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Shear Wave Elastography for Detection of Prostate Cancer: A Preliminary Study

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Objective: To assess the diagnostic value of shear wave elastography (SWE) for prostate cancer detection.

Materials and Methods: In this retrospective study, 87 patients with the suspicion of prostate cancer (prostate-specific antigen > 4 ng/mL and abnormal digital rectal examination) underwent a protocol-based systematic 12-core biopsy followed by targeted biopsy at hypoechoic areas on grey-scale ultrasound. Prior to biopsy, SWE was performed by placing two circular 5 mm-sized regions of interest (ROIs) along the estimated biopsy tract in each sector and one ROI for hypoechoic lesions. SWE parameters, S (mean stiffness) and R (mean stiffness ratio), were calculated and compared regarding different histopathologic tissues and their accuracy for diagnosing prostate cancer was analyzed. SWE parameters were correlated with Gleason score and were compared between indolent (< 8) and aggressive (≥ 8) tissues in prostate cancer patients.

Results: Prostate cancer was detected in 7.5% of 1058 cores in 29.9% of 87 patients. Seven (43.8%) of 16 hypoechoic lesions were confirmed as prostate cancer. SWE parameters were significantly different among the histopathologic entities (p < 0.001). Prostate cancer was stiffer than benign tissues ($p \leq 0.003$). Sensitivity, specificity and receiver operating characteristic curve area for diagnosing cancer were 43%, 80.8%, and 0.599, respectively, for a cutoff of S > 43.9 kPa and 60.8%, 66.4%, and 0.653, respectively, for R > 3. Both, S and R showed a significant correlation with Gleason score ($r \geq 0.296$, $p \leq 0.008$) and were significantly different between indolent and aggressive prostate cancer ($p \leq 0.006$).

Conclusion: Shear wave elastographic parameters are significantly different between prostate cancer and benign prostate tissue and correlate with Gleason score.

Index terms: *Prostate cancer; Shear wave elastography; Young modulus; Ultrasonography; Gleason score*

INTRODUCTION

Prostate cancer is the most common malignancy in men in the western world (1). Serum prostate-specific antigen (PSA) with levels > 4.0 ng/mL considered as abnormal has been used as a screening test for prostate cancer. However, various benign diseases such as acute prostatitis, benign prostatic hypertrophy and previous therapeutic intervention of the prostate can lead to elevated PSA levels; therefore false-positive results from PSA test are not uncommon. On the contrary, prostate cancer can also present in approximately 20% of the patients with PSA levels < 4.0 ng/mL (2). Digital rectal exam (DRE) has been implemented into the process of prostate cancer screening in order to increase accuracy. This has led to an increased positive predictive value (PPV) of 60.6% compared with DRE (31.4%)

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or PSA (PPV, 42.1%) alone (2, 3). A standard grey-scale (B-mode) transrectal ultrasound (TRUS)-guided biopsy is currently offered when prostate cancer is suspected using one of these methods (4). However, grey-scale ultrasound can only detect approximately 50% of prostate cancer and biopsies yield at least 1 positive biopsy in only 25% of the patients (5, 6). To reduce false-negative results, investigators have performed biopsies with an increased number of systematic cores (7, 8). Although TRUS-guided biopsy is considered a safe procedure, it is invasive and always involves some risk of complication such as post-biopsy rectal bleeding or urosepsis. Therefore biopsy protocols should be optimized to accurately detect prostate cancer while reducing the number of prostate biopsy specimens and the biopsy-related patient morbidity (9).

Recently, shear wave elastography (SWE) which can provide quantitative information on tissue elasticity in real time has been gaining much interest for prostate cancer diagnosis (10). A few investigators reported SWE possessed high diagnostic accuracy and that it may play a role to spare patients with high PSA levels but negative SWE results from unnecessary biopsies (11, 12). Despite those promising results, we believe that additional investigation with a larger study population is necessary to assess the diagnostic value of SWE in the detection of prostate cancer and this was the purpose of the present study.

MATERIALS AND METHODS

Patient Selection

Institutional Review Board approval was obtained for this retrospective study and the requirement for an informed consent was waived. All patients who were scheduled for TRUS-guided biopsy for suspected prostate cancer at our institution during the period of January 2012 to January 2013 were enrolled in this study. The indications for TRUS-guided biopsy were elevated serum PSA (> 4 ng/mL) or abnormal DRE. Of initial 107 patients who were referred to our department for TRUS-guided biopsy, 20 patients were excluded from the study for the following reasons: 1) SWE imaging was not performed (n = 8), 2) SWE parameters were not acquired according to the study protocol (n = 7), 3) discrepancy was present between the location of SWE measurement and where the core biopsy was performed (n = 5). Finally, the remaining 87 patients were included in the study.

Transrectal Ultrasound, Shear Wave Elastography

Transrectal ultrasound was performed with an ultrasound system (SuperSonic Imagine, Aix en Provence, France) by one radiologist with 5 years' experience in genitourinary ultrasonography with a SE12-3 MHz transrectal probe including grey-scale, color Doppler and SWE imaging. Imaging was performed in the axial and sagittal planes, from the seminal vesicles to the apex of the gland. After volume measurement and routine imaging, the prostate was divided into 12 sectors for both SWE imaging and biopsy of the prostate (13).

