**Rationale and Objectives:** To correlate prognostic histologic features and immunohistochemical biomarkers of breast cancer with quantitative shear wave elastography (SWE) parameters.

**Materials and Methods:** B-mode ultrasound (US) and SWE were performed before core biopsy on 72 cancers in 68 patients. Mean cancer size was determined from US. Histologic grade, lymph node status, lymphovascular invasion (LVI), histologic type, and immunohistochemical biomarkers (estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 [HER2]) were determined from surgical pathology reports. Correlation between these features and quantitative SWE parameters (mean elasticity [E mean], maximum elasticity [E max], and elasticity ratio [E ratio]) was made.

**Results:** There was significant correlation of mean cancer size with E mean, E max, and E ratio (correlation, 0.492, 0.500, and 0.435, respectively; all $P < .001$). Lymph node involvement was associated with significantly higher E max ($P = .040$). LVI was associated with significantly higher E mean, E max, and E ratio ($P = .002, .004, \text{ and } .042$, respectively). There was no significant correlation of histologic grade with SWE parameters. HER2+ cancers were associated with significantly higher E ratio ($P = .030$). In multivariate analysis, only mean cancer size was significantly correlated with E mean and E max ($P < .001$).

**Conclusions:** There was significant correlation of cancer size with SWE parameters. There was significant correlation of lymph node status and LVI with SWE, but only on univariate analysis. SWE has the potential to provide prognostic information of breast cancer in a noninvasive manner, but further study is required.

**Key Words:** Breast cancer; prognostic features; elastography.

Original Investigations

**Quantitative Shear Wave Elastography:**

*Correlation with Prognostic Histologic Features and Immunohistochemical Biomarkers of Breast Cancer*

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Breast cancer is a heterogeneous disease, with different histologic types, clinical course, response to treatment, and prognosis. The prognostic histologic features of breast cancer include invasive size, lymph node status (1), histologic grade (2), lymphovascular invasion (LVI), (3) and histologic type (4,5). Molecular profiling of breast cancer by gene expression array analysis classifies breast cancers into different subtypes. There is correlation of the different molecular subtypes with the response to systemic therapy (6–9). There is also a significant correlation between the different histologic types of breast cancer and their molecular subtypes (10). Because gene expression array analysis has strict tissue requirements and is not always available, immunohistochemical study is used as a surrogate with determination of the expression of the following cancer biomarkers: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) (11–13). Three major subtypes are defined: ER positive (ER+ [ER+, PR+/-, and HER2−/+] ), HER2 positive (HER2+ [ER−, PR−, and HER2+] ), and triple negative (TN [ER−, PR−, and HER2−] ). These immunohistochemical subtypes correspond approximately to the molecular subtypes of luminal A (ER+, PR+/-, HER2−; low grade)/luminal B (ER+, PR+/-, HER2−; high grade or ER+, PR+/-, HER2+), HER2 enriched and basal-like, respectively. The luminal A subtype has the best prognosis and the basal-like subtype the worst prognosis (14,15).

Core biopsy is performed to obtain samples for analysis of histologic and immunohistochemical features of breast cancer. However, these limited biopsy samples are inadequate for assessment of the entire range of intratumoral heterogeneity, which can influence the course of tumor progression and...
Shear wave elastography (SWE) provides quantitative information of tissue stiffness (elasticity) from the speed of shear wave propagation in tissues. Shear waves (transverse waves) are generated by the acoustic radiation force of a focused ultrasound (US) beam passing into the breast. They travel faster in stiff tissue compared to soft tissue. By capturing the propagation of the shear waves, an elasticity map is produced. This is a color overlay of the US image, with different colors representing the speed of the shear waves (in m/s) or the tissue stiffness (Young modulus $E$ in kilopascals or kPa) (17–20). From the elasticity map, the stiffness of a mass can be assessed from the color score or the color pattern (21,22), or from quantitative parameters (23–25).

Many studies have shown that the color score or color pattern (21,22) and quantitative parameters from SWE can aid in the differentiation of benign and malignant breast lesions (23–25). It has been shown that adding SWE features to US improved specificity of breast US assessment without loss of sensitivity (26).

