Original Article

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The Correlation of Magee Equations™ and Oncotype DX® Recurrence Score From Core Needle Biopsy Tissues in Predicting Response to Neoadjuvant Chemotherapy in ER+ and HER2- Breast Cancer

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ABSTRACT

Objective: Oncotype DX® recurrence score (RS) can be predicted from Magee Equations™ (MS) postoperatively. The aim of this study is to investigate correlation of MS with RS from pretreatment core needle biopsy (CNB) tissues, and their clinical usefulness in prediction of response to neoadjuvant chemotherapy (NCT) in estrogen receptor-positive and human epidermal growth factor receptor 2-negative (ER+/HER2-) breast cancer (BC).

Materials and Methods: Pretreatment CNB tissue samples from 60 patients with ER+/HER2- invasive BC were analyzed for MS and RS correlation. MS and RS were categorized as follows: low (<18), intermediate (18–30), and high (≥ 31). Percentage Tumor size Reduction (%TR) was used to assess tumor response to NCT, and substantial %TR was defined as at least 50% reduction (≥50%TR). Correlation between MS and RS, and predictive factors for the ≥50%TR achievement were assessed.

Results: MS and RS represented a strong correlation (Spearman's correlation; r=0.58, p<0.0001) as a continuous variable. As a categorical variable, the concordance between MS and RS was 43.3%, and it increased to 80% (r=0.61, p=0.003) with the exclusion of the intermediate risk categories. Although, there was pathologic complete response (pCR), MS showed the highest predictive power for the ≥50% TR achievement, none of the factors were statistically significant (p≥0.07).

Conclusion: Our study demonstrated that there was a strong correlation between MS and RS from pretreatment biopsy tissue samples in ER+ and HER2- invasive BC.

Keywords: Breast cancer, Magee Equations™, Oncotype DX® recurrence score, pretreatment biopsy, neoadjuvant chemotherapy

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Introduction

Oncotype DX® (Genomic Health, Redwood City, CA, USA) is a commercially available reverse transcriptase-polymerase chain reaction-based assay that provides a recurrence score (RS) which ranges from 0 to 100 based on the expression of 21 genes, using RNA extracted from formalin fixed paraffin embedded (FFPE) tumor tissues. It classifies patients into low-, intermediate- and high-risk of recurrence for women with hormone receptor positive (HR+) early stage breast cancer (BC) who are treated with adjuvant endocrine therapy. More importantly, Oncotype DX® can predict the magnitude of chemotherapy (CT) response and identify HR+ early stage BC patients who will benefit from CT (1-5). However, two considerable drawbacks of Oncotype DX® are its high cost and the time required for processing of the specimens.

Although several guidelines recommend Onctype DX® use for lymph node negative HR+ early stage BC (6-9), considering its cost and time, clinicians should identify patients who are unlikely to benefit from Oncotype DX® testing even when the test is available. Additionally, Oncotype DX® assay is not currently reimbursed/readily available in most of countries. Efforts have been put forth to determine if routinely available pathologic parameters could predict RS. Some studies have shown that estrogen receptor (ER) levels, progesterone receptor (PR) levels, human epidermal growth factor receptor 2 (HER2) score, Ki67, Nottingham grade, tubule formation, mitosis and nuclear pleomorphism had a correlation with RS (10-16). Previous studies from our group showed that RS could be predicted by Magee Equations™ in combination with standard morpho-immunohistological variables from surgical pathology (17, 18). The correlation between RS and Magee Equations™ score (MS) seems appealing given its simplicity and potential cost savings (19-21).

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While neoadjuvant chemotherapy (NCT) have several advantages including to monitor response to treatment and shrinks the tumor, some studies questioned the benefit of NCT for patients with HR+ BC overall. These studies showed that pathological complete response (pCR) was less likely to occur in luminal patients and did not confer with a survival benefit (7, 22-24). However, the main objective of NCT for HR+ cancers is to increase breast conserving surgery (BCS) rate. In addition, there is a subset of HR+ BC patients who benefit from NCT (25) such as luminal B patients. RS has been proposed to also select HR+ HER2- BC patients who will benefit from NCT. The correlation between multi-gene assays such as Oncotype DX® RS from pretreatment biopsy tissue and tumor response to neoadjuvant therapy has been studied previously (26-34).