Shear wave elastography image acquisition is performed by generating shear wave using a sonographic push pulse. Then it expresses the tissue stiffness in a color-coded map of Young modulus, which is simply the ratio of stress put on a material to the deformation caused by stress, overlaid on grey-scale images (14, 15). Because of high prevalence of enlarged prostate volume, the field of view of SWE imaging was not wide enough to cover the entire prostate. Therefore, right and left lobes were measured separately with a limitation of acquiring SWE mapping in the more anterior portions of the prostate. To ensure stable acquisition of SWE data, the least possible pressure was applied to the prostate while maintaining contact with the probe for 5 to 10 seconds. For each of the 12 sectors, two 5 mm-sized circular regions of interest (ROIs, R1 and R2) were placed along the estimated path for biopsy to calculate the Young modulus (kPa) (Fig. 1). R1 and R2 were generally placed at a depth of approximately 2.5–3 cm and 3.5–4 cm, respectively, and their average value was calculated to represent each sector. In addition, we searched for any focal lesions on grey-scale ultrasound or SWE. First, hypoechoic areas with nodular or clustered shape and irregular margin on grey-scale ultrasound were evaluated by placing a 5 mm-sized circular ROI at the stiffest portion within the lesion (16). Furthermore, we identified areas stiffer than the background prostate gland on SWE but had negative findings on grey-scale ultrasound within the peripheral zone and if present, measured the Young's modulus. We limited this assessment within the peripheral zone because the central and transitional zones tend to be complex, deep and resultantly lend itself to poor SWE imaging (11). To minimize the possible measurement variability from timing of color mapping and motion from bowel peristalsis effects, measurements were performed three times with the corresponding mean value used to represent the stiffness of each ROI.

