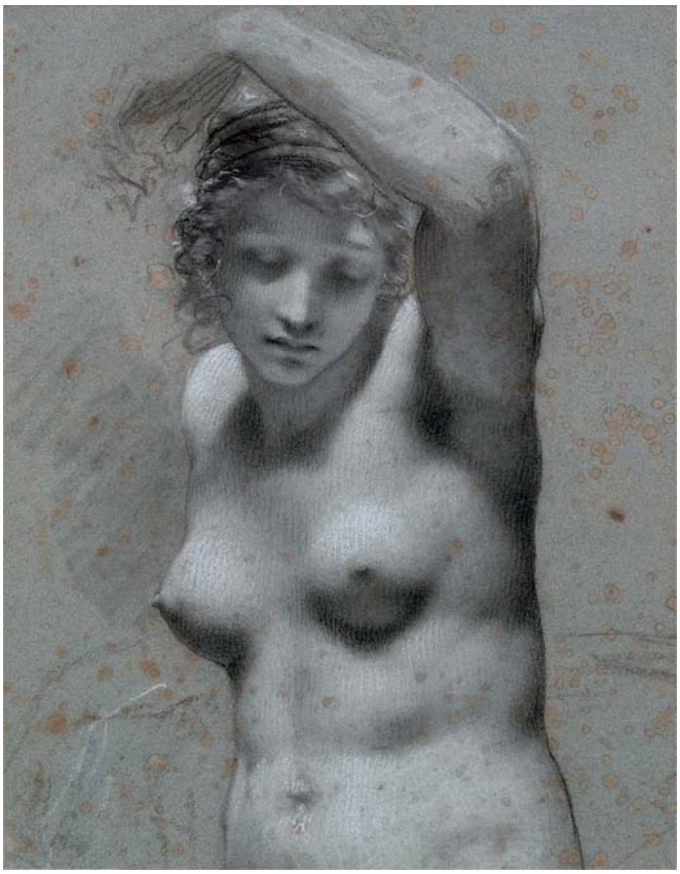
SHEARWAVE™ ELASTOGRAPHY IN THE PROSTATE

PUBLICATIONS AND ABSTRACTS



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Trans-rectal quantitative Shear Wave Elastrography : application to prostate cancer - A feasibility study

Poster No.: C-1748

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Type: Scientific Exhibit

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Keywords: Ultrasound, Elastography, Urinary Tract / Bladder, Oncology

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Purpose

Prostate cancer is the 2nd leading cause of cancer death in men. It is also the most common diagnosed malignancy in men with near 190.000 new cases in the USA in 2008. Despite the larger use of biological tests (such as prostate specific antigen (PSA)) and imaging modalities (trans-rectal ultrasonography (TRUS) and Magnetic Resonance Imaging (MRI)), there is a slight increase in the annual death rate while the mortality remains stable. Due to the limited sensibility of TRUS (60 to 70%), a normal examination should not delay the systematic biopsies if digital rectal examination or PSA are abnormal.

The purpose of our study was to evaluate the feasibility of trans-rectal quantitative Shear Wave Elastography (SWE) for prostate cancer evaluation.

Methods and Materials

21 patients presenting with increased PSA values (4-10 ng/mL) were prospectively enrolled after signing an informed consent form. The prostate was studied using trans-rectal ultrasound (TRUS) with spatial compounded B-mode, colour Doppler US (CDUS) and SWE on the Aixplorer system (Supersonic Imagine, Aix-en-Provence, France; transducer SE12-3). Elasticity measurements and ratios between nodules and adjacent parenchyma were calculated.

Contrast-enhanced US (CEUS) was performed using low MI pulse subtraction after injection of 4.8-9.6 ml of SonoVue® (Bracco, Milan, Italy) using an Aplio XG system (Toshiba MS, Nasu, Japan).

Imaging findings were correlated to sextant prostate biopsies (n=12) and targeted biopsies on suspicious areas (n=2-6) detected at SWE and CEUS. MRI with axial and coronal T2w acquisition, axial T1w acquisition, diffusion and dynamic contrast-enhanced MRI (Signa 1.5T and Discovery MR450, GE HealthCare, Milwaukee, WI, USA) was also evaluated.

