Liquid-biopsy based proteomic analysis for early detection of breast cancer

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Background

Widespread mammography has enabled the early diagnoses of breast cancer which drastically improves patient outcomes; however, it is distinctly less accurate in women with dense breast tissue. Alternative imaging methods such as ultrasound and MRI are available, but with their increased cost they are often not covered by insurance for the general population. One possible solution is to introduce a blood-based screening assay. Recent research has indicated the possibility of detecting cancer from blood even at early stages. Much of this research has focused on isolating cell free DNA (cfDNA); however, genomic analysis has not resulted in the sensitivity needed for early detection. Further, cfDNA does not correlate with protein abundance leading to the possibility that analyzing blood-based proteins may lead to higher sensitivity, especially in early-stage cancers. We analyzed the plasma proteome in a cohort of women with newly diagnosed early-stage breast cancer (Stage 0-2).

Methods

Blood samples were drawn and shipped to Astrin for plasma isolation and processing. Proteins from the plasma were enriched, digested, and de-salted using Astrin's proprietary sample preparation method prior to loading on the mass spectrometer. Raw mass spectrometry (MS) data was processed and mapped to a proprietary, Astrin developed spectral library to identify and quantify greater than 7,000 proteins per patient. Machine learning and AI was used to develop a protein-based classifier that identified early-stage breast cancer patients.

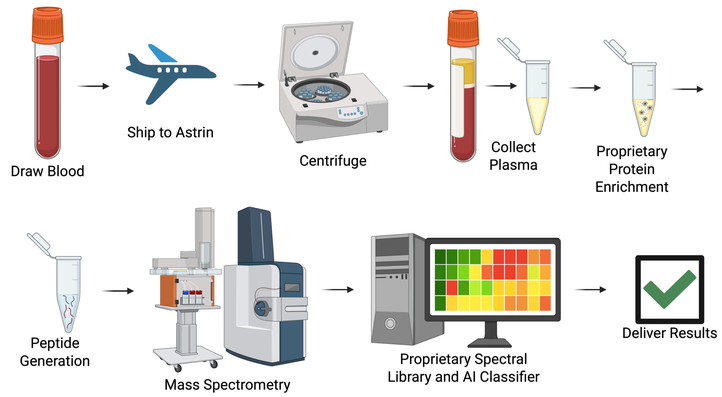


Figure 1. Workflow of Astrin's Blood-based Proteomic Assay for Early Detection

Conclusions and Future Directions

The initial findings from 284 women, comprising 116 with **newly diagnosed and treatment naïve Stage 0-2** [stage 0 (n=31), I (n=72), II (n=13)] breast cancer and 168 healthy controls demonstrated a 90.5% sensitivity with a 90.5% specificity using a leave-one-out cross-validation (LOOCV) approach. When divided by stage, all stages had above 90% sensitivity while maintaining the 90.5% specificity. Overall, this assay underscores the groundbreaking potential of this liquid biopsy platform using proteomics.

To further validate this assay, we are looking to recruit larger prospective cohorts to enable integration of our assay into the clinic.

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Data and Findings

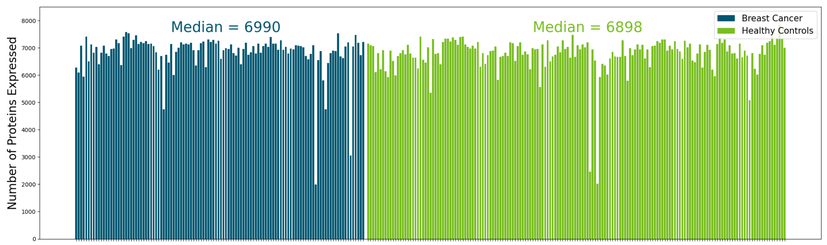


Figure 2. Number of proteins detected in each sample indicates both the consistency in our sample preparation and our mass spectrometry sensitivity across healthy and breast cancer cohorts.