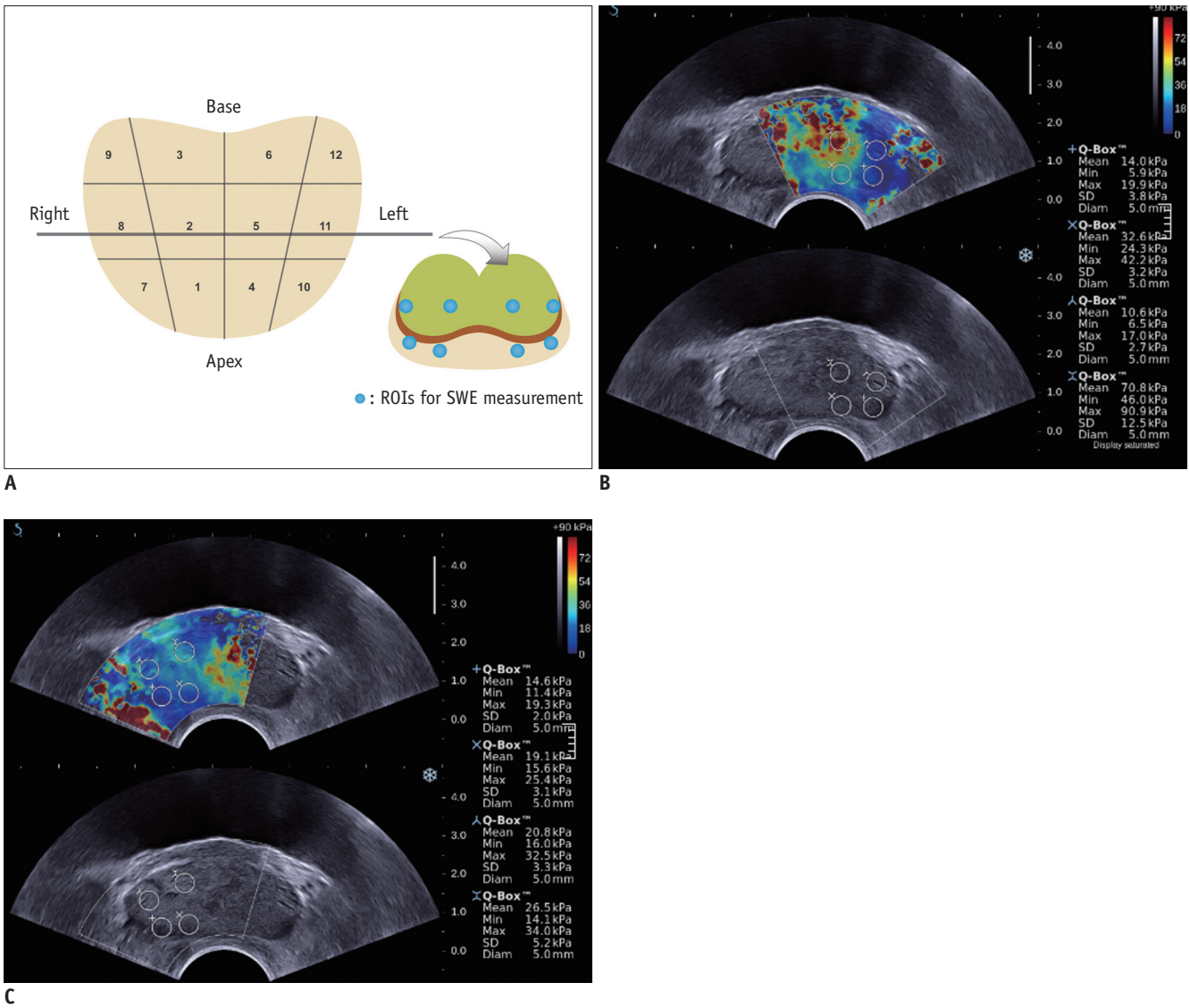

Fig. 1. Distribution of 12 sectors for systematic 12-core biopsy and acquisition of shear wave elastographic (SWE) parameters.
A. Twelve systematic cores consisting of paramedian (1–6) and lateral (7–12) cores from base, mid-level and apex at each side of prostate gland. Image on lower right is representative axial slice at mid-level of prostate gland which is demonstrated as with line traversing schematic drawing of prostate on left. **B, C.** SWE images acquired in 57-year-old man demonstrate total of four 5-mm-sized regions of interest (ROI), two each at paramedian and lateral sectors, placed along estimated path of core biopsy at left **(B)** and right **(C)** prostate glands. Left upper paramedian ROI demonstrates higher stiffness (red color) than surrounding prostate tissue (blue color) in left lateral and right areas. Quantitative SWE parameters of this sector were 52.9 kPa and 6.4 for S and R, respectively. Upon 12-core biopsy, this area was confirmed as prostate cancer with Gleason score of 7.

Transrectal Ultrasound-Guided Prostate Biopsy

All TRUS-guided prostate biopsies were performed by one radiologist after performing the routine grey-scale, color Doppler and SWE imaging. Before performing biopsies, 5 mL of 1% lidocaine (Dai Han Pharm, Seoul, Korea) was administered via a 22-gauge, 14-cm Chiba needle (Becton Dickinson, Franklin Lakes, NJ, USA). An 18-gauge, 20-cm automatic cutting needle and automated biopsy gun (Pro-Mag 2.2; Manan Medical Products, Northbrook, IL, USA) were used to obtain biopsy cores. Biopsy specimens were generally obtained from 12 separate prostate regions, including three samples from the peripheral zone and three samples from the inner gland on each side. Core biopsy was performed at each sector targeted along the location where the aforementioned two ROIs were placed. In cases in which focal lesions were detected on TRUS, biopsies encompassing the lesions were obtained (Fig. 2). The biopsy specimen was numbered to match the focal lesion.

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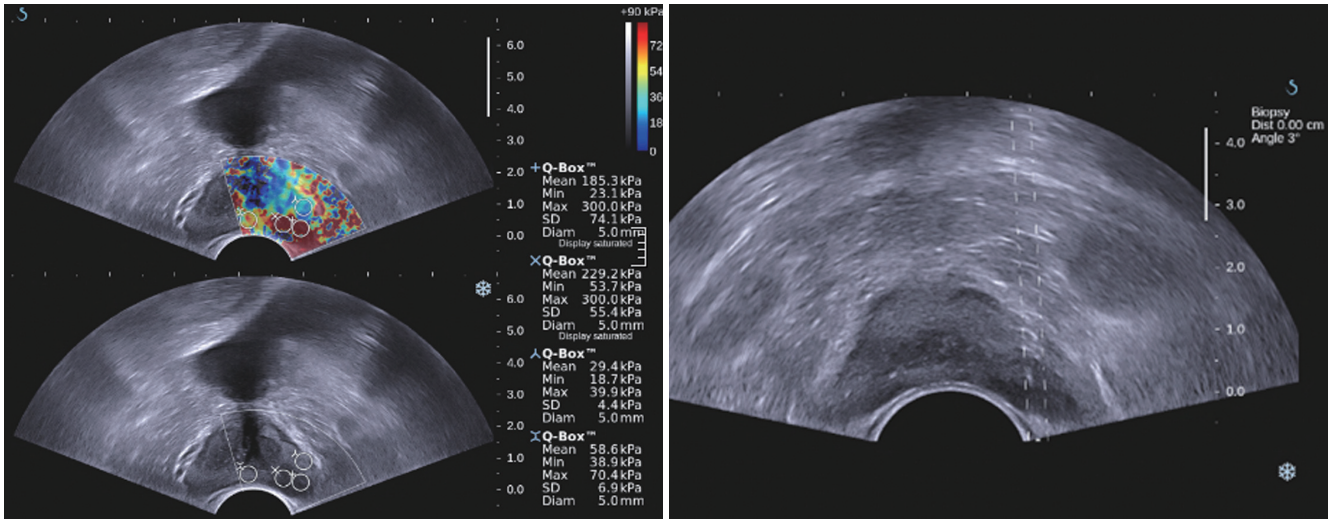

A B

Fig. 2. 80-year-old man with prostate cancer in focal lesion with hypoechogenicity and elevated stiffness on shear wave elastography.