The blinded analysis of the SWE acquisition was performed retrospectively from cineloops and frames. Normal and abnormal patterns were matched with pathology results.

Results

In 3 patients, it was not possible to localize normal and abnormal patterns using SWE due to a technical problem during the export of the data. The analysis was performed from the remaining 18 patients (mean age 65 ± 6 years, min 54 - max 79). The PSA values were 6.9 ± 2.2 ng/mL.

Eight patients exhibited significant prostate adenocarcinomas. Among the 26 nodules detected either at US or at pathology, 10 were adenocarcinomas with Gleason score above 6 and 16 were adenomatous hyperplasia or focal prostatitis. The correlation between B-mode + pathology and CDUS, CEUS or MRI could not be obtained for 3 / 3 / 4 nodules, respectively.

SWE was feasible in all patients. Signals were obtained in both the peripheral and the transition zones with good correlation to anatomical areas. Because of higher attenuation, the deepest transition zone was not correctly assessed over 4-5 cm. Macro-calcifications exhibited very high stiffness values.

Transition zone appeared heterogeneous with stiffness values above 40 kPa. SWE signals were adequate for all peripheral nodules. Limitations resulted from gas interposition and higher pressure of the end-fire transducer on the rectal wall and the adjacent posterior gland.

Prostate cancer nodules exhibited a high stiffness (mean 55 ± 45 kPa, min 23/ max 180 kPa) than the adjacent peripheral gland (mean 18 ± 9 kPa).

Peripheral adenomatous hyperplasia and focal prostatitis exhibited a significantly lower stiffness (mean 19 ± 5 kPa, min 12/ max 28 kPa; $p < 0.01$). The stiffness ratio between nodule and adjacent parenchyma was significantly higher for cancer (3.0 ± 1.0) compared to benign nodules (1.0 ± 0.20; $p < 0.01$). The cut-off value of 1.5 allowed the best discrimination of the two populations.

The sensitivity (Se), specificity (Spe), Positive predictive value (PPV) and Negative predictive value (NPV) were calculated for each modality: CDUS, CEUS, SWE and MRI.

CDUS: Se= 50%; Spe= 73%; PPV= 50%; NPV= 73%

CEUS: Se= 67%; Spe= 86%; PPV= 75%; NPV= 80%

SWE: Se= 90%; Spe= 100%; PPV= 100%; NPV= 94%

MRI: Se= 62%; Spe= 78%; PPV= 62%; NPV= 78%

Images for this section:

