on 114 Taiwanese females with biopsy-confirmed breast cancer, and 50 healthy controls confirmed by ultrasound or mammogram. Four milliliters of blood was collected prior to imaging and processed using the CellMax biometric platform (CMx Platform3) which enumerates CTCs utilizing selection criteria based on a set of markers (cytokeratin 18, mamacoglobin, CD45), cell morphology (size, N/C ratio) and nucleic morphology (Fig.3). Logistic regression models for CMx CTC counts and patient age were used to assess the classification performance of the CMx test (Fig.4).

RESULTS

Of the 114 cancer cases (80% were stage 0–2), the subtypes were confirmed for 102 (62% ER/PR+/HER2-, 22% HER2+, 16% TNBC). CTC count was a significant predictor of cancer status (Likelihood Ratio P-value = 0.0001). At 90% specificity (exact 95% CI: 78.2%, 95.6%) sensitivity was 56.3% (95% CI: 43.3%, 68.6%) for the most common subtype ER/PR+/HER2-; 36.4% (17.2%-59.3%) for HER2+; 43.8% (19.8%-70.1%) for TNBC, and 46.3% (37.1%-56.1%) overall.

CONCLUSIONS

Circulating tumor cells as a blood-based biomarker have great potential for use in the management of breast cancers. Testing for CTCs is efficient, non-invasive, and can improve the current standard of care. In this initial study, our CTC assay was shown to be a significant predictor of cancer status, demonstrating robust performance in distinguishing breast cancer patients from healthy controls. The CTC assay can easily be combined with cfDNA to enhance detection rates. Proof-of-concept data also suggests potential for a rule out test to avoid unnecessary follow-up biopsies in BIIRADS 3/4 patients. This assay is rapid, inexpensive, and easy to implement in most clinical labs. Given its broad applicability, this technology has the potential to have a substantive impact on the diagnosis and treatment of many cancers.

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DISCLOSURE

The authors declare no conflicts of interest.

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