Effect of a 21-Gene Reverse-Transcriptase Polymerase Chain Reaction Assay on Treatment Recommendations for Patients with Lymph Node–Positive and Estrogen Receptor–Positive Breast Cancer

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Background & Objectives

- The Onco*type* DX® Recurrence Score (RS) assay provides a reliable method of estimating the risk of distant recurrence for individual patients with node-negative, estrogen receptor–positive (N-/ER+) breast cancer and enables oncologists to identify specific patients with N-/ER+ breast cancer who are unlikely to benefit from chemotherapy.
- Preliminary data show that the Onco*type* DX® RS predicts low recurrence rates in a large proportion of node-positive, estrogen receptor–positive (N+/ER+) patients and may also predict chemotherapy benefit.[1-3]
- **Objectives:**
  1. Determine whether the Onco*type* DX® assay results affected adjuvant treatment recommendations for N+/ER+ patients.
  2. Identify reasons for ordering the assay in N+/ER+ breast cancer.

Methods

- Web-based survey that targeted medical oncologists who ordered Onco*type* DX® for patients with N+/ER+ breast cancer.
- Approved by an independent institutional review board.
- Survey items included physician demographics, general use and views of Onco*type* DX®, and recent use of the assay for patients with N+/ER+ breast cancer. Respondents were surveyed about their most recent patient with N+/ER+ breast cancer; the survey asked for clinical characteristics and what treatment recommendations were made before and after receiving the Onco*type* DX® assay results.
- 1,017 medical oncologists who had ordered Onco*type* DX® in patients with N+/ER+ breast cancer were invited to participate.
- Data were collected from May 2009 through June 2009. The survey was closed after reaching a prespecified minimum of at least 150 responses.
- Descriptive analyses summarized frequency and percentage distributions of the survey responses, classifying patients according to RS group: low (RS <18), intermediate (RS 18-30), and high (RS ≥31).
- Treatment recommendations were categorized as either:
  hormonal therapy alone or
  chemotherapy plus hormonal therapy.
- Decreased intensity of treatment recommendation was defined as a change from:
  chemotherapy plus hormonal therapy to hormonal therapy alone.
- Increased intensity was defined as a change from:
  hormonal therapy alone to chemotherapy plus hormonal therapy.

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Results

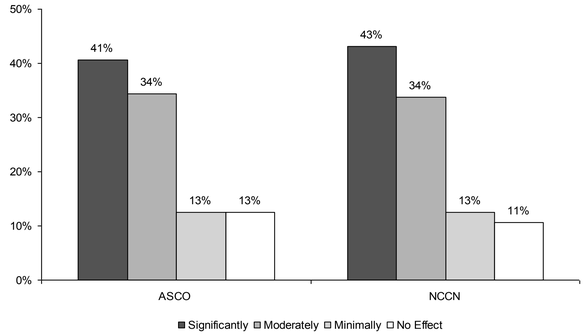
Table 1 - Physician Demographics

	All (N = 160) No. of responses (%)
Practice Setting	
Academic medical center	40 (25.0)
Community (multi-specialty, single-specialty, or solo practice)	114 (71.3)
Other	6 (3.8)
Years in Practice[a] mean (SD)	14.5 (10.3)
median (range)	11 (1−45)
Geographic Region	
East	41 (25.6)
Midwest	37 (23.1)
South	44 (27.5)
West	38 (23.8)

[a] 3 missing values

- 160 medical oncologists completed the survey (16% of those invited to participate). Most practiced in community (71%) or academic (25%) settings, and they had a median of 11 years of practice experience.

Figure 1 – Anticipated Extent of Increased Use of Onco*type* DX® in N+/ER+ Disease if Included in Clinical Practice Guidelines



- 75% (120/160) would moderately or significantly increase their use of Onco*type* DX® testing for patients with N+/ER+ disease if ASCO included the assay in their practice guidelines for this population.
- 77% (123/160) would moderately or significantly increase their use of Onco*type* DX® testing for patients with N+/ER+ disease if NCCN included the assay in their practice guidelines for this population.