SWE allows for quantitative assessment of stiffness of a mass, and as such, objective correlation between prognostic features of breast cancer and quantitative values of its stiffness can be performed. Evaluation of correlation between the prognostic features of heterogeneous groups of breast cancer and their SWE values is the subject of ongoing research. It was reported that breast cancers with poorer histologic prognostic features, immunohistochemical biomarkers, and subtypes with poorer prognosis showed higher mean elasticity ($E$ mean) values (27–30) and elasticity ratio ($E$ ratio) (31). Thus, several groups demonstrated significant correlation of histologic grade with elasticity value (27,28,30,31). However, there was a discrepant result with other prognostic features. Significant correlation of invasive cancer size with elasticity value was demonstrated by Evans et al. (27), Chang et al. (30), and Choi et al. (31), whereas Youk et al. (28) did not find an independent correlation of invasive cancer size with $E$ mean. For ER and PR status, Chang et al. (30) demonstrated significant correlation with $E$ mean, and Choi et al. (31) demonstrated significant correlation with $E$ ratio, whereas Youk et al. (28) did not find independent correlation of ER and PR status with $E$ mean. Given somewhat discrepant results in prior studies, we conducted a prospective study to evaluate correlation between the main prognostic features of breast cancer and the SWE parameters.

The purpose of our study is to correlate prognostic histologic features (cancer size, histologic grade, lymph node status, LVI, and histologic type) and immunohistochemical biomarkers (ER, PR, and HER2) of breast cancer with quantitative SWE parameters.

**MATERIALS AND METHODS**

An institutional research ethic board–approved prospective study of SWE in the evaluation of solid breast masses was performed from July 2011 to August 2013. Women aged ≥18 years, with a solid mass in the breast demonstrated on US, who underwent US-guided core biopsy for tissue diagnosis, and consented to participate in the study were enrolled. Women who were pregnant or lactating were excluded. In our institution, in accordance with the American College of Radiology guidelines, masses of Breast Imaging Reporting and Data System (BI-RADS) 4a category or above underwent core biopsy for tissue diagnosis. Patients with masses of BI-RADS 3 category underwent short interval follow-up at 6, 12, and 24 months (32). However, some patients with masses of BI-RADS 3 category elected to have a core biopsy for tissue diagnosis.

One hundred fifty-four women with 166 solid breast masses demonstrated on US after mammography or clinical finding of a palpable mass or thickening in the breast, who underwent US-guided core biopsy for tissue diagnosis, were enrolled. Sixty-eight patients with 72 breast cancers formed the subjects of this study.

The radiologists participating in the study have experience in breast imaging from 7 to 14 years. All radiologists have experience in SWE for 2 years. The technologists assisting in the study have experience in breast US for at least 4 years. The initial US was performed by a technologist. Subsequently, a radiologist performed US on the mass and determined its BI-RADS category. This was followed with SWE and then US-guided core biopsy.

US and SWE were performed with Aixplorer Multiwave V3 ultrasound machine from Supersonic Imagine (Aix-en–Provence, France). The linear-array transducer has a frequency range of 7.5–15 MHz, axial resolution of 0.3–0.5 mm, and a lateral resolution of 0.3–0.6 mm. In the Supersonic system, the SWE image is a semitransparent map of tissue stiffness overlaying the US image, with a color spectrum from dark blue (soft) to red (hard) and a default quantitative scale from 0 to 180 kPa.

SWE was performed by the radiologist who performed the US examination. SWE images were obtained with minimal pressure on the breast (33). The US probe was held over the mass for about 5–10 seconds for the image to stabilize before recording the image for quantitative SWE measurements. Three SWE images were obtained for the mass (with two in orthogonal planes). The image with color showing the highest stiffness and the least amount of artifact was selected for the study. Quantitative SWE parameters were obtained by placing a 2-mm round region of interest (ROI) on the hardest part of the mass or the adjacent tissue if it demonstrated higher stiffness than the mass and another ROI on the adjacent adipose tissue. The machine automatically displayed the SWE parameters such as mean elasticity ($E$ mean), maximum elasticity ($E$ max), elasticity ratio ($E$ ratio [ratio between $E$ mean of the mass/adjacent tissue and adipose tissue]), and these were recorded.