A. After acquisition of shear wave elastographic images, region of interest was placed at and around focal lesion with hypoechogenicity compared with surrounding prostate gland. After three region of interest measurements, mean S and R were 191.2 kPa and 11.2, respectively. **B.** Dotted line shows needle guide for real-time biopsy targeted at focal lesion which was confirmed as prostate cancer with Gleason score of 7 at pathology.

Image Analysis

All images (grey-scale ultrasound and SWE) were digitally stored and quantitative analyses of these images were independently performed at a later time point by one radiologist with 2 years' experience in genitourinary imaging who was not involved in the acquisition of the imaging data and was blinded to the pathologic results. The following four quantitative SWE parameters were evaluated in our study for evaluation of the stiffness:

Mean stiffness (S)
= (Young's modulus [R1] + Young's modulus [R2]) / 2
Mean stiffness ratio (R)
= S of sector / lowest S of patient

Of note, R was evaluated in order to measure the lesion-to-background ratio. The sector with the lowest S was selected as the reference to other lesions because it may be able to represent the normal background prostate tissue without involvement of pathology and because it is impractical to evaluate SWE in adjacent muscle or other organs when performing TRUS (17).

Pathological Analysis

Core biopsy specimens were evaluated independently and blinded to the quantitative SWE data by one pathologist with 9 years' experience in uropathology. Histological grading was based on the Gleason score (18).

Statistical Analysis

All statistical analyses were performed with PASW statistical software (version 18.0; SPSS, Chicago, IL, USA) and MedCalc version 11.1.1.0 for Windows (MedCalc Software, Mariakerke, Belgium). A two-tailed p value of < 0.05 was considered to indicate a statistically significant difference.

Baseline characteristics of patients with and without prostate cancer were compared with the unpaired t test. One way analysis of variance with Tukey-Kramer post hoc test was used to compare the quantitative SWE parameters between different pathologies on a per-core basis. The unpaired t test was used to compare the SWE parameters between benign and malignant prostate tissues and to compare them between tissues obtained from median and lateral cores. Receiver operating characteristic (ROC) curve analysis was performed for the SWE parameters that demonstrated significant differences between benign and malignant prostate tissues to obtain the sensitivity, specificity according to the threshold which yielded the greatest Youden index. The generalized estimating equation was used to adjust for the intrasubject correlation as 12 core biopsies were obtained in each patient. Each variable (S or R), used in the generalized estimating equation, had a binary value (greater than and less than the threshold value derived from ROC curve analysis). The Spearman correlation test was used in patients with prostate cancer to correlate SWE parameters with Gleason score and the unpaired t

test was used to compare these values between prostate cancer obtained from systematic biopsy and targeted biopsy and between indolent (Gleason score < 8) and aggressive (Gleason score ≥ 8) prostate cancer.

RESULTS

Patient Characteristics

A total of 87 patients with a mean age of 66 ± 9.0 years (range, 37–85 years) were included in our study. The mean serum PSA level was 12.8 ± 31.9 ng/mL (range, 1.13–259.15 ng/mL), and the mean prostate volume was 58.6 ± 22.2 mL (range, 23.3–156.4 mL). The mean PSA density was 0.24 ± 0.55/mL (range, 0.02–3.75/mL).

The mean age, prostate volume and PSA density were significantly different in the patients with and without prostate cancer; mean age: 70.1 ± 7.7 years vs. 64.8 ± 9.0 years (p = 0.012), prostate volume: 49.5 ± 21.2 mL vs. 62.2 ± 21.7 mL (p = 0.015) and PSA density 0.55 ± 0.95/mL vs. 0.12 ± 0.07/mL (p = 0.031). The PSA level of subjects with prostate cancer was higher (27.9 ± 57.2 ng/mL) than of subjects without prostate cancer (6.7 ± 4.1 ng/mL) with borderline significance (p = 0.076).

Relationship between Shear Wave Elastographic Parameters and Histopathology

A total of 87 patients with 1058 cores biopsies cores were evaluated. Two cores from one patient were not evaluated because the SWE parameters were not measured. A total of 79 (7.5%) prostate cancer foci were detected in 26 (29.9%) patients. There were a total of 16 hypoechoic lesions noted on grey-scale ultrasound. Among them, 7 lesions (43.8%) were confirmed as prostate cancer on pathology. The pathologic results also included 953 cores with normal prostate tissue, 23 with chronic inflammation and 3 with atypia.

The relationship between SWE parameters and histopathology is described in Table 1. The SWE parameters were significantly different among the entities (p < 0.001 for all). Prostate cancer showed significantly different SWE values upon pairwise comparison with the following benign categories: prostate cancer versus normal prostate tissue (p < 0.001 for all), prostate cancer versus chronic inflammation (p = 0.002 for R). Prostate cancer demonstrated borderline higher S compared with atypia (p = 0.09). Among the benign categories, S showed significant difference between normal prostate tissue and chronic inflammation (p = 0.021).

