IMPACT OF THE 21-GENE RECURRENCE SCORE ASSAY ON TREATMENT DECISION IN EARLY BREAST CANCER (EBC) PATIENTS WITH FAVORABLE PROGNOSTIC FACTORS

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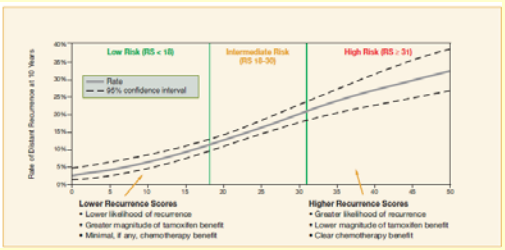
Background

• The 21-gene Onco*type* DX® assay is a clinically validated test that predicts the likelihood of chemotherapy benefit and the risk of distant recurrence for patients with early-stage estrogen receptor-positive (ER+) breast cancer.[1-5]
• It has been demonstrated that the result of the assay, the Recurrence Score® (RS) value, provides additional information independent of traditional prognostic markers.[1-6]
• The use of Onco*type* DX for adjuvant decision-making is described in several guidelines, including St Gallen, NCCN®, ASCO®, and ESMO.[7-10]
• The 2009 St Gallen guidelines state that "validated multigene tests, if readily available, could assist in deciding whether to add chemotherapy in cases where its use was uncertain after consideration of conventional markers."
• The NCCN guidelines describe the application of the Onco*type* DX assay for patients with node-negative or micrometastatic disease.
• Clinical utility studies have shown that use of the assay predominantly results in a reduction of adjuvant chemotherapy recommendations.[11]



Paik S, Shak S, Tang G, *et al.* A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. *N Engl J Med.* 2004;351(27):2817-26.

The RS is a Continuous Predictor of the Risk of Distant Recurrence and Likely Magnitude of Chemotherapy Benefit.

Objective

To describe the results from our institutions' three year experience using the Oncotype DX assay to identify patients who need chemotherapy despite the presence of primarily favorable characteristics

Patients and Methods

• All patients considered for evaluation with Onco*type* DX assay were pre- or post-menopausal with ER+, HER2-, early-stage breast cancer.
  - One patient was identified as HER2+ and was not included in the analysis.
• Unfavorable factors were defined as tumor size > 2cm, tumor grade II or III, Ki67 >10%, or the presence of lymph node micrometastasis.
• The Onco*type* DX assay was performed on formalin-fixed paraffin embedded tissue at the Genomic Health, Inc.® laboratory in Redwood City, California.
• The risks and benefit of adjuvant chemotherapy (CT) were discussed with each patient after knowledge of the RS results. All patients were treated with endocrine therapy.

Table 1. Patients' Characteristics

Characteristic		N=42
Age (years)	Mean	50.47 (range 35-67)
		N (%)
Tumor Size	≤ 2 cm	39 (92.9)
	> 2 cm	3 (7.1)
Tumor Grade	I	9 (21.4)
	II	17 (40.5)
	III	3 (7.1)
	Unknown*	13(31.0)
Progesterone Receptor	Positive	34 (81.0)
	Negative	8 (19.0)
Tumor Type	Lobular	13 (31.0)
	Ductal	28 (66.7)
	Hybrid	1 (2.4)
Nodal Status	Negative	38 (90.5)
	Micrometastasis in 1 node	2 (4.8)
	Micrometastasis in 2 nodes	2 (4.8)
Ki-67	< 10%	21 (50.0)
	10-20%	10 (23.8)
	> 20%	10 (23.8)
	Unknown	1 (2.4)

Figure 1. Distribution of Patients by Recurrence Score Risk Groups

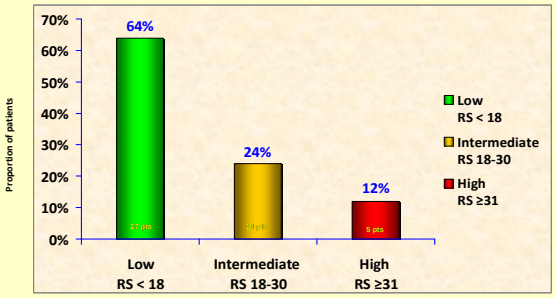


Table 2. Patients with No Unfavorable Characteristics

Patient ID	Age	Histology	Tumor Size	LN+	Grade	Ki67	RS	Adjuvant Chemotherapy Recommended or Received
209400	46	Ductal	1.1	0	I	<10%	19	Yes
208069	45	Lobular	1	0	n/a	<10%	21	Yes
209069	48	Ductal	1.1	0	I	<10%	13	No
209008	60	Lobular	1.5	0	n/a	<10%	9	No
208046	43	Lobular	2	0	n/a	<10%	9	No
209106	44	Lobular	1.2	0	n/a	<10%	9	No
207080	65	Lobular	1.6	0	n/a	<10%	15	No
208065	47	Lobular	1.7	0	n/a	<10%	15	No
208110	54	Lobular	1	0	n/a	<10%	16	No
208093	47	Lobular	1.5	0	n/a	<10%	16	No
208059	60	Ductal	0.8	0	I	n/a	17	No
209014	67	Lobular	1.7	0	n/a	<10%	18	No
208060	42	Ductal	0.7	0	I	<10%	18	No
209039	60	Lobular	1	0	n/a	<10%	20	No
210093	48	Lobular	1.3	0	n/a	<10%	13	No

