Will oncotype DX DCIS testing guide therapy? A single-institution correlation of oncotype DX DCIS results with histopathologic findings and clinical management decisions

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Given the increased detection rates of ductal carcinoma *in situ* (DCIS) and the limited overall survival benefit from adjuvant breast irradiation after breast-conserving surgery, there is interest in identifying subsets of patients who have low rates of ipsilateral breast tumor recurrence such that they might safely forgo radiation. The Oncotype DCIS score is a reverse transcription-PCR (RT-PCR)-based assay that was validated to predict which DCIS cases are most likely to recur. Clinically, these results may be used to assist in selecting which patients with DCIS might safely forgo radiation therapy after breast-conserving surgery; however, little is currently published on how this test is being used in practice. Our study examines traditional histopathologic features used in predicting DCIS risk with Oncotype DCIS results and how these results affect clinical decision-making at our academic institution. Histopathologic features and management decisions for 37 cases with Oncotype DCIS results over the past 4 years were collected. Necrosis, high nuclear grade, biopsy site change, estrogen receptor and progesterone receptor positivity < 90% on immunohistochemistry, and Van Nuys Prognostic Index score of 8 or greater were significant predictors of an intermediate–high recurrence score on multivariate regression analysis ($P < 0.02$). Low Oncotype DCIS scores and low nuclear grade were associated with lower rate of radiation therapy ($P < 0.008$). There were seven cases (19%) with Oncotype DCIS results that we considered unexpected in relation to the histopathologic findings (ie, high nuclear grade with comedonecrosis and a low Oncotype score, or hormone receptor discrepancies). Overall, pathologic features correlate with Oncotype DCIS scores but unexpected results do occur, making individual recommendations sometimes challenging.

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Breast ductal carcinoma *in situ* (DCIS) is diagnosed in over 60 000 women in the United States each year, with an incidence of more than 50 new cases per 100 000 for women over 50 years old.¹ The goal of DCIS therapy is to prevent invasive cancer in the ipsilateral breast and to minimize morbidity and

mortality associated with invasive cancer. Current treatment modalities include combinations of surgery (mastectomy vs breast-conserving surgery), radiation therapy (partial or whole breast), and endocrine therapy, all of which are associated with varying levels of morbidity. Clinical trials have shown that radiation therapy after breast-conserving surgery reduces local recurrence and subsequent ipsilateral breast cancer events by up to 50%.^{2,3}

Multiple studies have demonstrated that only 13–52% of patients with untreated DCIS eventually develop subsequent invasive breast cancer,^{2,4} suggesting that up to half of patients with DCIS may not require adjuvant treatment. Therefore, there is a

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clinical need to provide risk stratification for patients with DCIS. Oncotype DX DCIS (abbreviated as Oncotype DCIS in the following sections; Genomic Health, Redwood City, CA, USA), a commercially available, multi-gene expression assay, was clinically validated to predict risk of breast cancer recurrence after breast-conserving surgery for DCIS without radiation.^{5,6} This assay uses a subset of genes from the original Oncotype DX assay, a counterpart assay that predicts invasive breast cancer progression and the benefit of chemotherapy.⁷ The Oncotype DCIS assay also reports quantitative estrogen receptor (ER) and progesterone receptor (PR) hormone receptor expression results.

Oncotype DX testing of invasive ER-positive breast cancers has become a common clinical practice when the benefit of chemotherapy is in question. However, both Oncotype DX and Oncotype DCIS tests in the United States cost ~\$4500 per case.⁸ In an effort to improve cost-effectiveness and value-based care, several groups have designed tools that use clinical and pathologic features to predict Oncotype DX scores on invasive cancers.^{8–13} However, the clinical and pathologic correlates of Oncotype DCIS remain largely unexplored due to the limited clinical experience with the assay.¹⁴

In this study, we reviewed the clinical, morphologic, and immunophenotypic data of DCIS cases sent for Oncotype DCIS at our institution, and analyzed whether any features were predictive of the Oncotype DCIS results. We also re-evaluated any unexpected Oncotype DCIS test results on the basis of histopathologic findings. Finally, we examined whether any features, including both histopathologic features and Oncotype DCIS score, were predictive of the final clinical management decision to include or forgo radiation therapy. Because the length of follow-up in this study was < 4 years, outcomes data were not included at this time.