Differentiation of Benign and Malignant Prostate Tissue Using SWE Parameters

The differences of SWE parameters in benign and malignant prostate tissue are described in Table 2 and Figure 3. Both S and R were significantly greater in malignant than in benign prostate tissues. The mean S and R values were 54.6 kPa and 6.0 for prostate cancer and 33.4 kPa and 3.1 for benign prostate tissues (p < 0.001 and p = 0.003 for S and R, respectively). Prostate cancer tissues

Table 1. Relationship between Shear Wave Elastographic Parameters and Histopathology

Parameter	Normal Prostate Tissue (n = 953)	Chronic Inflammation (n = 23)	Atypia (n = 3)	Prostate Cancer (n = 79)	*P*
S (kPa)	33.2 ± 16.7 (2.3, 150.1)	45.8 ± 38.0 (14.0, 148.7)	25.8 ± 10.5 (18.0, 37.8)	54.6 ± 46.0 (13.5, 191.2)	< 0.001
R	3.1 ± 2.1 (1.0, 19.0)	3.4 ± 2.0 (1.6, 9.1)	2.4 ± 0.9 (1.5, 3.2)	6.0 ± 8.3 (1.2, 41.9)	< 0.001
Lowest S of patient (kPa)	12.1 ± 4.4 (1.8, 37.1)	12.1 ± 3.8 (8.9, 16.3)	10.7 ± 2.1 (8.3, 11.9)	12.8 ± 9.4 (1.8, 37.1)	0.633

Note.— Data are mean ± standard deviation. Mean stiffness (S) = (Young's modulus [R1] + Young's modulus [R2]) / 2, Mean stiffness ratio (R) = S of sector / lowest S of patient

Table 2. Differentiation of Benign and Malignant Prostate Tissue Using SWE Parameters

Parameter	Benign Prostate Tissue (n = 979)	Prostate Cancer (n = 79)	*P**
S (kPa)	33.4 ± 17.6 (2.3, 150.1)	54.6 ± 46.0 (13.5, 191.2)	< 0.001
R	3.1 ± 2.1 (1.0, 19.0)	6.0 ± 8.3 (1.2, 41.9)	0.003

Note.— Data are mean ± standard deviation. *Difference between grades was evaluated by using Student *t* test. Mean stiffness (S) = (Young's modulus [R1] + Young's modulus [R2]) / 2, Mean stiffness ratio (R) = S of sector / lowest S of patient. SWE = shear wave elastography

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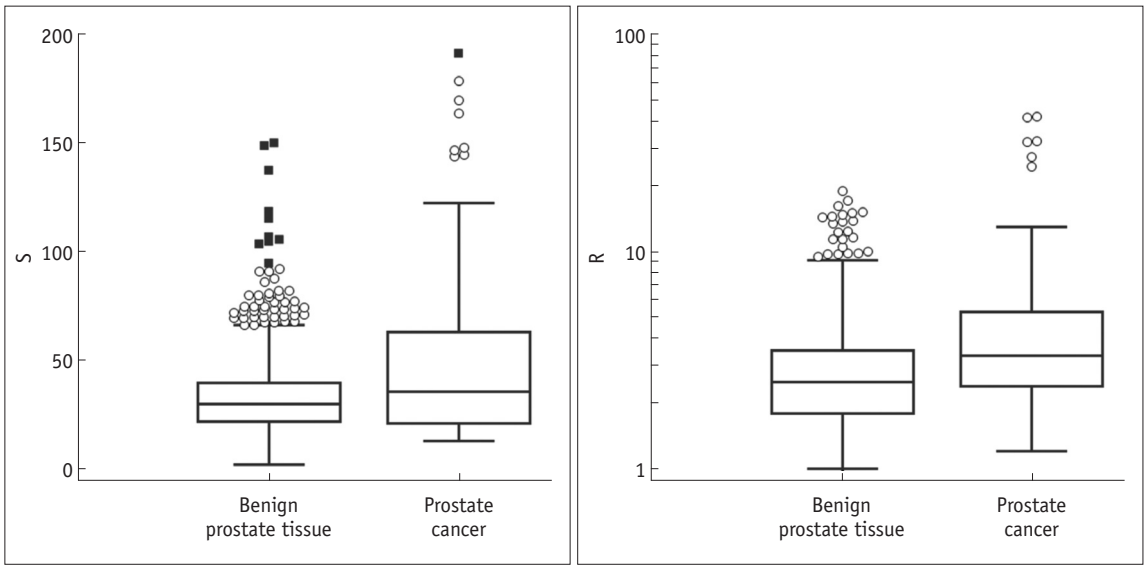

Fig. 3. Shear wave elastographic parameters according to histopathology. Shear wave elastographic parameters were significantly different between prostate cancer and benign prostatic tissue. Mean S and R values were 54.6 kPa and 6.0 for prostate cancer, and 33.4 kPa and 3.1 for benign prostate tissues ($p < 0.001$ and $p = 0.003$ for S and R) respectively. Mean stiffness (S) = mean value of Young' modulus measured from two regions of interest placed along estimated path for core biopsy for each of 12 sectors. Mean stiffness ratio (R) = ratio of S of sector to that of lowest S of patient.