MS from post- surgical pathology and Oncotype DX® RS are highly concordant and this encourages us to evaluate the possibility of similar association from pretreatment biopsy tissue samples. There has been no study to identify the correlation between MS and Oncotype DX® RS from pretreatment tissue samples. If there is a significant correlation between these two calculations and Oncotype DX® is unavailable, MS may give additional information for decision making of NCT to clinicians with no cost.

The aim of this study is to investigate the correlation of MS with RS from pretreatment core needle biopsy tissues and its clinical usefulness in prediction of response to neoadjuvant chemotherapy in ER+ and HER2- invasive BC.

Materials and Methods

Patient selection and clinicopathological data

Clinicopathological data was collected retrospectively for 71 female patients with ER+/HER2- invasive carcinoma of the breast diagnosed with core needle biopsy (CNB) and treated with NCT. All patients were ≥18 years of age without prior history of any cancer including BC. Patients were diagnosed with T1-3 N0-1 M0 tumor, in which the tumor size was recorded based on preoperative images. All patients had unifocal tumors. Pathological data required for MS calculation such as H-scores for ER and PR, HER2, and tumor size were obtained from pretreatment slide review or medical record. These data were blinded to RS evaluation.

Score assessment

Both MS and RS were obtained from pretreatment CNB tissues. Pretreatment paraffin-embedded tissue samples were sent to Genomic Health, Inc. for Oncotype DX® RS. MS was calculated from Magee Equations™ (http://path.upmc.edu/onlineTools/mageeequations.html). The recurrence score risk categories were as follows: low (<18), intermediate (18–30), and high (≥31). We also investigated low- and midrange-risk groups as follows: low (<11), intermediate (11–25), and high (>25) (35-37).

Response assessment

All patients received standard NCT. Pathologic complete response (pCR) was defined as complete absence of viable invasive tumor cells both in the breast and lymph nodes on pathologic examination. We used Percentage Tumor Size Reduction (%TR) to assess tumor response to NCT in this study. %TR was based on pretreatment size (the largest dimension) and pathology evaluation of the resected specimen. The pretreatment tumor size was abstracted from clinical charts as a maximum dimension (unidimensional measurement). Imaging modality considered for tumor size measurements was selected in the following preferential order: Magnetic resonance imaging, ultrasound, mammogram or physical examination. The post-treatment tumor size was defined as the product of: maximum dimension of tumor-bed (or area of fibrosis)* percentage cellularity (compared with pretreatment biopsy) of the tumor-bed (or area of fibrosis) by microscopic exam. %TR was calculated as the difference between the pre- and post- treatment tumor size divided by pre-treatment tumor size, multiplied by 100 (available at http://path.upmc.edu/onlineTools/ptvr.html). Substantial %TR was defined as at least 50% reduction in tumor size (≥50%TR).

Statistical analysis

We assessed the correlation of MS with RS and predictive factors for clinicopathological response to NCT. Categorical comparisons between the categories were tested by the Pearson Chi-Square test. Correlations between MS and RS were determined using the Spearman's correlation coefficient both as continuous and categorical variables. The predictive power of variables on the ≥50%TR achievement was assessed based on multiple logistic and linear regression analyses. The Area Under the ROC (Receiver Operating Characteristic) Curve (AUC) values were calculated by plotting cumulative distribution function of sensitivity vs. '1-specificity'. The p-values were derived from two-tailed tests, and $p<0.05$ was considered significant. All statistical tests were performed using SAS/STAT version 9.3 (SAS Institute, Inc., North Carolina, USA).

Key Points

- Guidelines recommend Onctype DX® use for lymph node negative HR+ early stage breast cancer.
- Oncotype DX® assay is expensive and it is not currently reimbursed/readily available in most of the countries.
- Previous studies from our group showed that recurrence score could be predicted by Magee Equations™.
- Magee Equations™ is a simple method that takes no additional cost and waiting time.
- The present study demonstrated that there was a strong correlation between Magee Score and Recurrence Score from pretreatment biopsy tissue samples in ER+ and HER2- invasive breast cancer.
- Magee Score from pretreatment biopsy tissue can be a useful decision-making tool in the neoadjuvant setting, especially for low- or high-Magee Score patients.

Results

Pretreatment core biopsy samples were obtained and sent for Oncotype DX® testing from 71 patients. Two samples failed RNA extraction and the remaining 69 patient samples were processed by RT-PCR. There was no PCR failure, however, 9 samples were identified as HER2 positive by RT-PCR. The final sample size analyzed was 60 cases.