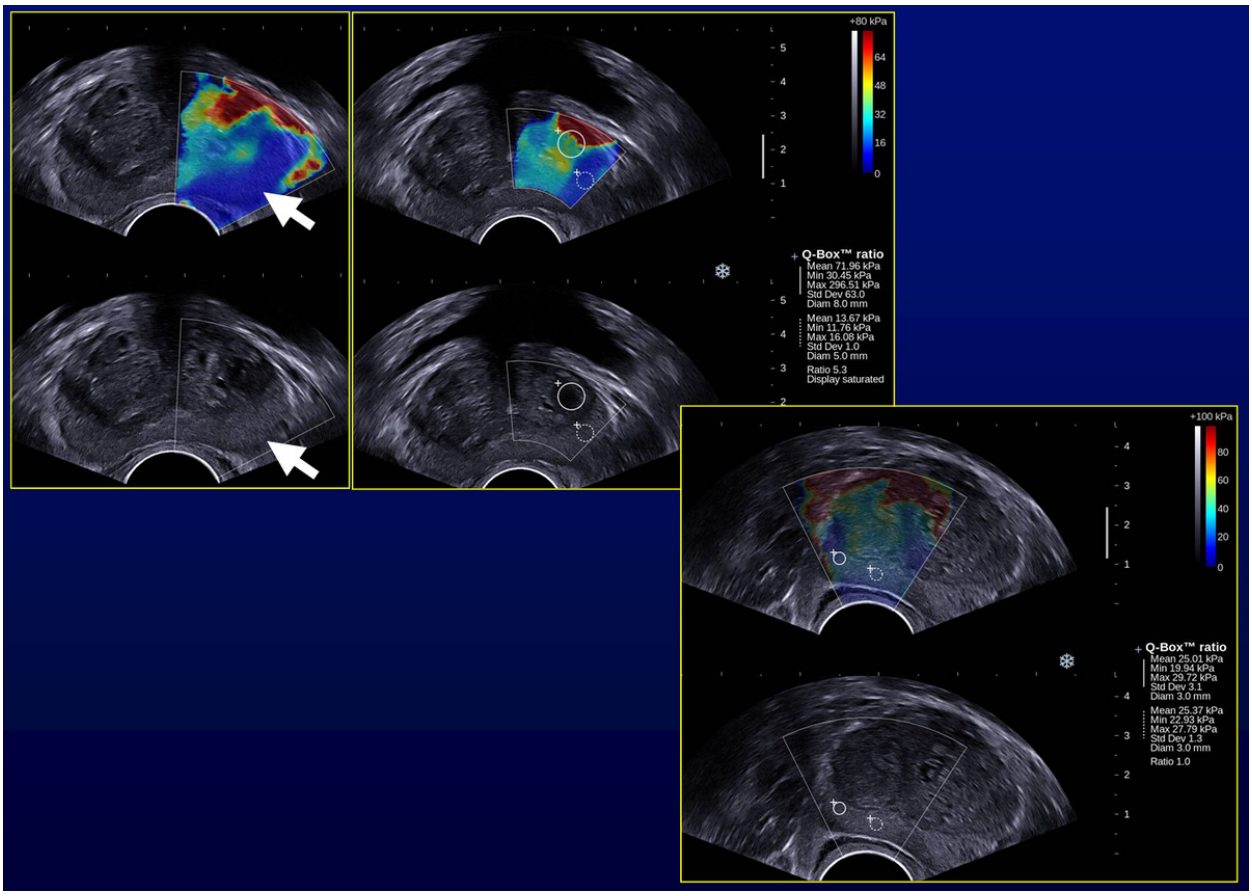

Fig. 1: SWE study of a normal prostate. Note the homogeneous coding of the SWE signals in the peripheral zone and the matching between SWE pattern and anatomical morphology

