P2-06-21: Preliminary validation of a multi-modal AI for stratification of early-stage breast cancer patients utilizing a foundation model for digital pathology

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Introduction

- Early breast cancers are risk-stratified based on clinicopathological characteristics and refined by genomic assays that predict risk of recurrence. These are often insufficient to fully personalize treatment.
- Digital pathology captures information about tissue morphology and the tumor microenvironment, providing valuable insights into tumor biology and patient outcomes.
- Artificial intelligence (AI), specifically self-supervised learning, have enabled researchers to train models to extract meaningful histopathological features by learning over large unlabeled datasets of pathology slides, providing a path to overcoming the limitations presented by traditional assays.

Methods

We developed an AI model that integrates digital pathology with clinical information to predict risk of breast cancer recurrence. We extracted pathology imaging features using our AI foundation model, Kestrel, trained on 500 million image patches derived from 80,000 pan-cancer WSIs.

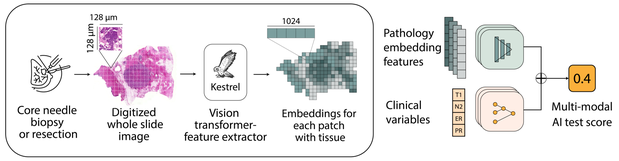


Figure 1: Imaging-based features from Kestrel were combined with clinical information to generate our multimodal AI test score

Patients

The AI test has been trained to predict recurrence and survival using 4,659 patients across 10 cohorts from six countries.

The external evaluation sets included five cohorts (n=3,502):

- Providence (n=1733) and TCGA (n=911) cohorts comprised all invasive breast cancer subtypes
- UChicago (n=421), Basel (n=269), and Karmanos (n=168) cohort included only HR+ HER2− patients previously tested with Oncotype DX as part of the standard diagnostic workflow.

Results

Performance robust in all external validation cohorts

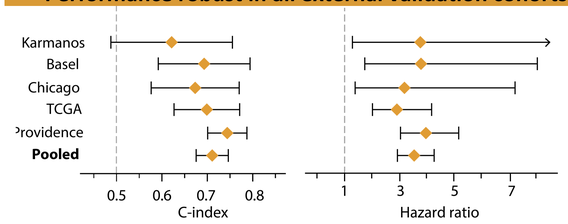


Figure 2: The AI test was found to be prognostic in all five patient cohorts used as external evaluation sets, for both C-index and hazard ratio. Pooled results are computed using random effects model. Hazard ratio are computed for every 0.2 increase in our AI test score.

Consistent performance across subgroups

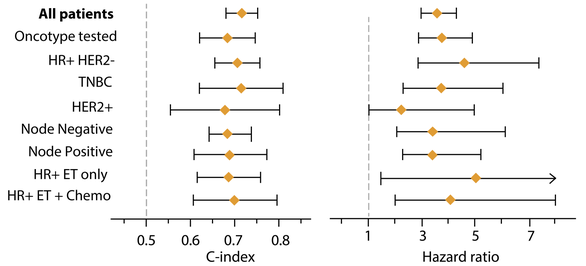


Figure 3: Our test demonstrates strong performance across clinically relevant subgroups, including HR+ HER2-, TNBC, and HER2+ patients.

Comparison to Oncotype DX

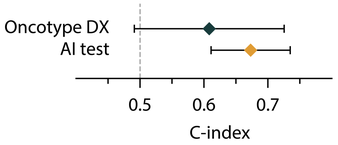


Figure 4: The AI test is a better predictor of recurrence than Oncotype DX.

All endpoints

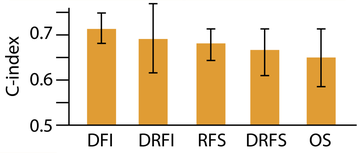
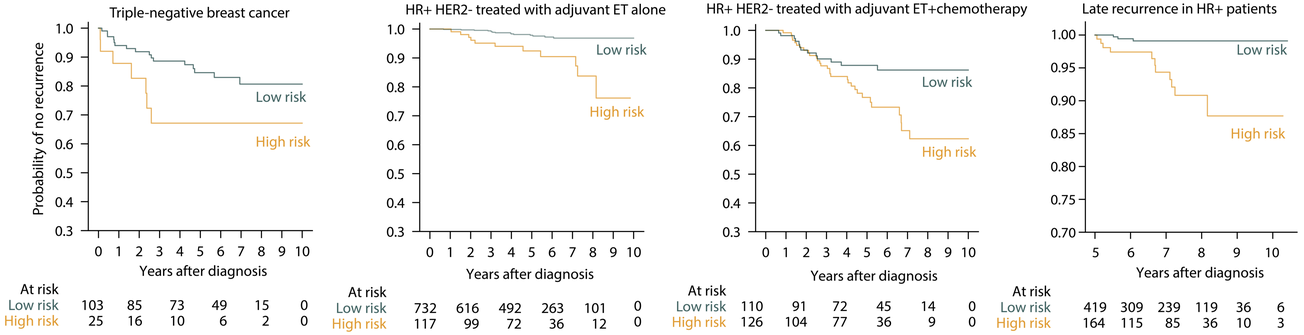


Figure 5: Our test is also prognostic for all secondary endpoints, including distant recurrence-free interval (DRFI), overall survival (OS) and recurrence-free survival (RFS).

Clinical use cases



In TNBC, there is an ongoing discussion about potential strategies to de-escalate the KEYNOTE-522 regimen, for example with shorter or anthracycline-free chemotherapy regimens or complete omittance of adjuvant treatment.

In hormone receptor-positive (HR+) patients, treatment selection questions revolve around the addition of adjuvant chemotherapy, extended endocrine therapy, and new agents like CDK4/6 inhibitors. We hypothesize that high-risk HR+ patients treated with adjuvant ET alone may benefit from adding chemotherapy, while high-risk HR+ patients who received both chemotherapy and endocrine therapy may see improved outcomes with the addition of CDK4/6 inhibitors

HR+ patients who completed five years of adjuvant ET could be candidates for extended endocrine therapy.

Conclusion

The AI test (Ataraxis Breast):

- Is predictive of recurrence and survival in non-metastatic invasive breast cancer
- Is more accurate in predicting recurrence than Oncotype DX
- Performs consistently in all major breast cancer groups across age, nodal status, molecular subtype, and received adjuvant treatment
- Works in HR+ HER2-, TNBC, and HER2+ patients
- Has potential to improve treatment selection

References

Read our full paper

Jan Witowski, Ken Zeng, Joseph Cappadona, Jailan Elayoubi, Elena Diana Chiru, Nancy Chan, Young-Joon Kang et al. "Multi-modal AI for comprehensive breast cancer prognostication." *arXiv preprint arXiv:2410.21256* (2024).

More information