A summary of clinicopathologic features of the study is detailed in Table 1. The mean patient age was 52±13 years. The mean pre-NCT tumor size was 48±36 mm. The median %TR was 42% (range 0–97%) and ≥50%TR was observed in 27 (45%) patients. There was neither pathological complete response nor disease progression.

Table 2 shows the categorical distribution of MS and RS. The 21-gene assay demonstrated a low RS (<18) in 27 (45%), intermediate RS (18–30) in 10 (17%) and high RS (≥31) in 23 (38%) tissues. Magee Equations™ demonstrated a low MS in 16 (27%), intermediate MS in 40 (67%) and high MS in 4 (7%) tissues.

Correlation between MS and RS

The mean MS was 22.0 compared with 27.7 for RS (Table 1). As a continuous variable, MS significantly correlated with RS (Pearson's correlation; r=0.58, p<0.0001). When analyzed as categorical variables, the overall concordance between MS and RS was 43.3% (Table 2). The Pearson's correlation coefficient between MS and RS was 0.38 (p=0.001). One-step discordance was 50% (30/60), and two-step discordance was 6.6% (4/60). With the exclusion of the intermediate risk categories for both MS and RS, the concordance between the two variables increased to 80% (r=0.61, p=0.003).

When MS fell in the intermediate category, RS was either the low or intermediate category in 63% (25/40) of the cases. Focusing on the intermediate MS category, median MS for the low/intermediate RS category was 21 (range 18-31), and median MS for the high RS category was 25 (20-31). With 15 cases represented the lower range of the intermediate MS category (score of 18–21), 14 cases (93%) were reported as the low/intermediate RS category, and only 1 case (7%) was reported as the high RS category. Additionally, in the intermediate MS category, median PR H-score for the low/intermediate RS category is 120 (0-300), and median PR H-score for the high RS category is 23 (2-200). With 11 cases presented PR ≤23 in the intermediate MS category, 8 cases (73%) grouped to the high RS category, and 3 cases (27%) case grouped to the low/intermediate RS category.

Table 1. Summary of clinicopathologic features (n=60)

	Total		<50%TR (n=33)		≥50%TR (n=27)	
	Mean	(range)	Mean	(range)	Mean	(range)
Recurrence score	27.7	(3.3-69.9)	25.6	(6.0-69.9)	30.4	(3.3-66.6)
Magee score	22.0	(10.2-39.0)	20.6	(10.2–34.9)	23.7	(13.6-39.0)
Ki67	42.2	(5.0-85.0)[a]	35.0	(5.0-60.0)[b]	50.4	(8.0-85.0)[c]
ER (H-score)	234.7	(216.2-253.1)	257.7	(130-300)	206.5	(35-300)
PR (H-score)	131.6	(0-300)	149.8	(0-300)	109.3	(0-300)
Tumor size (cm)	4.8	(1.0-23.0)	4.7	(1.0-14.0)	5.0	(2.0-23.0)
Nottingham Score	6.6	(5.0-9.0)	6.6	(5.0-9.0)	6.5	(5.0-9.0)

[a]n=15, [b]n=8, [c]n=7

Table 2. Comparison between numbers of low, intermediate and high-risk categories based on Oncotype DX® recurrence score (RS) and Magee score (MS) (n=60)

	RS			
MS	Low (<18)	Intermediate (18-30)	High (≥31)	Total
Low risk (<18)	12 (20%)	0	4 (7%)	16 (27%)
Intermediate risk (18-30)	15 (25%)	10 (17%)	15 (25%)	40 (67%)
High risk (≥31)	0	0	4 (7%)	4 (7%)
Total	27 (45%)	10 (17%)	23 (38%)	60 (100%)

Pearson's correlation: 0.38 (±0.12). Table Likelihood Chi-Square p=0.001. Concordance: 43.3% (26/60); one-step discordance: 50% (30/60); two-step discordance: 6.6% (4/60).