US-guided core biopsy was performed with 14-G needle and automated Bard Magnum biopsy gun. Four specimens were obtained from different parts of the mass, deposited in formalin, and sent for pathologic examination. Masses with pathologic diagnosis of breast carcinoma were included in this study.

Mean cancer size was determined from the US images (average of length × height × width). Histologic grade, lymph node...
status, LVI, histologic type, and immunohistochemical biomarkers (ER, PR, and HER2) of the cancer were determined from the surgical pathologic reports. Correlation between these prognostic features and quantitative SWE parameters was made.

**Statistical Analysis**

Statistical analysis was performed using SPSS software, version 20 (IBM SPSS Statistics 20, 2011). Continuous variables were described using mean and standard deviation and categorical variables using frequency and percentage. The Spearman correlation coefficient was used to assess the correlation between the size of malignant lesions and the SWE parameters.

The Kruskal–Wallis test and the Mann–Whitney U test or the two-sample t test were used to assess the univariate association between SWE parameters and histologic characteristics of malignant lesions.

Multiple linear regression analysis with stepwise selection was used to determine a set of histologic characteristics that can predict SWE parameters. A P value of <.05 was considered statistically significant.

**RESULTS**

**Descriptive Statistics of Demographic and Clinical Characteristics**

The mean age (±standard deviation) of the 68 patients was 58 ± 13.0 years (range, 32–83 years).

The mean size of the 72 cancers was 14.6 ± 8.5 mm (range, 3.2–51.0 mm).

Twelve (16.7%) cancers were well differentiated (grade 1); 29 (40.3%) were moderately differentiated (grade 2); and 26 (36.1%) were poorly differentiated (grade 3). Four (5.6%) were of indeterminate grade (grade 1 or 2). The histologic grade was not available for one (1.4%) cancer.

The results of lymph node excision were available for 58 cancers in 55 patients. Thirty-six (50.0%) had a negative lymph node status, whereas 22 (30.6%) had a positive lymph node status.

LVI was absent for 43 (59.7%) cancers and present for 27 (37.5%) cancers. LVI information was not available for two (2.8%) cancers.

There were 64 (88.9%) invasive ductal cancers (IDCs; 62 IDC not otherwise specified (NOS), one tubular carcinoma, and one medullary carcinoma); five (6.9%) ductal carcinoma in situ (DCIS), one (1.4%) invasive lobular carcinoma (ILC); and two (2.8%) invasive mucinous carcinoma (IMC).

Immunohistochemical biomarkers were determined for 67 cancers (all the non-DCIS cases). Fifty-seven (85.1%) were ER+, 10 (14.9%) were ER–; 50 (74.6%) were PR+, 17 (25.4%) were PR–; and 14 (20.9%) were HER2+, 53 (79.1%) were HER2–.

Immunohistochemical subtypes were determined as follows: 11 (16.4%) cancers were luminal A (ER+, PR+/–, HER2–; grade 1); 22 (32.8%) cancers were luminal B (ER+, PR+/–, HER2–; grade 3 or ER+, PR+/–, HER2+); one (1.5%) cancer was HER2+ (ER–, PR–, HER2+), and nine (13.4%) cancers were TN (ER–, PR–, HER2–). The subtype of 24 (35.8%) cancers was indeterminate.

The quantitative SWE parameters of the 72 cancers were as follows: E mean (mean value) 141.54 ± 77.54 kPa (range, 16.20–300.00 kPa), E max (mean value) 169.21 ± 89.10 kPa (range, 20.00–300.00 kPa), and E ratio (mean value) 11.33 ± 10.29 (range, 1.83–62.63).

**Mean Cancer Size**

The mean cancer size was moderately correlated with each of the SWE parameters. The Spearman correlation coefficient between the mean cancer size and E mean, E max, E ratio was 0.492, 0.500, 0.435, respectively (all P < .001). In general, a larger cancer was stiffer than a smaller cancer, with significantly higher values of the SWE parameters.

**Histologic Grade**

There was no significant difference in the SWE parameters between the three histologic grades. However, grade 3 cancers tended to have higher values of all three SWE parameters (Table 1).

**Lymph Node Status**

There was significant difference in E max between cancers with a positive lymph node status and cancers with a negative lymph node status. Cancers with a positive lymph node status tended to have significantly higher values. There was also a trend toward a significant difference in E mean between these two types of cancers (Table 2).