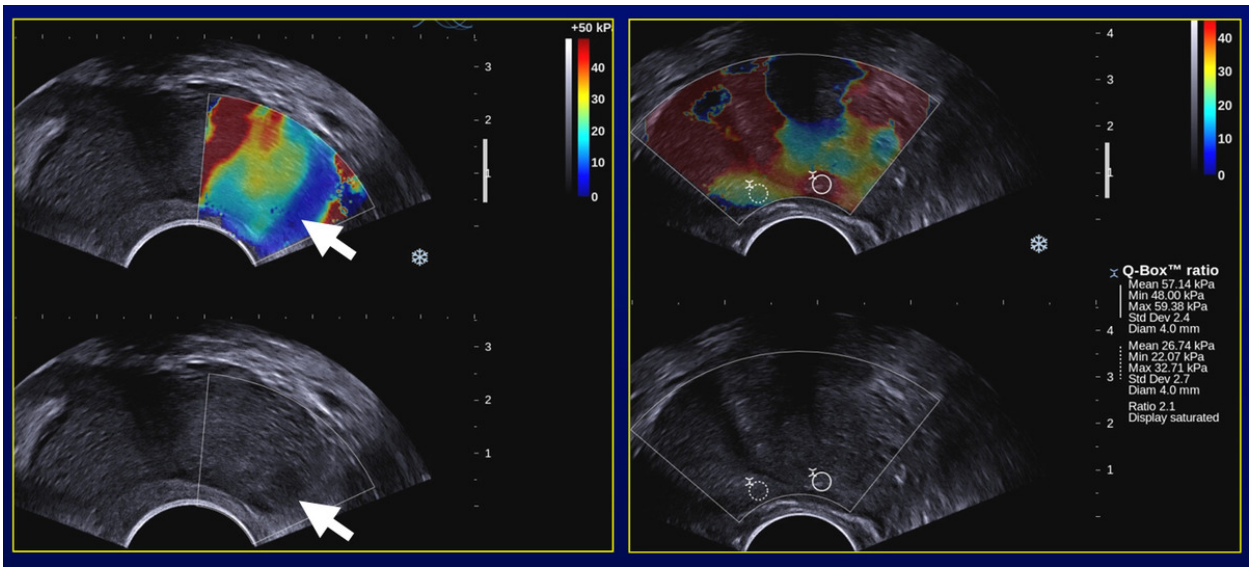

Fig. 2: Patient presenting a soft benign nodule in mid peripheral prostate zone (left picture, straight arrow). Close to the apex, a stiff area was detected and biopsy revealed a Gleason 7 adenocarcinoma (right picture).

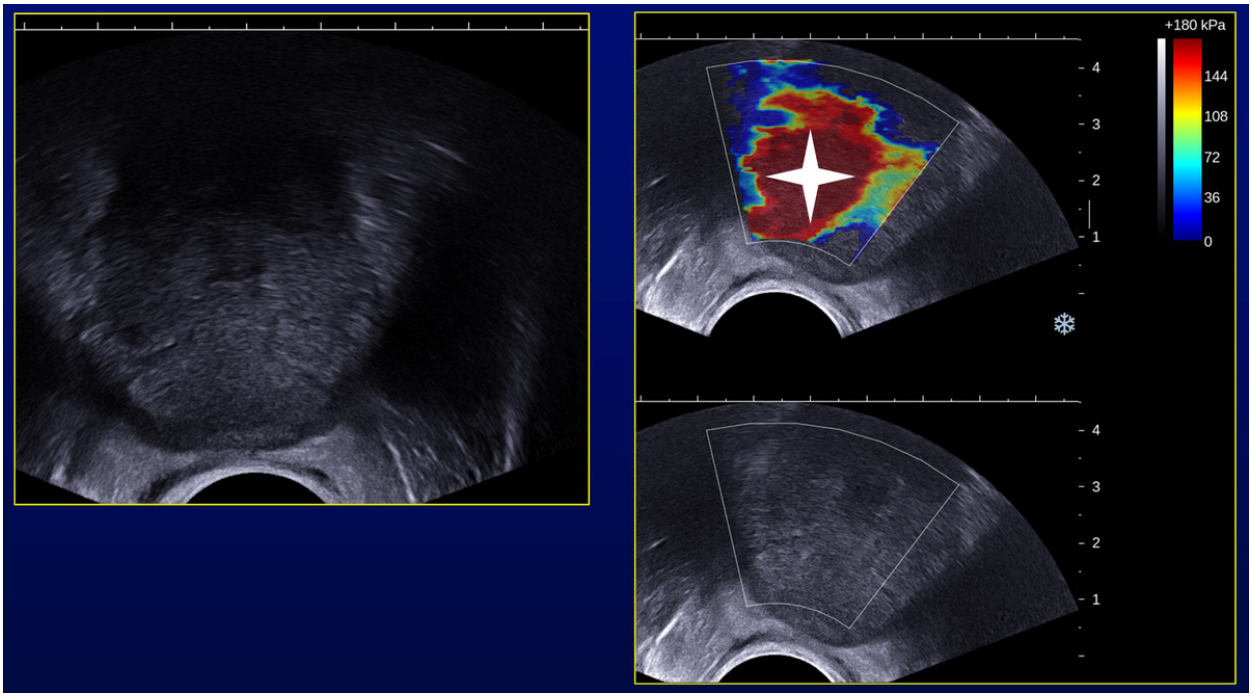

Fig. 3: Patient with no detected nodule on B-mode imaging. However, SWE revealed a diffuse increase in stiffness values over 180 kPa within the entire prostate. All biopsies showed the presence of adenocarcinoma with a Gleason score of 9.