Table 3. Comparison between numbers of low (<11), midrange (11-25) and high-risk (>25) categories based on Oncotype DX® recurrence score (RS) and Magee score (MS) (n=60)

	RS			
MS	Low (<11)	Intermediate (11-25)	High (≥25)	Total
Low risk (< 11)	1 (2%)	0	0	1 (2%)
Intermediate risk (11-25)	6 (10%)	21 (35%)	15 (25%)	42 (70%)
High risk (≥25)	1 (2%)	4 (7%)	12 (20%)	17 (28%)
Total	8 (13%)	25 (42%)	27 (45%)	60 (100%)

Pearson's correlation: 0.35 (±0.12). Table Likelihood Chi-Square p=0.04. Concordance: 56.7% (34/60); one-step discordance: 41.7% (25/60); two-step discordance: 1.7% (1/60).

In order to investigate the low and midrange risk categories, we used the other cutoff as follows: low (<11), intermediate (11–25), and high (>25) (Table 3). Oncotype DX® assay demonstrated a low RS (<11) in 8 (13%), intermediate RS (11–25) in 25 (42%) and high RS (>25) in 27 (45%) samples (Table 3). Magee Equations™ demonstrated a low MS (<11) in 1 (2%), intermediate MS (11–25) in 42 (70%) and high MS (>25) in 17 (28%) tissues. By using this cutoff, the concordance between MS and RS as a categorical variable was increased to 56.7%. One-step discordance was 41.7% (25/60), and two-step discordance was 1.7% (1/60). With the exclusion of the intermediate risk categories for both MS and RS, the concordance further increased to 92.9%.

Correlation between MS and RS in the patients achieved ≥50%TR

Twenty-five percent (4/16) of the low MS category patients, 50% (20/40) of the intermediate MS category patients, and 75% (3/4) of the high MS category patients achieved ≥ 50%TR, compared with 37% (10/27) of the low RS category patients, 60% (6/10) of the intermediate category RS patients and 48% (11/23) of the high RS category patients achieved ≥ 50%TR (Table 4, 5). Focusing on the ≥50%TR achieved patients, the correlation between MS and RS was marginally significant (Table 4; r=0.42, p=0.05). The concordance between MS and RS was 44.4%. One-step discordance was 51.9% (14/27), and two-step discordance was 3.7% (1/27). With the exclusion of the intermediate risk categories for both MS and RS, the concordance increased to 86% (r=0.75, p=0.002).

We also investigated the low and midrange risk categories (Table 5). Oncotype DX® assay demonstrated a low RS (<11) in 2 (7%), intermediate RS (11–25) in 11 (41%) and high RS (>25) in 14 (52%) samples. Magee equation demonstrated a low MS (<11) in 0 (0%), intermediate MS (11–25) in 16 (59%) and high MS (>25) in 11 (41%) tissues. In this cutoff, the concordance between MS and RS as a cat-

Table 4. Comparison between numbers of low, intermediate and high-risk categories based on Oncotype DX® recurrence score (RS) and Magee score (MS) among samples with tumor volume reduction ≥50% (n=27)

	RS			
MS	**Low (<18)**	**Intermediate (18-30)**	**High (≥31)**	**Total**
Low risk (<18)	3 (11%)	0	1 (4%)	4 (15%)
Intermediate risk (18-30)	7 (26%)	6 (22%)	7 (26%)	20 (74%)
High risk (≥31)	0	0	3 (11%)	3 (11%)
Total	10 (37%)	6 (22%)	11 (41%)	27 (100%)

Pearson's correlation: 0.42 (±0.16). Table Likelihood Chi-Square p=0.05. Concordance: 44.4% (12/27); one-step discordance: 51.9% (14/27); two-step discordance: 3.7% (1/27).

Table 5. Comparison between numbers of low (<11), midrange (11-25) and high-risk (>25) categories based on Oncotype DX® recurrence score (RS) and Magee score (MS) among samples with tumor volume reduction ≥50% (n=27)

	RS			
MS	**Low (<11)**	**Intermediate (11-25)**	**High (≥25)**	**Total**
Low risk (<11)	0	0	0	0 (0%)
Intermediate risk (11-25)	1 (4%)	7 (26%)	8 (30%)	16 (59%)
High risk (≥25)	1 (4%)	4 (15%)	6 (22%)	11 (41%)
Total	2 (7%)	11 (41%)	14 (52%)	27 (100%)

Pearson's correlation: 0.01 (±0.19). Table Likelihood Chi-Square p=0.91. Concordance: 48.1% (13/27); one-step discordance: 48.1% (13/27); two-step discordance: 3.7% (1/27).