Materials and methods

After obtaining IRB approval, our pathology database was queried for Oncotype DCIS testing from December 2012 to October 2016. No specific selection criteria are currently used in our institution for Oncotype DCIS case selection, and test requests are clinician- and patient-dependent. Pathology reports, medical records, and the Oncotype DCIS assay reports were reviewed to document demographic data, histologic findings, and treatment recommendations. Cases with previous or concurrent invasive breast carcinoma, or with invasive carcinoma diagnosed on following excision, were excluded. Representative H&E-stained slides from the block sent for Oncotype DCIS testing, as well as ER and PR immunohistochemical stained slides, were available and reviewed for 35 of 37 cases by CL, KM, and KA. The diagnosis and hormone receptor expression

status were confirmed. In addition, mitotic figures, periductal inflammation, biopsy site change, microcalcification, and DCIS cellularity were documented. Dense periductal inflammation was defined as three layers of lymphocytes surrounding at least 75% of the duct.¹⁴ The Van Nuys Prognostic Index score was calculated using patient age, tumor size, margin width, and pathologic classification.^{15–17} For this study, we selected a binary cutoff score of 8, as radiation or mastectomy was recommended for patients with score equal or higher than 8. The presence of biopsy site changes was also documented, as studies have shown that the presence of biopsy site change might affect Oncotype DX recurrence score for invasive breast cancer.⁹

For categorical variables, statistical comparisons between groups were made using χ^2 or Fisher's exact test, where appropriate. Multivariate analysis was conducted using stepwise logistic regression. All tests of significance were two-tailed, and significance was set at $P < 0.05$. The decision was made to do no further testing in the setting of the perfect predictor 'complete separation' problem precluding successful regression analysis. Statistical analysis was performed with SPSS statistical software (Statistical Package for the Social Science, IBM, Version 22.0, Armonk, NY, USA).

Results

Clinical Parameters and Histopathological Features

During the study period, 42 DCIS cases were identified with an Oncotype DCIS test ordered. Three cases were canceled by patients, and two cases were rejected due to insufficient material for testing. In all, 37 (90.2%) cases had an Oncotype DCIS test result, either on the initial biopsies (11%) or on the excision specimens (91%). All cases involved female patients, with a mean age of 57.7 years with a range of 34–82 years. The majority of the patients are over 50 years old (68%), with ER-positive (99%), intermediate-grade (57%) DCIS spanning a mean of 1.5 cm (0.3–5.0 cm). The histopathological features of the DCIS are listed in Table 1. Oncotype DCIS scores were reported with three tiers: low risk (score < 39, 25 cases, 68%); intermediate (score 39–54, 7 cases, 19%); and high risk (score > 54, 5 cases, 14%; Table 1).

Univariate and Multivariate Analysis

Univariate analysis was performed to assess for differences in clinical, histologic, and immunohistochemistry findings between the low, intermediate, and high Oncotype DCIS score groups (Table 2). Features that were significantly different among the three groups included the following: nuclear grade ($P < 0.001$); necrosis ($P = 0.008$); biopsy site change ($P = 0.005$); ER ($P = 0.025$); Van Nuys Prognostic

Table 1 Clinicopathologic features and Oncotype DCIS results

	n = 37, no. (%)
<i>Patient age (years) (34–82)</i>	
≥ 50	25 (68)
< 50	12 (32)
<i>Nuclear grade</i>	
Low	5 (14)
Intermediate	21 (57)
High	11 (30)
<i>ER immunohistochemistry status</i>	
Positive	36 (97)
Negative	1 (3)
<i>PR immunohistochemistry status</i>	
Positive	34 (94)
Negative	2 (6)
<i>Size</i>	
≥ 1 cm	22 (59)
< 1 cm	15 (41)
<i>Margin status (cm)^a</i>	
≥ 0.3	20 (54)
< 0.3	17 (46)
<i>Oncotype DCIS result (score)</i>	
Low (< 39)	25 (68)
Intermediate (39–54)	7 (19)
High (score > 54)	5 (14)

^aFinal, after re-excision of positive margins, if applicable. Sums may not meet total *n* due to incompletely available data.