**Lymphovascular Invasion**

There was significant difference in all three SWE parameters between cancers with and without LVI. Cancers with LVI tended to have significantly higher values (Table 3).

**Immunohistochemical Biomarkers**

There was no significant difference in the SWE parameters between cancers that were ER+ and ER–, PR+, and PR–. HER2+ cancers tended to have significantly higher values of E ratio compared to HER2– cancers. There was no significant difference in E mean or E max between HER2+ and HER2– cancers (Table 4).

We did not perform statistical analysis to correlate immunohistochemical subtypes with SWE parameters because there was only one cancer of HER2+ subtype (ER–, PR–, and HER2+). It is not valid to use a group of one case to compare to the other groups.
### Histologic Type

There was a trend toward significant difference in E mean and E max between DCIS and IDC ($P = .076$ and $.067$, respectively). DCIS had lower values of E mean and E max. There was significant difference in E ratio between DCIS and IDC ($P = .031$), with DCIS having significantly lower values (Table 5).

### Multivariate Analysis

Multiple linear regression analysis demonstrated that only mean cancer size was significantly correlated with E mean and E max ($P < .001$; Figs 1 and 2). Lymph node status and LVI no longer had significant correlation with SWE parameters. We determined mean cancer size from US images by averaging length × height × width. Chang et al. (31) also determined cancer size (maximal diameter) from US. The other studies determined cancer size from pathologic reports (27,28,31).

### DISCUSSION

We demonstrated significant correlation of mean cancer size with SWE parameters, with a larger cancer demonstrating significantly higher values of E mean, E max, and E ratio (all $P < .001$). Lymph node involvement was associated with significantly higher E max ($P = .040$). LVI was associated with significantly higher E mean, E max, and E ratio ($P = .002$, $.004$, and $.042$, respectively). Our findings are similar to other studies. Evans et al. (27) demonstrated association of larger invasive cancer size ($P < .0001$), lymph node involvement ($P < .0001$), and vascular invasion ($P = .0077$) with significantly higher E mean. Youk et al. (28) demonstrated that larger invasive cancer size ($P = .013$), lymph node involvement ($P < .0001$), and LVI ($P < .0001$) were associated with significantly higher E mean. Chang et al. (30) demonstrated that larger invasive cancer size ($P = .012$) and lymph node involvement ($P = .018$), and LVI ($P < .0001$) were associated with significantly higher E mean. Choi et al. (31) demonstrated that larger invasive cancer size ($P = .009$) was associated with significantly higher E ratio. We determined mean cancer size from US images by averaging length × height × width. Chang et al. (30) also determined cancer size (maximal diameter) from US. The other studies determined cancer size from pathologic reports (27,28,31).

In multiple linear regression analysis, only mean cancer size was significantly correlated with E mean and E max ($P < .001$; Figs 1 and 2). Lymph node status and LVI no longer had significant correlation with SWE parameters. We demonstrated that cancers with lymph node involvement showed significantly higher E mean, E max, and E ratio ($P < .001$). Our findings are similar to other studies that have associated larger cancer size with increased E values (27,28,31).

### TABLE 1. Correlation of Histologic Grade with SWE Parameters

<table>
<thead>
<tr>
<th>SWE Parameter</th>
<th>Grade</th>
<th>$n$</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>E mean</td>
<td>1</td>
<td>12</td>
<td>127.37 ± 76.82</td>
<td>26.90–286.30</td>
</tr>
<tr>
<td>$P^* = .247$</td>
<td>2</td>
<td>29</td>
<td>131.48 ± 78.52</td>
<td>16.20–292.90</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>26</td>
<td>163.39 ± 77.86</td>
<td>32.70–300.00</td>
</tr>
<tr>
<td>E max</td>
<td>1</td>
<td>12</td>
<td>150.65 ± 86.33</td>
<td>29.80–300.00</td>
</tr>
<tr>
<td>$P = .241$</td>
<td>2</td>
<td>29</td>
<td>156.60 ± 89.39</td>
<td>20.00–300.00</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>26</td>
<td>193.87 ± 89.15</td>
<td>37.10–300.00</td>
</tr>
<tr>
<td>E ratio</td>
<td>1</td>
<td>12</td>
<td>7.23 ± 3.34</td>
<td>2.30–13.01</td>
</tr>
<tr>
<td>$P = .152$</td>
<td>2</td>
<td>29</td>
<td>12.28 ± 12.83</td>
<td>1.83–62.63</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>26</td>
<td>13.18 ± 9.48</td>
<td>2.55–41.43</td>
</tr>
</tbody>
</table>

