Prediction of the 21-gene recurrence score by a non-genomic approach in stage I estrogen receptor-positive, HER2-negative breast cancer

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Introduction

- The recurrence score (RS), which is derived from the results of an assay of 21 genes, predicts the likelihood of recurrence in patients with breast cancer, thus potentially helping clinicians decide when to recommend chemotherapy.
- However, non-genomic clinicopathologic prognostic markers may also be able to distinguish patients with low, intermediate, and high risk of recurrence without the added cost of genetic testing.

Objectives

Develop a novel non-genomic tool called **predicted RS (pRS)** and investigate the relationship between RS and pRS among patients with **stage I estrogen receptor-positive, human epidermal growth factor receptor 2-negative (HER2) breast cancer**.

Methods

- We reviewed the records of 1055 patients at The University of Texas MD Anderson Cancer Center with estrogen receptor-positive, HER2-negative stage I breast cancer who had RS results available.
- We used multivariable linear regression to develop pRS in this population.
- We then validated our models in a cohort of 242 patients from Anne Arundel Medical Center with the same characteristics.

Results

Table. 1 Baseline characteristics of the patients.

Characteristic	No. (%) MDA cohort, n = 1055	AAMC cohort, n = 242	P- value
Median RS *(interquartile range)*	17 (12-22)	15.5 (11-23)	0.1212
Categorical RS			0.0083
Low (<18)	585 (55.5)	148 (61.2)	
Intermediate (18-30)	380 (36.0)	64 (26.4)	
High (>30)	90 (8.5)	30 (12.4)	
Median age *(interquartile range)*	54 years (47-62)	58 years (50-66)	<0.0001
Median tumor size *(interquartile range)*	13 mm (10-16 mm)	12 mm (9-15 mm)	0.0058
Pathologic stage*			<0.0001
IA	1006 (95.4)	227 (100)	
IB	49 (4.6)	0 (0)	
Missing sentinel lymph node status	0	15	
Histologic grade			0.0044
I	254 (29.5)	98 (40.7)	
II	464 (53.8)	109 (45.2)	
III	144 (16.7)	34 (14.1)	
Unknown	193	1	
Nuclear grade			<0.0001
1	154 (16.7)	132 (54.5)	
2	596 (64.6)	79 (32.6)	
3	173 (18.7)	31 (12.8)	
Unknown	132	0	
Median Ki67 *(interquartile range)*	11 (5-25)	15 (8-31)	0.0091
Median ER expression *(interquartile range)*	95% (90-99%)	95% (90-99%)	0.0128
Median PR expression *(interquartile range)*	80% (32-95%)	90% (50-97%)	0.0017

The pRS model is :

$$pRS = 26.089 - 0.071ER - 0.092PR + 0.132Ki67 + 1.08\ I\ [HG=II] + 7.129\ I\ [HG=III]$$

where **I** is an indicator function.

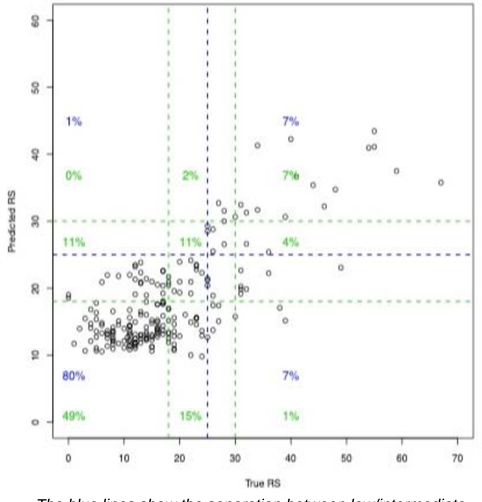
- The pRS had a Pearson correlation coefficient of 0.7352 with RS in our validation cohort ($p < 0.0001$).
- Among the 242 patients in the validation cohort, 209 (86.4%) had all covariates available to calculate pRS.

Table. 2 - Correlation between recurrence score (RS) and predicted RS (pRS) in the Anne Arundel Medical Center validation cohort using two risk categories.*

	RS		
pRS	High	Low	Total
High	24 (92%)	2 (8%)	26
Low/intermediate	15 (8%)	168 (92%)	183
Missing data	6	27	33
Total	45	197	242

- Two (1.2%) of the 170 patients with low/intermediate RS (RS ≤25) were classified into the high pRS group (P-value <0.0001).
- None of the patients with a pRS >30 were considered low/intermediate risk (RS ≤ 25) as defined in the TAILORx trial.

Figure. 1 – Discrimination plot for true recurrence score (RS) and predicted RS as calculated using the MD Anderson cohort in 242 patients from Anne Arundel Medical Center.



The blue lines show the separation between low/intermediate-risk (RS ≤ 25) and high-risk (RS > 25) patients according to TAILORx data (see text). The green lines show low-risk (RS < 18), intermediate-risk (RS = 18-30), and high-risk (RS > 30) patients according to the standard RS cutoffs.

Conclusion & Future Perspective

- **Our results indicate that the pRS tool accurately identified a subset of patients who had an RS >25 and thus would not need to undergo the genetic test to determine their high-risk status.**
- **The cost of the 21-gene assay to determine RS is an important consideration.**
- **Our results suggest that it would be cost-effective without substantial risk to avoid using the 21-gene assay in certain patient populations, which in our results represented 9% of the validation cohort.**

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