Index class ($P=0.040$); and PR ($P=0.016$). In addition, a Spearman's rank-order correlation demonstrated a statistically significant negative linear relationship between Oncotype DCIS score and percent positive cells on PR immunohistochemistry (correlation of -0.485 , $P=0.003$). Comparing the low Oncotype DCIS score vs intermediate- to high-score groups, the low-score group was more likely to have no necrosis (52% vs 0%, $P=0.002$), low/intermediate nuclear grade (92% vs 25%, $P<0.001$), ER positivity 90% or greater (96% vs 67%, $P=0.03$), PR positivity 90% or greater (58% vs 8%, $P=0.005$), no biopsy site change (75% vs 25%, $P=0.010$), and a Van Nuys Prognostic Index score < 8 (76% vs 33%, $P=0.027$). Similar results are observed when we analyzed the data using three-tier Oncotype DCIS score groups. Of note, all cases of DCIS without necrosis had a low Oncotype DCIS recurrence score ($N=13$, average score = 15, 100% specificity). No other characteristics, including patient age, mitoses, DCIS size, final margin, DCIS cellularity, dense inflammation, or calcification were significantly different between the Oncotype DCIS low-, intermediate-, and high-score groups. On multivariate logistic regression analysis, (i) necrosis, (ii) high nuclear grade, (iii) biopsy site change, (iv) ER, and (v) PR positivity $< 90\%$ on immunohistochemistry, and (vi) Van Nuys Prognostic Index score of 8 or greater were significant predictors of an

intermediate to high Oncotype DCIS score (P -values all < 0.02 ; Table 3). Other factors, including dense inflammation, DCIS span and cellularity, mitoses, patient age, final margin status, and calcification were not significant predictors.

Radiation Therapy Decision-Making

Per electronic medical record, the Oncotype DCIS results were discussed with 73% of patients (27/37 patients). Radiation treatment decision data were available for all the patients, and 54% of patients (20/37 patients) received adjuvant radiation therapy. With the exception of two patients who opted for mastectomy, 5 out of 15 patients made the decision of forgoing radiation therapy based on the Oncotype DCIS results.

All patients with intermediate to high Oncotype DCIS scores were offered radiation therapy, and only 1 patient declined (1/12, 8.3%). For patients with low Oncotype DCIS scores, 36% of the patients (9/25 patients) received adjuvant radiation therapy despite low scores. The documented reasons for opting for radiation treatment despite a low score (as noted in the medical record review) were patient wishes and younger patient age (< 50 years old) in the majority of cases (89%). In some of these cases, testing was initially ordered by a physician other than the radiation oncologist (such as the medical oncologist).

Univariate analysis demonstrated significant differences in radiation therapy management in different Oncotype DCIS score groups ($P=0.005$; Table 4). In addition, cases with higher nuclear grade were significantly more likely to receive radiation therapy ($P=0.008$; Table 4). Necrosis, patient age, DCIS size, and final margin status variables individually were not significantly different among the radiation and no radiation groups.

Comparison of Histology and Hormone Status with Unexpected Oncotype DCIS Results

The initial histology, immunohistochemistry, and Oncotype DCIS results (scores and ER and PR results) were reviewed, and seven cases with unexpected results were identified (Table 5). No cases with low nuclear grade and high Oncotype DCIS score were present. However, there were two cases with high nuclear grade and comedonecrosis that showed low Oncotype DCIS scores of 32 (upper threshold of the low-risk category being 38). On histology, the first case had intermediate to high nuclear grade. This patient received radiation therapy despite the low Oncotype DCIS score. The second case had a spectrum of low- to high-grade DCIS. The second patient did not receive radiation therapy.

Five cases showed discrepancy in hormone receptor results by immunohistochemistry and RT-PCR-based scores from Oncotype DCIS testing. One case with a negative ER immunohistochemistry ($< 1\%$)

Table 2 Comparison of Oncotype DX DCIS score with clinical and pathologic features