E max, maximum elasticity; E mean, mean elasticity; E ratio, elasticity ratio; SD, standard deviation; SWE, shear wave elastography.

$^*P$ value from the Kruskal-Wallis test.

### TABLE 2. Correlation of Lymph Node Status with SWE Parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Negative Lymph Node Status ($n = 36$)</th>
<th>Positive Lymph Node Status ($n = 22$)</th>
<th>$P^*$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>E mean</td>
<td>129.99 ± 76.41 (16.20–292.90)</td>
<td>169.85 ± 78.86 (39.60–300.00)</td>
<td>.062</td>
</tr>
<tr>
<td>E max</td>
<td>154.40 ± 87.21 (20.00–300.00)</td>
<td>204.07 ± 87.70 (46.80–300.00)</td>
<td>.040</td>
</tr>
<tr>
<td>E ratio</td>
<td>12.18 ± 12.62 (1.83–62.63)</td>
<td>12.40 ± 8.15 (5.36–34.52)</td>
<td>.941</td>
</tr>
</tbody>
</table>

E max, maximum elasticity; E mean, mean elasticity; E ratio, elasticity ratio; SD, standard deviation; SWE, shear wave elastography.

$^*P$ value from the two-sample $t$ test.
involvement were significantly larger than cancers without lymph node involvement \((P < .001)\); similarly cancers with LVI were significantly larger than cancers without LVI \((P < .001)\). It would appear that cancer size is the main factor associating with stiffness as demonstrated on SWE. The variables of lymph node status and LVI were included when cancer size is considered. We postulate that a larger cancer elicits more desmoplastic reaction in it and in its periphery compared to a smaller cancer. There is also increased cellularity, angiogenesis, and edema in a larger cancer. Together, these findings likely contribute to the increased stiffness of a larger cancer compared to a smaller cancer.

In multiple linear regression analysis, other studies showed inconsistent results regarding association of prognostic features with E mean. Evans et al. (27) demonstrated that invasive

<table>
<thead>
<tr>
<th>TABLE 3. Correlation of LVI with SWE Parameters</th>
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<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>E mean (SD)</td>
</tr>
<tr>
<td>E max (SD)</td>
</tr>
<tr>
<td>E max (SD)</td>
</tr>
<tr>
<td>E ratio (SD)</td>
</tr>
</tbody>
</table>

\(E\) max, maximum elasticity; \(E\) mean, mean elasticity; \(E\) ratio, elasticity ratio; LVI, lymphovascular invasion; SD, standard deviation; SWE, shear wave elastography.

\(*P^*\) value from the two-sample t test.

<table>
<thead>
<tr>
<th>TABLE 4. Correlation of Immunohistochemical Biomarkers with SWE Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomarker Variable</td>
</tr>
<tr>
<td>E mean (SD)</td>
</tr>
<tr>
<td>ER ((n = 10)), ER+ ((n = 57)) E mean ((P^* = .438))</td>
</tr>
<tr>
<td>E max ((P^* = .629))</td>
</tr>
<tr>
<td>E ratio ((P^* = .941))</td>
</tr>
<tr>
<td>PR ((n = 17)), PR+ ((n = 50)) E mean ((P^* = .980))</td>
</tr>
<tr>
<td>E max ((P^* = .930))</td>
</tr>
<tr>
<td>E ratio ((P^* = .700))</td>
</tr>
<tr>
<td>HER2 ((n = 53)), HER2+ ((n = 14)) E mean ((P^* = .259))</td>
</tr>
<tr>
<td>E max ((P^* = .162))</td>
</tr>
<tr>
<td>E ratio ((P^* = .030))</td>
</tr>
</tbody>
</table>

\(E\) max, maximum elasticity; \(E\) mean, mean elasticity; ER, estrogen receptor; \(E\) ratio, elasticity ratio; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor; SD, standard deviation; SWE, shear wave elastography.