Table 3. Patients with One Unfavorable Characteristic

Patient ID	Age	Histology	Tumor Size	LNmic	Grade	Ki67	RS	Adjuvant Chemotherapy Recommended or Received
210076	53	Ductal	2	0	I	10-20%	19	Yes
210047	53	Ductal	0.9	0	II	<10%	20	Yes
210081	43	Ductal	1	0	I	10-20%	10	No
210017	49	Lobular	2.2	0	n/a	<10%	13	No
210071	47	Ductal	0.8	0	II	<10%	13	No
209016	54	Ductal	0.8	0	II	<10%	16	No
208108	41	Ductal	1.2	0	II	<10%	16	No
209033	45	Lobular	1.2	0	n/a	10-20%	16	No
210028	53	Ductal	0.8	2	I	<10%	17	No
209019	35	Ductal	1	0	I	>20%	12	No

Table 4. Patients with Two or Three Unfavorable Characteristics

Patient ID	Age	Histology	Tumor Size	LNmic	Grade	Ki67	RS	Adjuvant Chemotherapy Recommended or Received	Number of Unfavorable characteristics
210029	47	Ductal	1	1	II	10-20%	9	Yes	3
210010	57	Ductal	1.5	0	II	10-20%	5	No	2
208117	52	Ductal	1	0	II	10-20%	10	No	2
209005	47	Ductal	2.2	0	I	10-20%	11	No	2
209036	47	Ductal	1.6	0	II	10-20%	16	No	2
209030	53	Hybrid	2	0	II	10-20%	16	No	2
209080	54	Ductal	2	1	II	<10%	24	No	2
208048	51	Ductal	1	0	II	10-20%	6	No	2
209051	55	Ductal	1.7	0	III	>20%	12	Yes	2
208097	36	Ductal	1.5	2	II	>20%	25	Yes	3
210079	43	Ductal	1.2	0	II	>20%	29	Yes	2
210078	53	Ductal	1.2	0	II	>20%	34	Yes	2
209113	62	Ductal	1.2	0	II	>20%	37	Yes	2
208063	54	Ductal	0.8	0	III	>20%	39	Yes	2
210038	55	Ductal	1.5	0	III	>20%	40	Yes	2
209046	41	Ductal	3	0	II	>20%	42	Yes	3
209053	64	Ductal	1.8	0	II	>20%	11	No	2

- One patient, not included in the analyses, was assayed due to conflicting clinocopathologic characteristics (young age, small tumor size, LNmic in 1 node, high ER & PgR expression, HER2(+). The RS was high (35) and she received Chemotherapy followed by Hormonal treatment.

Results

• **There was a range of OncotypeDX Recurrence Scores for all patients, regardless of the presence of unfavorable characteristics.**
  - This distribution is comparable to previously described cohorts ascertained in a clinical setting.
• Among the 15 patients with No Unfavorable Characteristics:
  - 10 patients had a Low RS (RS<18); CT* was not recommended.
  - 5 patients had an Intermediate RS (RS 18-30); CT was recommended in two.
• Among the 10 patients with One Unfavorable Characteristic:
  - 8 patients had a Low RS (RS<18); CT was not recommended.
  - 2 patients had an Intermediate RS (RS 18-30); both received CT.
• Among the 17 patients with 2 or 3 Unfavorable Characteristics:
  - 9 patients had a Low RS (RS<18); CT was not recommended but 2 patients chose to receive CT.
  - 3 patients had an Intermediate RS (RS 18-30); CT was recommended in two.
  - 5 patients had a High RS (RS≥31); all of them received CT.

*CT= Chemotherapy

Summary and Conclusions

• This small study of a non-randomized series of early breast cancer patients shows the experience of a single institution and further reinforces that the clinicopathologic criteria for categorizing patients does not predict the RS from the 21-gene Oncotype DX assay.
• The majority of the patients with one or more unfavorable prognostic factors would be classified as "intermediate risk" by St Gallen criteria.
  - For patients with an intermediate risk by St Gallen criteria, there is no clear cut recommendation regarding the choice of adjuvant chemotherapy; recommendation is either hormonal therapy alone or chemotherapy followed by hormonal therapy.
    • In this study, approximately 41% of patients with one or more unfavorable prognostic factor was recommended or received chemotherapy.
  - The RS classified 80% of patients with One Unfavorable Characteristic to low risk and thus spared them exposure to chemotherapy.
  -The RS classified 52.9% with Two or Three Unfavorable Characteristics as Low Risk, 17.7 % as Intermediate Risk and 29.4% as High Risk.
  - Among all patients, only in 26.2% of them CT was recommended following the result of the OncotypeDX RS (two more patients with low RS chose to receive adjuvant CT).
• The results from this study indicate that Oncotype DX may be a useful decision tool in clinical practice.

References

(1) Paik S, et al. *N Engl J Med.* 2004;351(27):2817-26. **(2)** Paik S, et al. *J Clin Oncol.* 2006;24(23):3726-34. **(3)** Habel LA, et al. *Breast Cancer Res.* 2006;8(3):R25. **(4)** Dowsett M, et al. *J Clin Oncol.* 2010;28(11):1829-34. **(5)** Albain K, et al. *Lancet Oncology.* 2010;11(1):55-65. **(6)** Goldstein LJ, et al. *J Clin Oncol.* 2008 ;26(25):4063-71. **(7)** Harris L, et al. *J Clin Oncol.* 2007;25(33):5287-5312. **(8)** NCCN Guidelines. *Breast Cancer.* www.nccn.org, v2.2011. **(9)** Aebi S, et al. *Ann Oncol.* 2010;21(Suppl 5):v9 – v14. **(10)** Goldhirsch A, et al. *Ann Oncol.* 2009;20(8):1319-29. **(11)** Hornberger J and Chien R. SABCS 2010. **(12)** Palmer G, et al. ECO & ESMO 2009.

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