Breast Cancer Whole Blood Screening

Analytical and Clinical Performance from Early Analysis of the International Identify Breast Cancer (IDBC) Study

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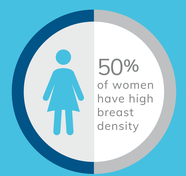
The Gap – underserved populations

60%
of women 35-50 detected after stage 1



70%
death rate if detected distant[1]

New tools are needed to address these groups. Blood tests also have potential to increase overall access, participation, and performance.

Study objective

Evaluate analytical and clinical performance of the Syantra DX™ Breast Cancer test for detecting an active breast cancer signature.

Molecular blood test (Syantra DX™ Breast Cancer)

Transcript quantification → AI/ML-enabled software → Positive/negative breast cancer

Non-fractionated whole blood samples were collected and analyzed as part of the IDBC prospective international clinical study (NCT04495244). Study sites are in Manchester (UK), Calgary (Canada), Oklahoma (USA) and Seoul (South Korea). The test uses custom reagents to analyze a gene expression panel (12 targets). Raw instrument data is fed to customized machine learning-informed algorithms that indicate presence or absence of an active breast cancer signature.

Methodology

Women aged 25 – 80 were consented and had blood drawn near the time of a screening mammogram (BI-RADS 1–2) or negative physical exam, or with a BI-RADs 3–5 score and prebiopsy. The clinical performance study and all subsequent amendments were reviewed by Institutional Ethics Boards and the following approvals were issued: Alberta, HREBA CC-17-0032; UK, 18/NW/0357-241391.

Blood collected from enrolled study participants → Shipped to the ACRB for registration → Sent to Syantra for extraction of nucleic acids → Aliquots sent for randomization, blinding & storage → Aliquots requested and the DX Breast Cancer Test is run → Test predictions reported to the study coordinator → Sample unblinding and correlation to participant status → Computation of perfomance metrics

Figure 1: Summary description of the IDBC prospective clinical study

Clinical study design

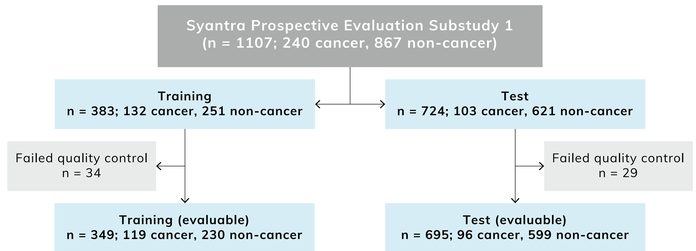


Figure 2: Data analysis plan for the IDBC study

Independent Test Set: 59% of breast cancer subjects were Stage 1 and 25% stage 2, and the median tumor size was 18 mm. 75% were hormone receptor positive, 10% were HER2 positive, and 5% were triple negative.

- Samples were randomized and double blinded (at collection sites and by the Alberta Cancer Research Biobank) prior to analyses.
- All clinical results presented are from the independent test set and are inferred results from the interim analysis. Performance metrics are reported for the test set with 99.5% confidence intervals (CI) computed through an exact binomial test (a = 0.005).

Results – high analytical performance

Robust and reproducible performance

- Work performed under an ISO 13485:2016 Quality Management System.
- Lab accreditation through College of Physicians and Surgeons of Alberta (CPSA).

Analytical performance of the test was demonstrated by evaluating linearity, reportable range of targets, analytical specificity, sample stability, reagent stability, repeatability, and reproducibility. Internal quality control checks were implemented within custom software for quantitative steps of the process to ensure consistency and validity of results.

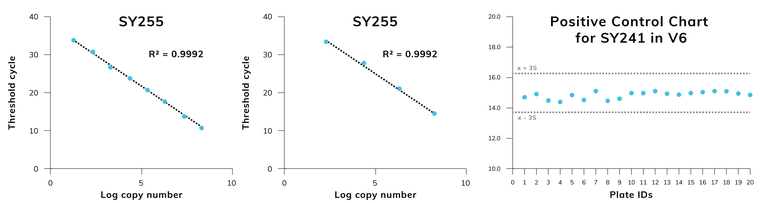


Figure 3: Linear regression data of tenfold dilution series spanning 8 orders of magnitude for SY255 (left) and 4 dilution points that span the amplification range in clinical samples representing the reportable range of amplification of the target (middle). Representative positive control chart (right) of a target control point (V6) in the test. Trends were evaluated by monitoring target amplification for the previous 20 plates and assessed against stringent predetermined criteria.

Results – strong clinical performance

Women aged 25-80:

- **Accuracy 92.2% (CI: 88.9% – 94.6%)**
  Specificity = 94.3% (CI: 91.0%-96.4%)
  Sensitivity = 79.2% (CI: 65.5%-88.4%)

Women aged 25-49:

- **Accuracy 98.5% (CI: 93.8% – 99.7%)**
  Specificity = 99.0% (CI: 94.2%-99.8%)
  Sensitivity = 91.7% (CI: 51.1%-99.1%)
- **D density**
  Specificity = 95.3% (CI: 77.4%-99.2%)
  Sensitivity = 88.9% (CI: 42.6%-98.9%)
- **Small tumors (<10 mm; n=19)**
  Sensitivity = 68.4%

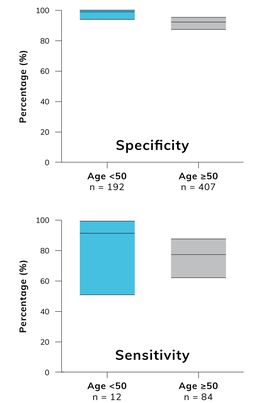


Figure 4: Performance of the test for participants under 50 and those aged 50 and over. Medians represent the specificity or sensitivity for each group and the whiskers represent the CIs computed through an exact binomial test. n = sample size.

Intended use

For European markets, the Syantra DX™ Breast Cancer test is intended to detect an active breast cancer signature and provide information to clinicians that might be used in directing further detection tests required to make a diagnosis.

Conclusions

The whole blood molecular test demonstrated high diagnostic specificity and sensitivity for breast cancer detection, including women:

- **With early-stage cancers,**
- **Under 50 and/or with dense breast tissue**

Acknowledgements

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References

1. SEER 17, Relative Survival by Stage (2012-2018).
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3. Pisano et al., DMIST Trial, Radiology, 2008, 246(2): 376–383

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