\(*P^*\) value from the Mann–Whitney U test.

<table>
<thead>
<tr>
<th>TABLE 5. Correlation of Histologic Type with SWE Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWE Parameter</td>
</tr>
<tr>
<td>E mean (SD)</td>
</tr>
<tr>
<td>(P^* = .076) E max (SD)</td>
</tr>
<tr>
<td>(P^* = .067) E max (SD)</td>
</tr>
<tr>
<td>(P^* = .031) E max (SD)</td>
</tr>
<tr>
<td>(P^* = .031) E ratio (SD)</td>
</tr>
<tr>
<td>(P^* = .007) E ratio (SD)</td>
</tr>
<tr>
<td>(P^* = .031) E ratio (SD)</td>
</tr>
<tr>
<td>(P^* = .031) E ratio (SD)</td>
</tr>
</tbody>
</table>

DCIS, ductal carcinoma in situ; \(E\) max, maximum elasticity; \(E\) mean, mean elasticity; \(E\) ratio, elasticity ratio; IDC, invasive ductal cancer; IMC, invasive mucinous carcinoma; SD, standard deviation; SWE, shear wave elastography.

\(*P^*\) value from the Mann–Whitney U test (comparing ductal carcinoma in situ and invasive ductal cancer).
cancer size ($P < .0001$), but not lymph node involvement, maintained independent association (however, in a later article, Evans et al. demonstrated E mean was an independent predictor of lymph node involvement [$P = .035$] (29)); Youk et al. (28) demonstrated LVI ($P = .002$), but not invasive cancer size or lymph node involvement, maintained independent association; Chang et al. (30) demonstrated invasive cancer size ($P < .0001$), but not lymph node involvement, maintained independent association.

Yoshihara et al. (34) demonstrated that axillary lymph node involvement was significantly associated with larger tumor size and the presence of LVI (both $P < .0001$). Klevesath et al. (35) demonstrated that increasing tumor size was significantly associated with lymph node positivity ($P = .003$); the presence of LVI correlated significantly with lymph node positivity ($P = .01$).

We demonstrated that grade 3 cancers tended to have higher SWE values compared to grade 1 and 2 cancers, but there was no significant difference between the three histologic grades (all $P > .05$; Figs 1 and 2). This finding is in contrast to other studies. Evans et al., Youk et al., and Chang et al. all demonstrated that a higher histologic grade was associated with significantly higher E mean; all $P < .0001$, (27,28,30). Choi et al. demonstrated that a higher histologic grade was associated with significantly higher E ratio ($P = .015$) (31). The smaller number of cancers in our study may explain the lack of significant correlation of histologic grade with SWE parameters.

Barr suggested that stiffness in the cancer was due to desmoplastic reaction (33). Desmoplastic reaction is more marked in grade 1 cancers compared to grade 3 cancers (36), and one would expect grade 1 cancers to be harder than grade 3 cancers (29).
cancers. This is opposite to the reported results. Chang et al. (30) suggested that stiffness of the high-grade cancers may be due to a combination of cellularity, microvessel density, necrosis, and fibrosis. High-grade cancers have increased cellularity compared to low-grade cancers. Jin et al. (37) demonstrated that certain types of vascular endothelial growth factor (VEGF) were significantly associated with large tumor size and high histologic grade (P < .01). There is also increased interstitial edema due to the “leaky” wall of the tumor vessels (38). All these factors likely contribute to the stiffness of the high-grade cancers. A recent study suggested that abnormal extracellular matrix plays an important role in cancer progression. It also deregulates behavior of stromal cells and facilitates tumor-associated angiogenesis and inflammation (39).