Table 6. Comparison between 50%TR achievement and Oncotype DX® recurrence score (RS) and Magee score (MS) categories (focused on low and midrange risk categories)

	RS categories				**MS categories**			
	Low <11	**Intermediate 11-25**	**High >25**	**p**	**Low <11**	**Intermediate 11-25**	**High >25**	**p**
<50%TR (n=33)	6 (18%)	14 (42%)	13 (39%)	0.20	1 (3%)	26 (79%)	6 (18%)	0.04
≥50%TR (n=27)	2 (7%)	11 (41%)	14 (52%)		0	16 (60%)	11 (40%)	
Total	8 (13%)	25 (42%)	27 (45%)		1 (2%)	42 (70%)	17 (28%)	

Table 7. Univariate analysis of predictive factors for tumor volume reduction ≥50% (n=60)

	Model P[a]	AUC (95% CI)[b]	AIC
Recurrence score categories (<18, 18-30, ≥31)	0.43	0.56 (0.42, 0.69)	86.90
Magee score categories (<18, 18-30, ≥31)	0.13	0.63 (0.52, 0.75)	83.95
Low risk Magee score category (<18)	0.07	0.61 (0.50, 0.72)	82.90
ER (H-score <100, ≥100)	0.97	0.59 (0.52, 0.67)	78.03
PR (H-score <120, ≥120)	0.12	0.60 (0.48, 0.73)	84.05

[a]Logistic regression modeling tumor volume reduction ≥50% as the outcome. [b]95 % Wald Confidence Intervals
AUC: Area Under the ROC (Receiver Operating Characteristic) Curve, AIC: Akaike Information Criterion

egorical variable was increased to 48.1%. One-step discordance was 48.1% (13/27), and two-step discordance was 3.7% (1/27). With the exclusion of the intermediate risk categories for both MS and RS, the concordance increased to 85.7%. Table 6 shows comparison between 50%TR achievement and RS (p=0.20) and MS (p=0.04) categories, focused on low and midrange risk categories.

Predictive factors for the ≥50%TR achievement

Predictive factors for the ≥50%TR achievement from univariate analysis are listed in Table 7. Although MS showed the highest predictive power, none of the factors such as RS, MS, ER and PR were statistically significant. The AUC values for RS, MS, ER and PR were 0.56, 0.63, 0.59, 0.60, respectively. Focusing on the low risk MS category, it did not lead to a significant improvement as a predictive factor (p=0.07, AUC=0.61). Low level of ER H-score (<100) was not a statically significant factor for the ≥50%TR achievement, whereas all patients who had low level (<100) of ER H-score (n=5, the median MS=30 [range 21.5–39]) achieved ≥50%TR.

Discussion and Conclusion

Patients must pay out of pocket for Oncotype DX® test in most of the countries as the insurance companies don't reimburse this high-cost test. In this study, we investigate the correlation between MS and RS from pretreatment biopsy tissue samples. In a continuous variable analysis, MS correlated significantly with RS. As a categorical variable, the Pearson's correlation coefficient between MS and RS dropped (Table 2). With the exclusion of the intermediate risk categories for both MS and RS, the concordance increased to 80%, and MS and RS showed strong correlation. Therefore, one can conclude that if MS is clearly in the high or low categories, it is predictive of the RS categories with 80% certainty.

MS tends to report more intermediate risk category patients than Oncotype DX® testing. Focusing on the intermediate MS category in our study, with 15 patients represented the lower range of the intermediate MS category (score of 18–21), 14 cases (93%) were reported as the low/intermediate RS category and only 1 case (7%) was reported as the high RS category. Therefore, patients who represent the lower range of the intermediate MS category (score of 18–21) can be categorized into the low/intermediate risk RS with an over 90% possibility. In addition, with 11 cases presented PR H-score ≤23 in the intermediate MS category, 8 cases (73%) grouped to the high RS category, and 3 cases (27%) grouped to the low/intermediate RS. Therefore, when MS is calculated as the intermediate group, low PR H-score patients may be grouped into the high RS category with an over 70% possibility. Others have also found similar strong correlations of lower PR scores with higher RS similar to our findings (10, 12, 13, 15–17).