acquired from targeted biopsy for hypoechoic lesions (n = 7) tended to show higher stiffness than those obtained from systematic biopsy (n = 72) however, without statistical significance: mean S = 81.4 ± 59.8 kPa vs. 52.0 ± 44.1 kPa ($p = 0.107$) and R = 7.5 ± 4.4 vs. 5.9 ± 8.6 ($p = 0.632$), for systematic biopsy and targeted biopsy, respectively. There was no significant difference in mean S and R values between prostate cancer tissues in the paramedian and lateral cores: mean S = 55.5 ± 40.6 vs. 48.6 ± 47.8 ($p = 0.516$) and mean R = 6.3 ± 8.6 vs. 5.4 ± 8.8 ($p = 0.636$) for paramedian versus lateral cores, respectively. However, the benign prostate tissues from the paramedian cores were significantly stiffer than those from lateral cores: mean S = 37.6 ± 16.6 vs. 29.2 ± 17.3 ($p < 0.001$) and mean R = 3.5 ± 2.4 vs. 2.6 ± 1.6 ($p < 0.001$) for paramedian versus lateral cores, respectively.

The ROC curve analyses for differentiation between benign and malignant prostate tissue using the SWE parameters are shown in Figure 4. Prostate cancer could be predicted with a sensitivity of 43.0% and a specificity of 80.8%, PPV of 13.5% and negative predictive value (NPV) of 94.8% using a cutoff value of S > 43.9 kPa. The sensitivity was 60.8% and the specificity 66.4%, the PPV was 11.5% and NPV was 95.8% when cutoff value of R > 3 was used. When paramedian and lateral sectors were separately evaluated, the lateral sectors yielded lower sensitivity and higher specificity compared with the paramedian sectors: 33.3% and 85.8% using S and 44.4% and 75.5% using R in the lateral sectors; 47.2% and 75.9% using S and 77.8% and 54.8% using R in the paramedian sectors. The area under the ROC curve (Az) was significantly higher ($p = 0.048$) using R (Az = 0.653; $p < 0.0001$) than using S (Az = 0.599; $p = 0.0122$).

These findings were confirmed to be independent from within subject clustering effects by using generalized estimating equation analysis. It demonstrated that S > 43.9 kPa (95% confidence interval [CI]: 1.2, 5.8; $p = 0.021$) and R > 3 (95% CI: 1.6, 4.9; $p = 0.001$) were significantly associated with prostate cancer.

Correlation of Shear Wave Elastographic Parameters with Gleason Score

The relationship between SWE parameters and Gleason score are shown in Table 3. Both S and R demonstrated a significant linear trend with Gleason score ($r = 0.343$, $p = 0.002$ for S, and $r = 0.296$, $p = 0.008$ for R). In addition, aggressive prostate cancer showed significantly higher values than indolent prostate cancer: the mean values for indolent versus aggressive prostate cancer were 46.3 ± 40.8 kPa vs. 68.9 ± 51.5 kPa for S ($p = 0.048$) and 4.0 ± 2.6 vs. 9.5 ± 12.8 for R ($p = 0.03$).

Focal Lesions on Shear Wave Elastography but Negative on Grey-Scale Ultrasound

There was a focal lesion in the peripheral zone of only

one patient which demonstrated higher stiffness than the surrounding prostate tissue without abnormal finding on grey-scale ultrasound (Fig. 5). The measured S and R values were 35.1 kPa and 3.1 and it was confirmed as prostate cancer with Gleason score of 7.

DISCUSSION

In our study, we evaluated the diagnostic value of SWE of the prostate for detection of prostate cancer. Our results demonstrated that the SWE parameters of S and R were significantly different between prostate cancer and chronic inflammation or benign prostate tissue. However, despite these promising results, the diagnostic value of SWE in the detection of prostate cancer was with a low sensitivity and variable specificity limited to be used as a tool to reliably differentiate between benign and malignant prostate tissue. We believe that further studies and technological improvements are warranted for real-time quantitative SWE to become a part of the standard protocol in prostate cancer management.