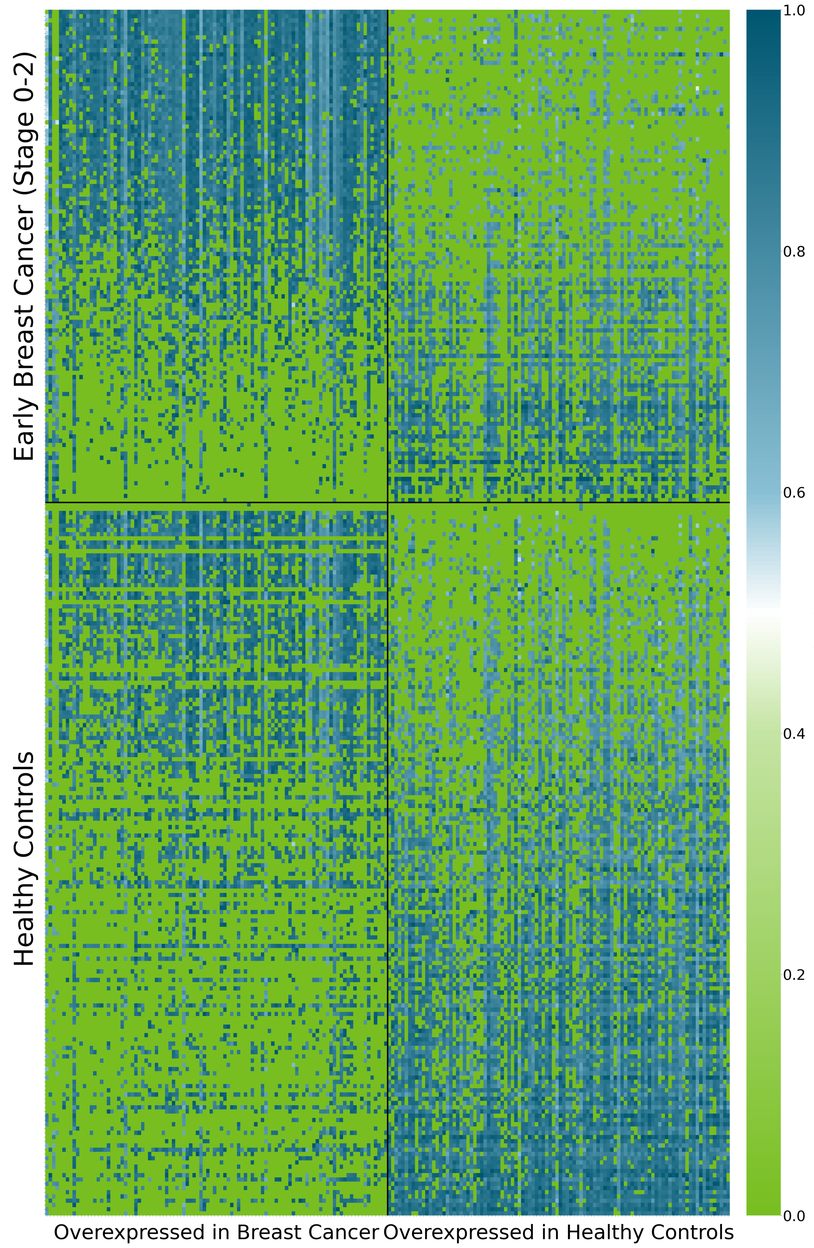


Figure 3. Differential proteomic profiles between cancer and healthy controls.

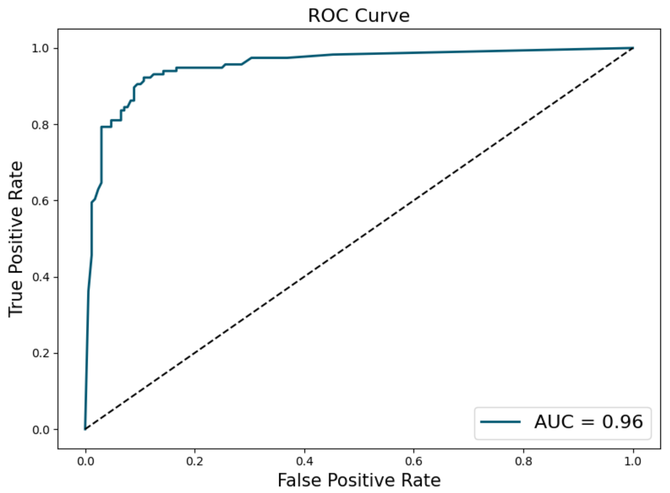


Figure 4. ROC curve demonstrating the accuracy of predicting a true positive at a given false positive rate

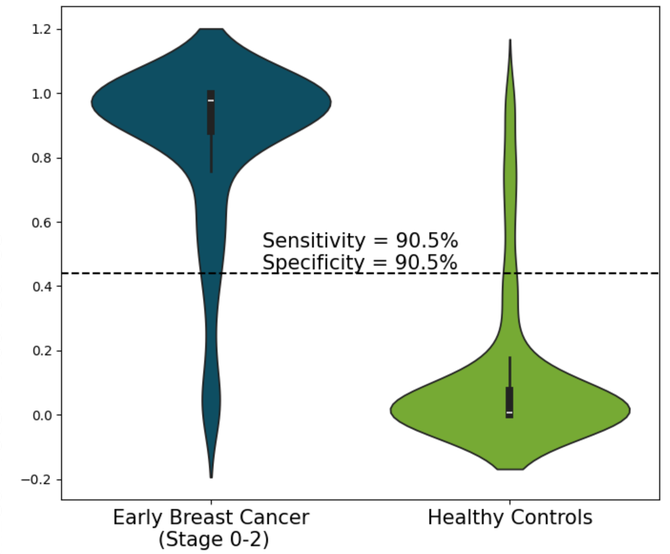


Figure 5. Sensitivity and specificity for entire cohort

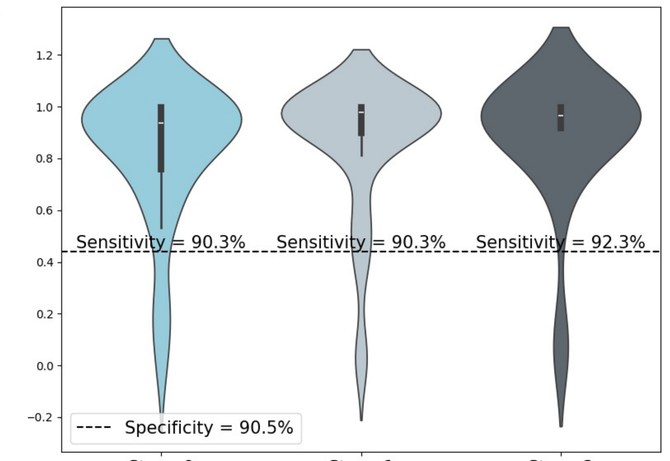


Figure 6. Sensitivity remains above 90% across all stages at >90% specificity.