Figure 2 – Reasons for Ordering Onco*type* DX® for Patients with N+/ER+ Breast Cancer

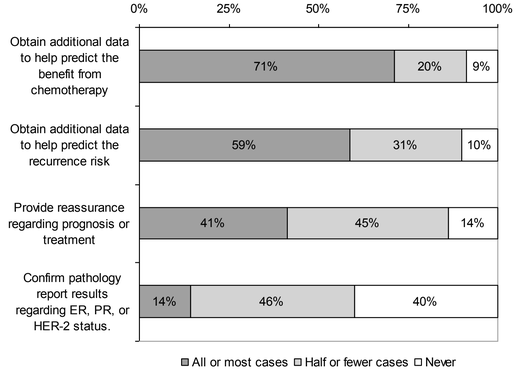


Table 2 – Characteristics of Patients with N+/ER+ Breast Cancer

	All (N = 160)
Age, mean (SD)	60.2 (11.2)
median (range)	61 (34-82)
	No. (%)
Menopausal status	
Postmenopausal	126 (78.8)
Premenopausal	30 (18.8)
Unknown	4 (2.5)
Tumor classification	
T1 (≤2 cm)	99 (61.9)
T2 (> 2 but ≤5 cm)	56 (35.0)
T3 (>5 cm)	4 (2.5)
Unknown	1 (0.6)
Positive axillary lymph nodes*	
1	110 (68.8)
2	28 (17.5)
3	10 (6.3)
≥4	4 (2.5)
Unknown	8 (5.0)
Comorbidities	
Any listed comorbidity	34 (21.3)
Diabetes mellitus	26 (16.3)
Uncontrolled hypertension	8 (5.0)
History of stroke or other cerebrovascular disease	0 (0.0)
Congestive heart failure or other chronic heart disease	0 (0.0)
Pulmonary fibrosis or other chronic lung disease	5 (3.1)
Chronic renal insufficiency	5 (3.1)
Peripheral neuropathy	0 (0.0)
Cytopenias	0 (0.0)

*Excludes micrometastases and isolated tumor cells

Table 3 – Effect of Onco*type* DX® Recurrence Score on Treatment Recommendations

	Recurrence Score: Low (< 18) n=72	Intermediate (18 – 30) n=53	High (≥ 31) n=13	All[a] n=138
Effect on recommendation	*Number of Patients*			
Any change	43	20	7	70 (51%)
Decreased Intensity[b]	35	11	0	46
Increased Intensity[c]	4	6	3	13
Other[d]	4	3	4	11
No change	29	33	6	68 (49%)

[a] Excludes 22 patients with no treatment recommendations before assay
[b] Decreased intensity = chemotherapy plus hormonal therapy → hormonal therapy alone
[c] Increased intensity = hormonal therapy alone → chemotherapy plus hormonal therapy
[d] 11 patients with treatment changes did not fit our definitions of either increased or decreased intensity (e.g., changes in chemotherapy components only or changes from hormonal therapy alone to chemotherapy alone)

- After obtaining patients' RSs, recommended treatment changed for 51% of N+/ER+ patients (70/138).
  - When recommended treatment was altered, chemotherapy was excluded in the revised plan in 66% of such cases (46/70), most of which occurred in patients with a low RS.
- In 13/138 cases (9%), the recommended treatment intensity increased from hormonal therapy alone to chemotherapy plus hormonal therapy.
- For the remaining 11 of 138 patients (8%), physicians stated that they changed their treatment recommendation; however, those changes did not fit our definitions of either increased or decreased intensity (e.g., changes in chemotherapy components only or changes from hormonal therapy alone to chemotherapy alone).

Limitations

- Voluntary, web-based survey might have yielded a biased sample.
- Descriptions of the most recent N+/ER+ patient may have been affected by recall bias. We prompted respondents to use the patient's chart as they completed the survey to minimize this.

Conclusions

- Medical oncologists who order Onco*type* DX® for patients with N+/ER+ breast cancer use the RS results much in the same manner as they do for N-/ER+ breast cancer.
- In more than half of the cases, the information obtained from the Onco*type* DX® assay altered the oncologists' initial treatment recommendations.
- Most of the treatment changes involved the elimination of chemotherapy entirely.
- More information about the impact of Onco*type* DX® on adjuvant treatment recommendations and outcomes will be gathered as medical oncologists continue to order the assay for patients with N+/ER+ breast cancer.

References

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