An AI algorithm for breast cancer detection improves future BC risk prediction among women with benign breast disease

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Background

- Women with a benign breast biopsy are at increased risk of future breast cancer (BC).
- Artificial intelligence models based on deep learning applied to mammography have been shown to improve breast cancer detection and risk estimation.[1,2]
  - Complementary to breast density
- The Transpara artificial intelligence detection system (ScreenPoint Medical) identifies *calcifications and soft tissue lesions* to determine suspicious regional findings and assigns a 1-10 detection score based on the most suspicious finding present across mammographic views (Fig 1).
- Transpara score has been shown to be a risk factor for interval and advanced cancer.[3]
- Performance in high-risk populations, including women with benign breast disease (BBD) is not clear.

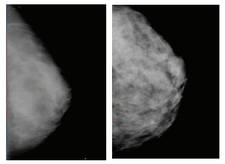


FIGURE 1: Mammograms
Craniocaudal view of mammograms with a Transpara score of 3 (on left) and 10 (highest, on right).

Objective

To evaluate if the addition of an AI cancer detection algorithm can improve risk prediction among women with BBD.

Methods

Study Design

- Participants were sampled from the Mayo Clinic Rochester BBD cohort.
- Cohort of 3,096 women with a diagnosis of BBD between 2002-2013 who also had a full field digital screening mammogram (FFDM).
- Follow-up for BC cases at least 2 years after BBD diagnosis.
  - Median follow-up is 12.9 years
  - 250 incident BC/ 134 invasive BC
- Imaging factors assessed on 4-view FFDM mammogram at time of BBD.
  - Transpara detection score (Raw score 0-10)
  - Volumetric Percent Density (VPD) using Volpara
- BBD severity/histologic impression assessed by three expert pathologists blinded to case status.
  - Non-proliferative (NP) findings
  - Proliferative disease without atypia (PDWA)
  - Atypical hyperplasia (AH)
- BMI obtained from electronic medical record.

Statistical Methods

- Cox proportional hazards regression models were applied to estimate hazard ratios (HRs) with 95% CIs.
- C-statistics estimated for models including the Transpara score, breast density and BBD severity to assess their contribution to risk prediction.
- Likelihood ratio tests (LRTs) and bootstrapping methods were used to compare model performance.
- Interactions evaluated between BBD severity with breast density and Transpara score by including an interaction term in the cox-proportional hazards model.

Results

TABLE 1. Characteristics of study sample.

Variable	Person Years	N Cases	Unadjusted HR (95% CI)	Age-Adjusted HR (95% CI)
Total	39307	219		
Age group				
Age <50 years	18013	83	1.0 (ref)	--
50-59 years	10347	68	1.50 (1.07, 2.10)	
60-69 years	7232	49	1.59 (1.09, 2.30)	
70+ years	3715	19	1.33 (0.79, 2.25)	
BMI Category				
<18.5	575	1	0.35 (0.05, 2.61)	0.35 (0.05, 2.56)
18.5-24.9	14016	69	1.0 (ref)	1.0 (ref)
25.0-29.9	10903	64	1.22 (0.86, 1.74)	1.15 (0.80, 1.65)
30.0+	11841	79	1.41 (1.01, 1.98)	1.35 (0.96, 1.89)
VPD quartile				
Q1	9579	48	0.88 (0.59, 1.32)	0.83 (0.55, 1.24)
Q2	9736	56	1.0 (ref)	1.0 (ref)
Q3	9770	56	1.00 (0.68, 1.47)	1.07 (0.72, 1.58)
Q4	10004	57	0.99 (0.67, 1.46)	1.15 (0.77, 1.71)
Transpara Score				
<5	9122	27	1.0 (ref)	1.0 (ref)
5-7	10454	47	1.86 (1.34, 2.60)	1.79 (1.28, 2.51)
8-10	19732	145	2.28 (1.61, 3.22)	2.22 (1.57, 3.15)

FIGURE 1. Association between Transpara Raw Score and Volpara volumetric percent density.