	Oncotype DCIS score									
	Low n = 25, no. (%)	Intermediate to high n = 12, no. (%)	P-value	High n = 5, no. (%)	Low to intermediate n = 32, no. (%)	P-value	Low n = 25, no. (%)	Intermediate n = 7, no. (%)	High n = 5, no. (%)	P-value
Nuclear grade			0.000			0.144				0.000
High	2 (8)	9 (75)		3 (60)	8 (25)		2 (8)	6 (86)	3 (60)	
Not high	23 (92)	3 (25)		2 (40)	24 (75)		23 (92)	1 (14)	2 (40)	
Necrosis			0.002			0.140				0.008
Present	12 (48)	12 (100)		5 (100)	19 (59)		12 (48)	7 (100)	5 (100)	
Absent	13 (52)	0 (0)		0 (0)	13 (41)		13 (54)	0 (0)	0 (0)	
Biopsy site change			0.010			0.008				0.005
Present	6 (25)	9 (75)		5 (100)	10 (32)		6 (25)	4 (57)	5 (100)	
Absent	18 (75)	3 (25)		0 (0)	21 (67)		18 (75)	3 (43)	0 (0)	
ER immunohistochemistry			0.030			0.583				0.025
≥ 90%	24 (96)	8 (67)		4 (80)	28 (87)		24 (96)	4 (57)	4 (80)	
< 90%	1 (4)	4 (33)		1 (20)	4 (13)		1 (4)	3 (43)	1 (20)	
PR immunohistochemistry ^a			0.005			0.062				0.016
≥ 90%	14 (58)	1 (8)		0 (0)	15 (48)		14 (58)	1 (14)	0 (0)	
< 90%	10 (42)	11 (92)		5 (100)	16 (52)		10 (42)	6 (86)	5 (100)	
Van Nuys Prognostic Index			0.027			0.346				0.040
Score ≥ 8	6 (24)	8 (67)		3 (60)	11 (34)		6 (25)	5 (71)	3 (60)	
Score < 8	19 (76)	4 (33)		2 (40)	21 (66)		19 (76)	2 (29)	2 (40)	
Dense inflammation ^b			0.149			1.000				0.096
Present	2 (8)	4 (33)		1 (20)	5 (16)		2 (8)	3 (43)	1 (20)	
Absent	22 (92)	8 (67)		4 (80)	26 (84)		22 (92)	4 (57)	4 (80)	
Span of DCIS			0.286			1.000				0.275
≥ 1 cm	13 (52)	9 (75)		3 (60)	19 (59)		13 (54)	6 (86)	3 (60)	
< 1 cm	12 (48)	3 (25)		2 (40)	13 (41)		12 (48)	1 (14)	2 (40)	
DCIS cellularity ^c			0.727			0.628				0.646
< 30%	10 (42)	4 (33)		1 (20)	13 (42)		10 (42)	3 (43)	1 (20)	
≥ 30%	14 (58)	8 (67)		4 (80)	18 (58)		14 (58)	4 (57)	4 (80)	
Mitoses			1.000			1.000				1.000
≥ 1	11 (46)	5 (42)		2 (40)	14 (45)		11 (46)	3 (43)	2 (40)	
0	13 (54)	7 (54)		3 (60)	17 (54)		13 (54)	4 (57)	3 (60)	
Patient age			1.000			0.295				0.252
≥ 50	17 (68)	9 (75)		5 (100)	21 (66)		17 (68)	4 (57)	5 (100)	
< 50	8 (32)	3 (25)		0 (0)	11 (34)		8 (32)	3 (43)	0 (0)	
Final margin status			1.000			0.348				0.417
≥ 0.3 cm	13 (54)	7 (58)		4 (80)	16 (50)		13 (54)	3 (43)	4 (80)	
< 0.3 cm	12 (48)	5 (42)		1 (20)	16 (50)		12 (48)	4 (57)	1 (20)	
Calcification			1.000			1.000				0.968
Present	11 (46)	5 (42)		2 (40)	14 (45)		11 (46)	3 (43)	2 (40)	
Absent	13 (54)	7 (58)		3 (60)	17 (54)		13 (54)	4 (57)	3 (60)	

Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

^aSpearman's rank-order test demonstrated a significant inverse linear relationship of moderate magnitude between percent positive cells on PR immunohistochemistry and Oncotype DCIS score (correlation = 0.485, $P = 0.003$).

^bDefined as three layers, periductal, >75%.

^cDefined as percent of cells in DCIS divided by total cells (including inflammation and stromal cells) on representative H&E from block sent for Oncotype DCIS testing.

had a positive Oncotype ER score of 7, which was near the threshold for positivity (6.5 or greater). Another case with a positive ER immunohistochemistry (5%, 3+) had a negative Oncotype ER score of

5.2. Three cases that were PR immunohistochemistry positive had negative Oncotype DCIS PR scores, all of which were close to the 5.5 score cutoff. All these cases had intermediate to high nuclear grade, high

Table 3 Predictors of intermediate to high Oncotype DCIS score

Predictor	Odds ratio	95% confidence interval	P-value
Necrosis	Perfect predictor ^a	Not applicable	0.000
High nuclear grade	22	3.72–130.23	0.001
Biopsy site change	9	1.81–44.59	0.007
ER immunohistochemistry < 90%	11.5	1.11–118.70	0.040
PR immunohistochemistry < 90%	15.4	1.70–139.28	0.015
Van Nuys Prognostic Index score 8 or greater	6	1.32–27.29	0.020

^aNecrosis was present in 100% of cases with intermediate or high scores, leading to the 'complete separation problem', which precludes successful regression analysis due to the stepwise nature of the function. Necrosis is a perfect predictor in this series.