In our study, there was no significant correlation of ER status and PR status with the SWE parameters. HER2+ cancers tended to have significantly higher values of E ratio compared to HER2− cancers. However, there was no significant difference in E mean or E max (Figs 1–4). This is in contrast to results from other studies: Chang et al. demonstrated significantly higher values of E mean of ER− cancers compared to ER+ cancers, PR− cancers compared to PR+ cancers (P < .0001, P = .015, respectively) (30). Choi et al. demonstrated similar results in E ratio for ER and PR status (P = .005 and .025, respectively) (31). Our study was limited by a smaller number of cancers compared to these two studies. However, our finding of correlation of HER2 status with E ratio was not demonstrated by the two previous studies. Youk et al. demonstrated ER status (P = .015) and PR status (P = .002) were significantly correlated with E mean on univariate analysis but not on multivariate analysis. They suggested that the correlation of ER and PR with E mean could be due to higher histologic grade of ER− or PR− cancers.

Figure 3. A 70-year-old woman with 19.3-mm, grade 3, invasive, ductal carcinoma (NOS) of the left breast. Shear wave elastography superimposed on ultrasound image (top) shows mean elasticity, 237.0 kPa; maximum elasticity, 272.9 kPa; and elasticity ratio, 13.77. Ultrasound image (bottom) shows the cancer with unknown lymph node status; negative lymphovascular invasion; estrogen receptor negative, progesterone receptor negative, and human epidermal growth factor receptor 2 positive; and human epidermal growth factor receptor 2 positive subtype. This cancer was extremely hard.

Figure 4. A 40-year-old woman with 12.3-mm, grade 3, invasive, ductal carcinoma (with medullary features) of the left breast. Shear wave elastography superimposed on ultrasound image (top) shows mean elasticity, 147.5 kPa; maximum elasticity, 165.5 kPa; and elasticity ratio, 15.29. Ultrasound image (bottom) shows the cancer with negative lymph node involvement (zero of four); negative lymphovascular invasion; estrogen receptor negative, progesterone receptor negative, human epidermal growth factor receptor 2 negative; triple negative subtype. This cancer was very hard.
Further studies are required to clarify the correlation of immunohistochemical biomarkers with SWE parameters.

We demonstrated that DCIS tended to be softer than IDC, with significantly lower E ratio \( (P = .031; \text{Fig } 5) \). There was only one case of ILC, which was very hard. On pathology, this was the classic type of ILC, with large sheets of fibrosis in the cancer. Evans et al. \( (27) \) also demonstrated increased stiffness of ILC compared to IDC \( (P < .0001) \). In our study, there were two cases of IMC, and they were very hard \( (\text{Fig } 6) \). This is unexpected because IMC was described as a relatively soft cancer \( (40) \). Chang et al. also demonstrated increased stiffness of IMC compared to IDC \( (30) \).

To summarize, our prospective study demonstrated a somewhat discrepant result from previous retrospective studies \( (27–31) \). Until this inconsistency is addressed with further studies, one should be prudent to apply results from these studies to one’s clinical practice to modify therapeutic approach.

There are several limitations of our study. First, the number of cancers is relatively small compared to other studies. The immunohistochemical subtypes were limited: there were only one HER2+ and nine TN subtypes. As a result, we did not analyze the correlation between immunohistochemical subtype and SWE parameters. The histologic types were also limited: most of the cancers were IDC; there were only five DCIS, one ILC, and two IMC. The small number of these cancers makes it difficult to make a definite conclusion about their stiffness. Second, SWE parameters of each cancer were obtained by only one radiologist. Repeated SWE by a second operator was not performed to confirm the results or if they were different, to obtain a second set of parameters to calculate an average with the first set. However, it was demonstrated that SWE for elasticity assessment within and between observers was highly reproducible \( (41) \). Third, mean cancer size was obtained from the US images, rather than maximal...
diameter from US or pathology report. We aimed to obtain prognostic information during the time of imaging and statistically significant results were obtained.

In conclusion, there was significant correlation of cancer size with the SSE parameters. There was significant correlation of lymph node status and LV1 with SSE, but only on univariate analysis. In our study subjects, SSE appeared to have limited correlation with prognostic features of breast cancer. Because SSE has the potential to provide prognostic information of breast cancer in a noninvasive manner to supplement that obtained from biopsy, further prospective study with a larger number of cancers is required to address the inconsistent results of different studies. Moreover, because sonographic features of invasive ductal carcinoma have been demonstrated to correlate with histologic grade and hormone-receptor status of the cancer (42), it would be of value to add stiffness to sonographic features to see if further information of cancer prognosis can be obtained.

REFERENCES
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