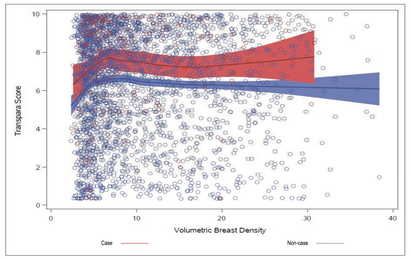


TABLE 2. Associations of BBD severity, Volumetric density and Transpara detection score with BC. Age and BMI adjusted.

Models	Cases/PY	HR (95% CI)	Model C-Stat
BBD Severity			.616 (.573, .659)
NP	78/19303	1.00 (REF)	
PDWA	108/17255	1.56 (1.15, 2.11)	
AH	33/2750	3.19 (2.05, 4.98)	
Log VPD per 1 SD	217/39089	1.27 (1.06, 1.52)	.577 (.537, .617)
Transpara (per 1 unit)	219/39307	1.16 (1.09, 1.24)	.628 (.588, .668)

FIGURE 2. Association of BBD severity (histologic impression) with Volumetric density.

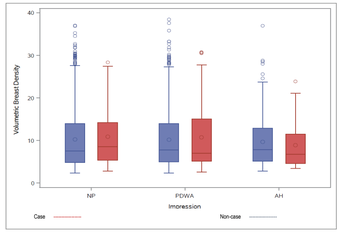


FIGURE 3. Association of BBD severity (histologic impression) with Transpara score.

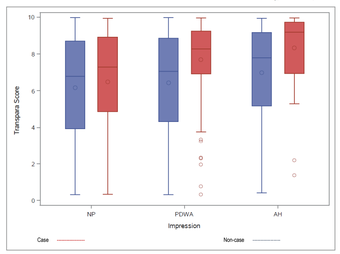


TABLE 3. Multivariate models: Imaging risk factors and BBD severity with BC risk. Age and BMI adjusted.

	Models	Cases/PY	HR (95% CI)	Model C-Stat
1	BBD Severity			.626 (.584, .668)
	NP	76/19207	1.00 (REF)	
	PDWA	108/17149	1.59 (1.17, 2.16)	
	AH	33/2733	3.25 (2.08, 5.07)	
	Log VPD per 1 SD	217/39089	1.26 (1.05, 1.52)	
2	BBD Severity			.650 (.608, .692)
	NP	78/19303	1.00 (REF)	
	PDWA	108/17255	1.51 (1.12, 2.05)	
	AH	33/2750	2.90 (1.86, 4.51)	
	Transpara (per 1 unit)	219/39307	1.15 (1.08, 1.22)	
3**	BBD Severity			.651 (.609, .694)
	NP	76/19207	1.00 (REF)	
	PDWA	108/17149	1.55 (1.14, 2.10)	
	AH	33/2733	2.95 (1.89, 4.60)	
	Log VPD per 1 SD	217/39089	1.14 (1.07, 1.21)	
	Transpara (per 1 unit)	217/39089	1.19 (0.99, 1.44)	

**Marginally significant improvement in C-statistic compared to model 1 (change =0.024, 95% CI: 0.000,0.047).

Evaluation of interactions:

- No evidence for interaction between VPD and BBD severity on BC risk.
- There was a statistically significant interaction between BBD severity and Transpara score on BC risk (P=0.02).
  - HR=1.04 (0.96, 1.14) per 1-unit Transpara score for NP
  - HR=1.17 (1.04, 1.33) per 1-unit Transpara score for PDWA
  - HR=1.30 (0.97, 1.74) per 1-unit Transpara score for AH
  - Almost no difference in C-statistic (C=.654) with interaction included.

Summary

- Among women with BBD, Transpara detection score provides similar information for risk prediction compared to models that include BBD severity and volumetric density.
- Stronger association of Transpara detection score with BC for women with PDWA and AH vs. NP.
- AI-models specifically trained for risk (vs. detection) are likely to improve risk prediction even further.

References

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