PD11-07

AI-Driven Risk Reclassification in HR+/HER2−Breast Cancer: Real-World Comparison with the 21-Gene Assay

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BACKGROUND

Risk stratification in HR+ BC is critical for tailoring adjuvant therapy, as administration of CHT often depends on genomic risk scores such as the Oncotype DX (ODX) assay. However, ODX has limited accessibility and interpretability—particularly in intermediate-risk pts—highlighting the need for alternative, scalable prognostic tools.

OBJECTIVES

Evaluate performance of the new multimodal artificial intelligence-based test, Ataraxis Breast RISK (ATX), in predicting disease-free interval (DFI) and compare its accuracy and risk stratification to ODX.

•**PRIMARY ENDPOINT:** DFI (disease-free interval), defined as time from diagnosis to first recurrence (locoregional or distant).

METHODS

- Retrospective single-center study of **269 HR+/HER2– BC pts** (Basel University Hospital, 2010–2024) with available H&E slides and **ODX RS** results.
- **Slides digitized (40×)** and >1,000 morphological features extracted using an AI foundation model.
- ATX integrated digital pathology and **baseline clinical data** (age, T/N stage, ER/PR/HER2, subtype) to produce a **continuous 5-year risk of recurrence score**.
- Prognostic accuracy for **DFI** assessed via **Cox models**, **Harrell's C-index**, and **KM curves**.
- **Comparative analysis:** Risk stratification, concordance, and **reclassification vs. ODX (TAILORx: low 0–10; int 11–25; high ≥26).**

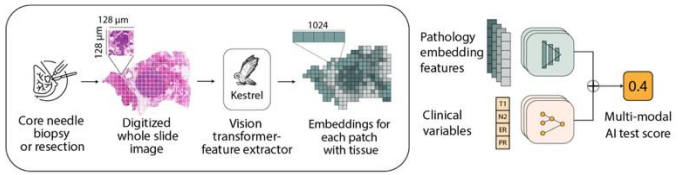


Fig. 1 Workflow of the ATX model, first extracting morphological features from H&E slides and integrating baseline clinical data

RESULTS

Demographics	
Median age n (range), (IQR)	59 (29-85), (IQR 17)
Tumor Characteristics	
pT1 n (%)	143 (53%)
pT2 n (%)	98 (36%)
Node positive n (%)	115 (43%)
Ductal histology n (%)	210 (78%)
Lobular Histology n (%)	47 (17.47%)
Grade 2 n (%)	146 (54%)
Ki-67% low n (%)	181 (67%)
Ki-67% high n (%)	88 (33%)
ODX low RS n (%)	59 (22%)
ODX intermediate RS n (%)	167 (62%)
ODX high RS n (%)	43 (16%)
ATX Breast Low Risk n (%)	187 (69.51%)
ATX Breast High Risk n (%)	82 (30.48%)
Treatment	
Chemotherapy n (%)	56 (21%)
Endocrine Therapy n (%)	257 (96%)
Outcome	
Any recurrence	25 (9%)
Cancer related deaths	3 (1.1%)

Table 1. Demographics, tumor characteristics, treatment and outcome

	without ATX Breast, HR (95%CI, p)	with ATX Breast, HR (95% CI, p)
ATX Breast	-	**4.18 (1.91-9.16, p<0.01)**
Grade	1.38 (0.66-2.88, p=0.39)	1.31 (0.61-2.80, p=0.48)
Age <50	2.07 (0.90-4.72, p=0.09)	2.44 (1.06-5.63, p=0.04)
ODX	1.60 (0.71-3.61, p=0.25)	1.15 (0.52-2.53, p=0.73)

Table 2. Multivariate Cox analysis with and without ATX model adjustments

High ATX risk patients showed higher recurrence rate than patients with low ATX risk (HR: 4.09, p<0.01; Figure 1).

ATX was prognostic of breast cancer recurrence with C-index of 0.70, while **Oncotype DX** showed a C-index of 0.55.

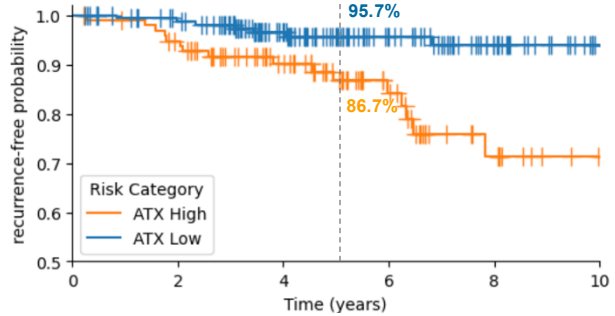


Fig. 2 Kaplan-Meier plot of disease-free interval (DFI) stratified by ATX Breast risk score. Pts. were classified into low/high risk ATX groups based on a predefined threshold of 10% 5-year risk of recurrence.

In multivariate analysis, ATX was a strong independent predictor - Table 2. Its scores correlated with higher tumor and nodal stage and showed variability within the ODX-intermediate group – Fig. 3.

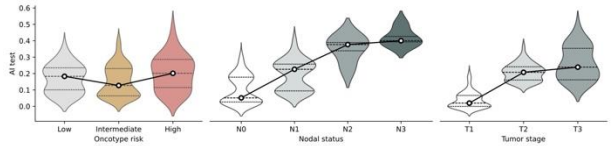


Fig. 3 ATX Breast distribution across ODX risk groups, node and tumor stage.

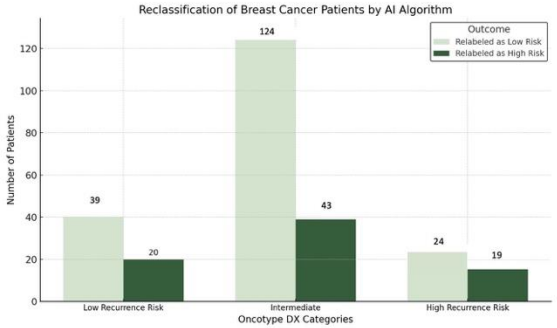


Fig. 4 Reclassification of the ODX risk categories according to ATX Breast

- **Low ODX group (n=59): 20 pts (33.9%)** reassigned to **high risk**
- **Intermediate ODX group (n=167): 124 pts (74.3%)** reclassified as **low risk**. **43 pts (25.7%)** reclassified as **high risk**.
- **High ODX group (n=43): 24 pts (55.8%)** reassigned to **low risk** by ATX.

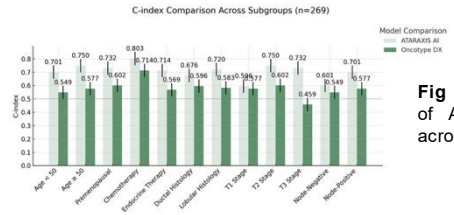


Fig 5. C-index comparison of ATX Breast and ODX across clinical variables

ATX Breast demonstrated superior predictive accuracy, particularly in chemotherapy-treated pts (C-index = 0.803), larger T2 tumors (C-index = 0.750) and node-positive subgroups (C-index = 0.701).

CONCLUSION

ATX Breast clarified risk for most intermediate ODX cases and may guide CHT administration.
These findings support ATX's clinical integration and prospective validation.

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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).