Table 4 Comparison of cases based on management

	Radiation therapy received n = 20, no.	No radiation therapy received n = 17, no.	P-value
<i>Oncotype DCIS score</i>			0.005
Low	9	16	
Intermediate	7	0	
High	4	1	
<i>Nuclear grade</i>			0.008
Low	3	2	
Intermediate	7	14	
High	10	1	
<i>Necrosis</i>			0.188
Yes	15	9	
No	5	8	
<i>Final margin</i>			0.325
≥ 0.3 cm	9	11	
< 0.3 cm	11	6	
<i>Van Nuys Prognostic Index score</i>			0.173
< 8	10	13	
≥ 8	10	4	
<i>Age</i>			1.000
≥ 50	14	12	
< 50	6	5	
<i>Size</i>			1.000
≥ 1 cm	12	10	
< 1 cm	8	7	

Oncotype DCIS scores, and documentation of radiation therapy offered. Repeat ER and PR immunohistochemistry performed on cases with discordant RT-PCR-based quantitative Oncotype DCIS results, supported the original immunohistochemistry diagnoses.

Discussion

In this study, we have reviewed our single-institution experience with Oncotype DCIS testing. We identified histopathologic correlates of the Oncotype DCIS scores, including nuclear grade,

necrosis, biopsy site changes, hormone status, and Van Nuys Prognostic Index scores. In our study, a low Oncotype DCIS score was associated with forgoing adjuvant radiation therapy after breast conservative surgeries. We also identified some cases with discordant histology/hormone status immunohistochemistry scores, the majority of which had borderline quantitative RT-PCR Oncotype DCIS results.

Oncotype DCIS was validated using retrospective data/samples from two cohorts of surgically treated DCIS patients that did not receive radiation therapy. The first validation study of Oncotype DCIS score was based on a subset of 327 patients from the Eastern Cooperative Oncology Group (ECOG) E5194 trial.⁵ This study included patients who were considered to have lower-risk DCIS based on size and nuclear grade, with ≤ 2.5 cm low- or intermediate-grade DCIS or ≤ 1.0 cm high-grade DCIS. In addition, a minimum negative margin width of 3 mm or no tumor on re-excision was part of the inclusion criteria. The second validation cohort included 718 DCIS patients from the Ontario population-based cohort of DCIS patients at multiple centers who did not receive radiation after surgery.⁶ This cohort had a higher portion of intermediate-high-grade DCIS, and margin status was defined as no tumor present at ink. These two studies found that Oncotype DCIS score could provide predictive value independent of clinicopathologic parameters such as age, tumor size, tumor grade, necrosis, focality, and tumor subtypes. As the Oncotype DCIS scores were validated using patients who did not receive radiation therapy, it is unclear whether and how the scores should be used for including or forgoing radiation therapy. However, newer data on groups that did vs did not receive radiation suggest that it may be predictive of radiation benefit.^{18,19}

The added predictive value of Oncotype DCIS scores remains unclear in the context of standard histopathologic and patient factors. In the invasive breast cancer setting, there have been multiple studies showing that certain pathological features are correlated with the Oncotype DX recurrence scores for invasive breast cancer (used to predict chemotherapy benefit in ER-positive invasive breast cancer patients).^{20–22} However, there is more limited experience with Oncotype DCIS score correlations

Table 5 Cases with Oncotype DCIS results discordant with histology or immunohistochemistry

