# 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

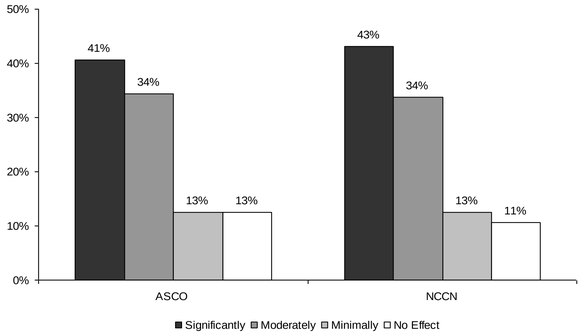
**Table 1 - Physician Demographics**

| | 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**

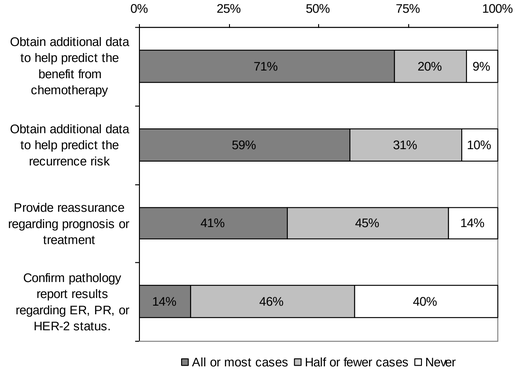



**Table 2 – Characteristics of Patients with N+/ER+ Breast Cancer**

| | 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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