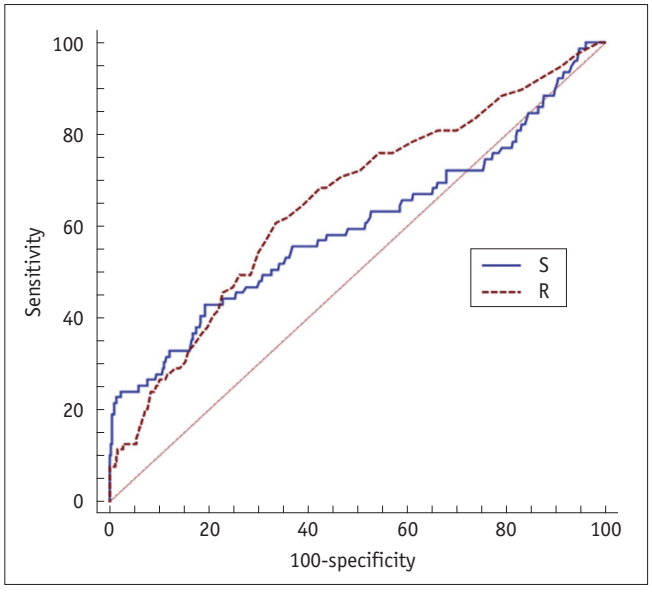

Fig. 4. Receiver operating characteristic curve analyses in differentiation of benign and malignant prostate tissue using shear wave elastography parameters. Prostate cancer could be predicted with sensitivity and specificity of 43.0% (95% confidence interval [CI], 31.9–54.7%) and 80.8% (95% CI, 78.2–83.2%) using cutoff value of S > 43.9 kPa (area under the curve [AUC] = 0.599; 95% CI, 0.569–0.629) and those of 60.8% (95% CI, 49.1–71.6) and 66.4% (95% CI, 63.3–69.4) with cutoff value of R > 3 (AUC = 0.653, 95% CI, 0.624–0.682). Mean stiffness (S) = mean value of Young' modulus measured from two regions of interest placed along estimated path for core biopsy for each of 12 sectors. Mean stiffness ratio (R) = ratio of S of sector to that of lowest S of patient.

Until now, few investigators reported that SWE can differentiate between prostate cancer and benign prostate tissue with a nearly perfect sensitivity (90–96.2%) and specificity (88–96.2%) (11, 12). The sensitivity and specificity was lower in our study although the SWE parameters were significantly different between cores with prostate cancer and those with benign tissues. Furthermore, it should be noted that the reference values were different among the two previous studies as well as ours. Barr et al. (11) used 37 kPa whereas we used 43.9 kPa (for S) or 3 (for R). Ahmad et al. (12) did not provide their reference value, but considering that benign areas and prostate intraepithelial neoplasia/atyipa demonstrated a mean Young modulus of 74.9 ± 47.3 kPa and 83.3 ± 38.6 kPa, respectively, the reference value seems to be much greater than the cutoff values in the study by Barr et al. (11) and in ours. We carefully speculate that these different study results may be partly attributed to the pressure applied to the prostate during the examination. Although it has been suggested that compared to quasistatic compression elastography and transrectal SWE does not require additional compression than the standard TRUS clinical examination, it is impossible to perform TRUS without applying any pressure at all to the prostate (12). Therefore, we cannot exclude the possibility that the size of the prostate and technique of the operator may cause variance in the SWE parameters even though the least possible pressure was applied during SWE measurement. Another important note is that the stiffness of the background prostate was significantly higher in the paramedian sectors than the lateral sectors, resulting in a significant overlap between

Table 3. Correlation of Shear Wave Elastographic Parameters with Gleason Score

Parameter	Gleason Score				R (rho)	*P**
	≤ 6 (n = 20)	7 (n = 30)	8 (n = 18)	≥ 9 (n = 11)		
S (kPa)	32.7 ± 19.4	55.4 ± 48.5	57.3 ± 39.4	88.2 ± 64.2	0.343	< 0.001
R	3.3 ± 2.2	4.4 ± 2.8	9.5 ± 12.4	9.5 ± 13.9	0.296	0.008

Note.— Data are mean ± standard deviation. *Trend of SWE parameter with Gleason score was evaluated by using Spearman's rank correlation test. Mean stiffness (S) = (Young's modulus [R1] + Young's modulus [R2]) / 2, Mean stiffness ratio (R) = S of sector / lowest S of patient

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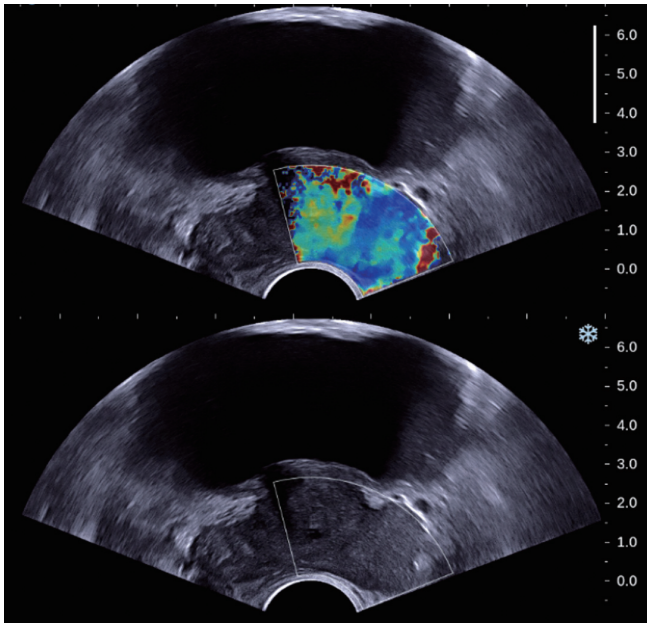

Fig. 5. 80-year-old man with prostate cancer in focal lesion in peripheral zone with elevated stiffness on shear wave elastography but negative findings on grey-scale ultrasound.
Focal lesion in peripheral zone at left lateral base demonstrated with persistent elevated stiffness but without abnormal finding on grey-scale ultrasound. S and R were calculated to be 29.2 kPa and 2.6. It was confirmed as prostate cancer on histopathology.

cores with prostate cancer and normal prostate in the paramedian cores. This may be because much of the inner glands are included in the paramedian sectors and also the paramedian sectors are more prone to the aforementioned applied pressure from the transducer. Correspondingly, the specificity of detecting prostate cancer was higher while the sensitivity was lower in the lateral sectors compared with the paramedian sectors. Taking into consideration that the paramedian sectors usually appear not only heterogeneous on grey-scale ultrasound, but also may show an elevated stiffness on SWE, the question remains if SWE should be implemented in the whole prostate including paramedian sectors.