Management for patients with intermediate risk disease by Oncotype DX® testing is published recently (37). Adjuvant endocrine therapy and CT had similar efficacy in women with HR (+), HER2-, axillary node negative BC who had RS between 11 and 25, although some benefit of CT was found in some women 50 years of age or younger. To investigate the low and midrange risk categories, we also used cutoff as low (<11), intermediate (11–25), and high (>25). By using this cutoff, the concordance between MS and RS as a categorical variable was increased to 56.7%. With the exclusion of the intermediate risk categories for both MS and RS, the concordance further increased to 92.9%. From these results, MS > 25 may be another cut off for predicting the high RS category (Table 3).

Focusing on the ≥50%TR achieved patients, the correlation between MS and RS was marginally significant (Table 3). The concordance between MS and RS was 44.4% due to one-step discordance. Excluding the intermediate categories for both MS and RS, the concordance increased to 86%, and MS and RS presented very strong correlation. According to this fact, when MS is in the high or low categories, it may predict the RS categories with 86% certainty for the achievement of ≥50%TR. The same was true of for the cutoff as low (<11), intermediate (11–25), and high (>25) (Table 3), and statistically significant correlation was found between 50%TR achievement and MS categories in terms of this cutoff (Table 3).

A number of conflicting results have been published on the usefulness of RS in predicting response to neoadjuvant therapy (26-34). Although two reports showed there was no statistically significant association between tumor response and RS (26, 27), some studies support the correlation between RS and tumor response to neoadjuvant systemic therapy (28-34). In univariate analyses of predictive factors for the ≥50%TR achievement from our study (Table 7), none of the models were statistically significant. However, the MS gave the best predictive power; 25% (4/16) of the low MS category patients and 75% (3/4) of the high MS category patients achieved ≥ 50%TR, compared with 37% (10/27) of the low RS category patients, and 48% (11/23) of the high RS category patients achieved ≥50%TR (Table 2, 4). Especially, in terms of predictive value of the ≥50%TR achievement, there is a possibility that MS can be superior to RS. Since small number of patients in our study may have affected not to reach statistical significance in MS and tumor response correlation, further larger studies are needed. Changing focus on another pathological factor for the ≥ 50%TR achievement, there was a trend that low level of PR H-score (<120) had the predictive power, but there was not significant. Although low level of ER H-score (<100) was not a statically significant factor for the ≥50%TR achievement probably due to smaller sample size, all patients who had low level of ER H-score (<100) (n=5) achieved ≥50%TR. These results are consistent with previous studies (28, 29).

Farrugia et al. (38) investigated an association between pCR after NCT and MS. They reported that pCR rate increased with higher MS, but this study had no genomic test. They concluded that MS can predict pCR, but this finding should be tested in a bigger study.

Some studies have been reported the association between RS and tumor response to neoadjuvant therapy, nevertheless, RS is not available for patients in almost most countries. Under such a situation, our results assure that MS gives an additional information in patient for NCT, especially for low or high MS score patients. The low or high MS categories are predictive of the RS categories with 80% certainty, and they may predict the RS categories with 86% certainty for the achievement of ≥50%TR. When MS is calculated to the intermediate risk category, patients who represented the lower range of the intermediate MS category (score of 18–21) can be categorized into the low/intermediate risk RS with an over 90% possibility, and low PR H-score may categorize the intermediate MS risk patients into the high RS category.

From our results, one can be speculated that the high MS category calculated from pretreatment biopsy tissue may enable us to predict high tumor response to chemotherapy. On the other hand, the low MS category may give small benefit of NCT, and initial surgery or neoadjuvant hormonotherapy may be recommended. Since none of factors including MS were not significantly correlated with tumor response in this small study, further studies are needed to determine whether MS can be a predictive marker for tumor response in neoadjuvant settings or not.

Our study has some limitations. At first, this is a small sample study from single institution. It was noteworthy that this result was achieved using limited amount of tissues obtained from pretreatment core needle biopsy. The second, we used an original method to evaluate tumor response (Magee Method; http://path.upmc.edu/onlineTools/ptvr.html). We cannot deny that different results will be come out with other assessment methods for tumor response.

The present study demonstrated that there was a strong correlation between MS and RS from pretreatment biopsy tissue samples in ER+ and HER2- invasive BC. Magee equation is a simple method that takes no additional cost and waiting time. When Oncotype DX® testing is not available readily, MS from pretreatment biopsy tissue can be a useful decision-making tool in the neoadjuvant setting, especially for low- or high-MS patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of University of Pittsburgh Institutional Review Board (IRB#:PRO09080144, August 3, 2010).

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