Pathology findings (no. of cases)	× 200 slide photograph	Oncotype DCIS result	Case review details
High nuclear grade with necrosis (2)		Low Oncotype DCIS score: both cases had a score of 32 (upper threshold of 'low-risk' category: 38)	Histology demonstrated a spectrum of nuclear grading (intermediate- to high-grade DCIS and low- to high-grade DCIS)
Negative ER immunohistochemistry (1)		Positive Oncotype DCIS ER: case score 7 (near 6.5 threshold for ER positivity)	ER stain re-performed with confirmation of negative test
Positive ER immunohistochemistry (1)		Negative Oncotype DCIS ER: case score 5.2 (near 6.5 threshold for ER positivity)	ER staining on immunohistochemistry was focal (5%, 3+). Repeat immunohistochemistry showed the same result
Positive PR immunohistochemistry (3)		Negative Oncotype DCIS PR: case scores 4.7, 4.8, and 5.4 (near 5.5 threshold for PR positivity)	PR staining on immunohistochemistry was focal for all cases (20%, 2+; 60%, 2+; 20%, 1–2%). Repeat immunohistochemistry showed the same result

with conventional characteristics. Knopfmacher *et al* reported the correlation of histopathological features with Oncotype DCIS score. They found that PR $\geq 90\%$, mitotic count < 1 , ER $\geq 90\%$, and low nuclear grade were associated with a low recurrent score. In addition, the presence of dense periductal inflammation was associated with higher scores.¹⁴ We saw similar trends in our cohort. However, we did not observe statistical significance of dense periductal inflammation or the presence of mitotic figures.

The clinical utility and cost-effectiveness of using Oncotype DCIS score for managing radiation treatment strategies are uncertain. One study looking at this question simulated a 10-year follow-up for DCIS patients that fit the ECOG E5194 trial criteria, to interrogate the cost-effectiveness of using Oncotype DCIS score to guide therapy. They found that it was not cost beneficial to either submit all DCIS patients or a subset of the patients based on histological grade to Oncotype DCIS testing.²³ While this study used several simplified assumptions and may not represent the daily clinical practice, it further highlighted the unmet need to develop a cost-effective strategy for selecting patients who may benefit from Oncotype DCIS testing. Our small, single-institution cohort data suggest that the absence of necrosis in DCIS could be used as a selective histopathology factor to forgo Oncotype DCIS testing due to the high likelihood it will return a low recurrence risk score. However, this finding requires further validation. We further identified cases in which radiation therapy decisions were incongruent with, or preceded, Oncotype DCIS assay results, highlighting a need for a more detailed understanding of the current

radiation therapy management decisions in the setting of Oncotype DCIS testing.

Some of the cases in our series had unexpected Oncotype DCIS scores or quantitative ER/PR results. It was helpful to re-review the histology and immunohistochemistry of stained slides in these cases as most of these cases showed contributing factors or potential explanations. Five cases with borderline hormone receptor immunohistochemistry results showed discordant results with the quantitative RT-PCR ER/PR results by Genomic Health. Borderline results, differences in testing methodologies, and tumor cellularity were seen as potential causes of these discordant results. Two cases categorized as high-grade DCIS with borderline low Oncotype DCIS scores were found to have a spectrum of DCIS grades (from low to high) on review of the histology. Heterogeneity of the DCIS was seen as a potential cause for a lower than expected Oncotype DCIS score in these cases.

Unexpected results from some of the cases highlight the importance of understanding the differences between testing methodologies, with RT-PCR-based assays generating a spatially indiscriminate score that includes ER/PR expression of all cells, including benign stromal cells and surrounding lymphocytes. In contrast, histology and immunohistochemistry review allows the interpreter to score the areas of interest only and to identify areas of regional heterogeneity (although is a subjective interpretation). Similar discordant results have been reported in the Oncotype DX assay recurrence score for invasive breast cancer, such as assigning an inappropriately increased recurrence risk in low-grade invasive breast carcinomas with biopsy site

change and false-negative quantitative RT-PCR HER2 results due to tumor dilution.^{21,24} When accounting for unexpected or discordant results, all of these factors should be taken into account on review of the pathology and in clinical decision-making.

Our cohort is limited in size and reflects the practices of a single institution. However, our data may provide valuable insight into the clinical application of the assay. On the basis of our experience, traditional histopathology predictors of DCIS outcome still have a critical role in clinical decision-making. Pathologic features can predict Oncotype DX DCIS scores but unexpected results do occur, making individual recommendations sometimes challenging. It appears that at our institution, Oncotype DCIS results are used in the context of the other histopathologic findings and patient preferences when making decisions for radiation therapy.

Disclosure/conflict of interest

The authors declare no conflict of interest.

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