Our study results showed that SWE parameters were significantly correlated with Gleason score in patients with prostate cancer. There was a significant linear trend of increasing stiffness with elevated Gleason score. In addition, the SWE parameters were significantly different between indolent and aggressive cancers. This may be attributed to the higher cell density and resultant stiffer tissue property of prostate cancer with higher grades (19). In a previous study it has been noted that prostate cancer with a Gleason score of seven was stiffer than those with a Gleason score of six although it was not significantly different from those with a Gleason score of eight (12). We speculate the higher proportion of aggressive cancers in our study (36.7%, 29/79) compared with the study of Ahmad et al. (12) (12.1%, 4/33) may have led to demonstrate this finding.

In our study we found that the mean stiffness ratio, R was also significantly different among the different histopathologic specimens and between prostate cancer and benign prostate tissue. R was evaluated with the intent to see whether the use of lesion-to-background ratio could maximize the differentiation of prostate cancer from benign prostate tissue compared with simple S. Until now, the lesion-to-background ratio of SWE has been used in other organs such as thyroid cancer but not in prostate cancer. In the study by Park et al. (17), the lesion-to-muscle ratio using SWE was helpful in differentiating thyroid cancers with pathologic extrathyroidal extension and central lymph node metastasis whereas the lesion-to-normal thyroid parenchyma was not useful. It is difficult to evaluate the SWE of adjacent muscles or other organs during TRUS performance. In addition, the sectors in the paramedian areas tend to show higher stiffness than the lateral sectors. This may be due to fact that a large portion of the inner glands are included in the paramedian sectors. Therefore, tumors in the paramedian cores may not evidently appear stiffer compared to the surrounding prostate upon visualization. As a result, we used the lowest S of the patients as normal background prostate tissue, because it may represent the area with no or the least involvement of pathologic process. However, this method has its intrinsic limitation that the normal background prostate may not be normal because of the common presence of benign prostate hypertrophy in old patients. Furthermore, the sector with the lowest S could even actually have cancer involvement in patients with diffuse prostate cancer. This was the case in 3 (3.1%) of 97 patients in our study. Exclusion of such patients from our study population would have resulted in greater differences in the stiffness between prostate cancer and benign tissues. However, we did not execute such exclusion as the operator will not be aware of whether the sector with the lowest S is normal, benign or malignant in the real clinical situation. Nevertheless, R showed significant differences between benign and malignant prostate tissues and also showed a correlation with Gleason score. Further studies may be warranted to validate the diagnostic value of R.

There are some limitations in our study. First, there is a

possibility of selection bias because of the retrospective nature of our study. However, it must be noted that all consecutive patients scheduled for TRUS-guided biopsy for suspected prostate cancer at our institution during the study period participated in this study. Therefore, despite of the retrospective design, it can be interpreted similarly to a prospective study. Second, our study population included a small proportion of patients with benign entities and this may have led to insufficient statistical power. In fact, while the SWE parameters were significantly different between prostate cancer and benign prostate tissue or chronic inflammation only borderline statistical differences were demonstrated between prostate cancer and atypia. We believe this may mainly have been due to the small number of patients with atypia (n = 3) and further studies with a larger number of patients in this category may be able to yield statistically significant results. Third, all SWE imaging and core biopsies were performed by a single radiologist, in contrast to a previous study in that they were independently performed each by a radiologist and an urologist (11). Imaging and SWE measurement by one person and systematic biopsy by another person may be of less bias. Fourth, there was a methodological challenge in correlating the pathologic specimen with the ROI for SWE measurement. In our study, we placed two ROIs along the estimated path for biopsy immediately before performing biopsy. In addition, we tried to include the area with increased stiffness compared with the surrounding prostate in at least one of the ROIs for each sector. On the contrary, previous studies used a single ROI to represent the sector. However, the specimen obtained from core-biopsy is not a single round structure but a long tract. Therefore, the mean value (S) of two ROIs along the estimated tract may be more representative of the core-biopsy specimen. Another issue regarding the ultrasonic-pathologic correlation is that the results of pathological analysis of prostate biopsy often show contradiction with prostatectomized specimens. Further studies are warranted based on step-section pathologic analysis after radical prostatectomy. Finally, we were not able to compare the diagnostic value of SWE and color Doppler ultrasound, because color Doppler ultrasound was not meticulously performed, especially for lesions detected on grey-scale ultrasound. We plan a further prospective study to compare their efficacy.

In conclusion, SWE parameters are significantly different between prostate cancer and benign prostate tissue and show significant correlation with Gleason score. However, the diagnostic accuracy is not high with low sensitivity and variable specificity.

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