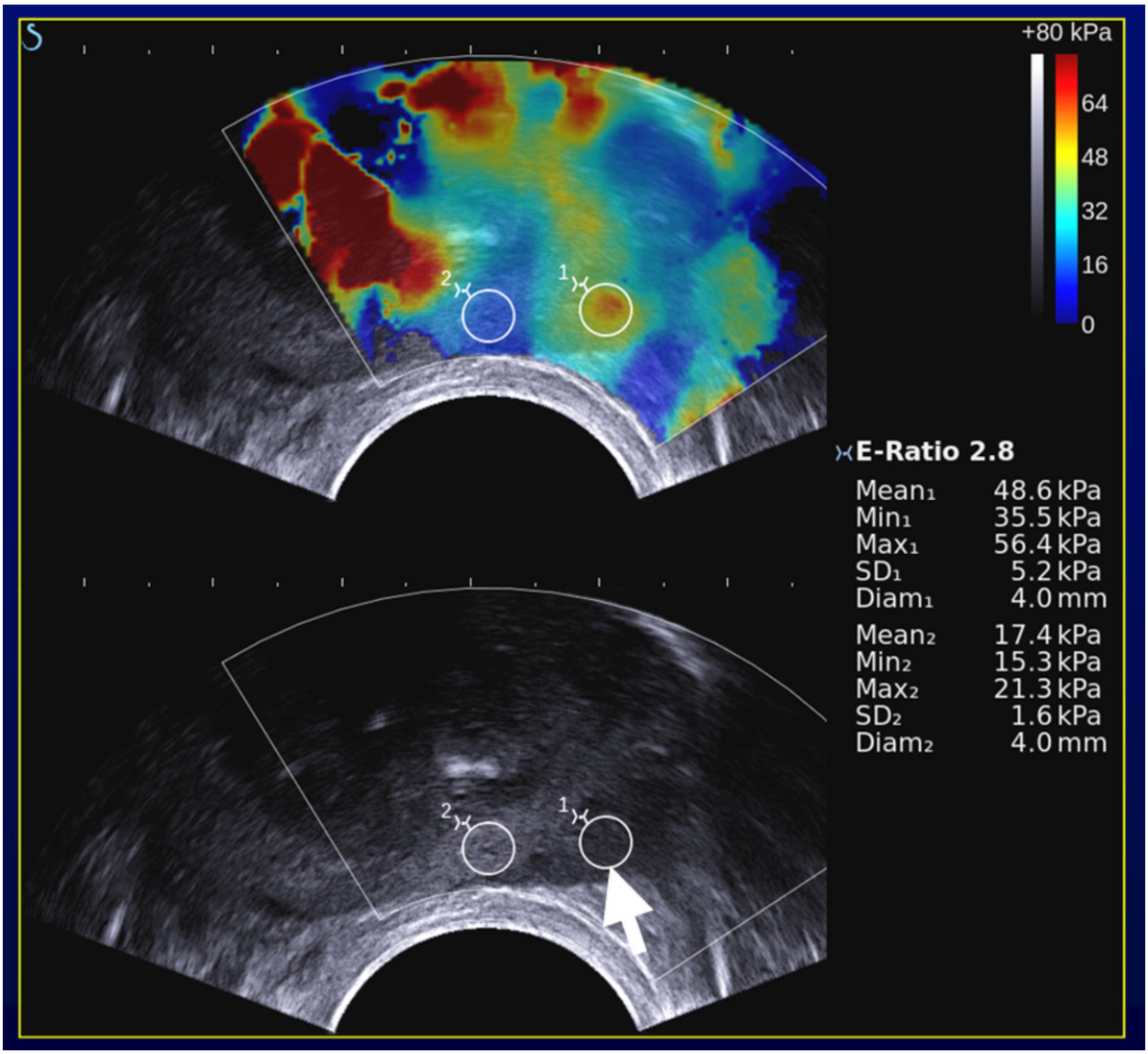

Fig. 4: The hypoechoic nodule in the peripheral zone at mid prostate exhibited a strong increase in stiffness values with a ratio of 2.8 compared to the surrounding peripheral parenchyma. This is the typical pattern of an adenocarcinoma.

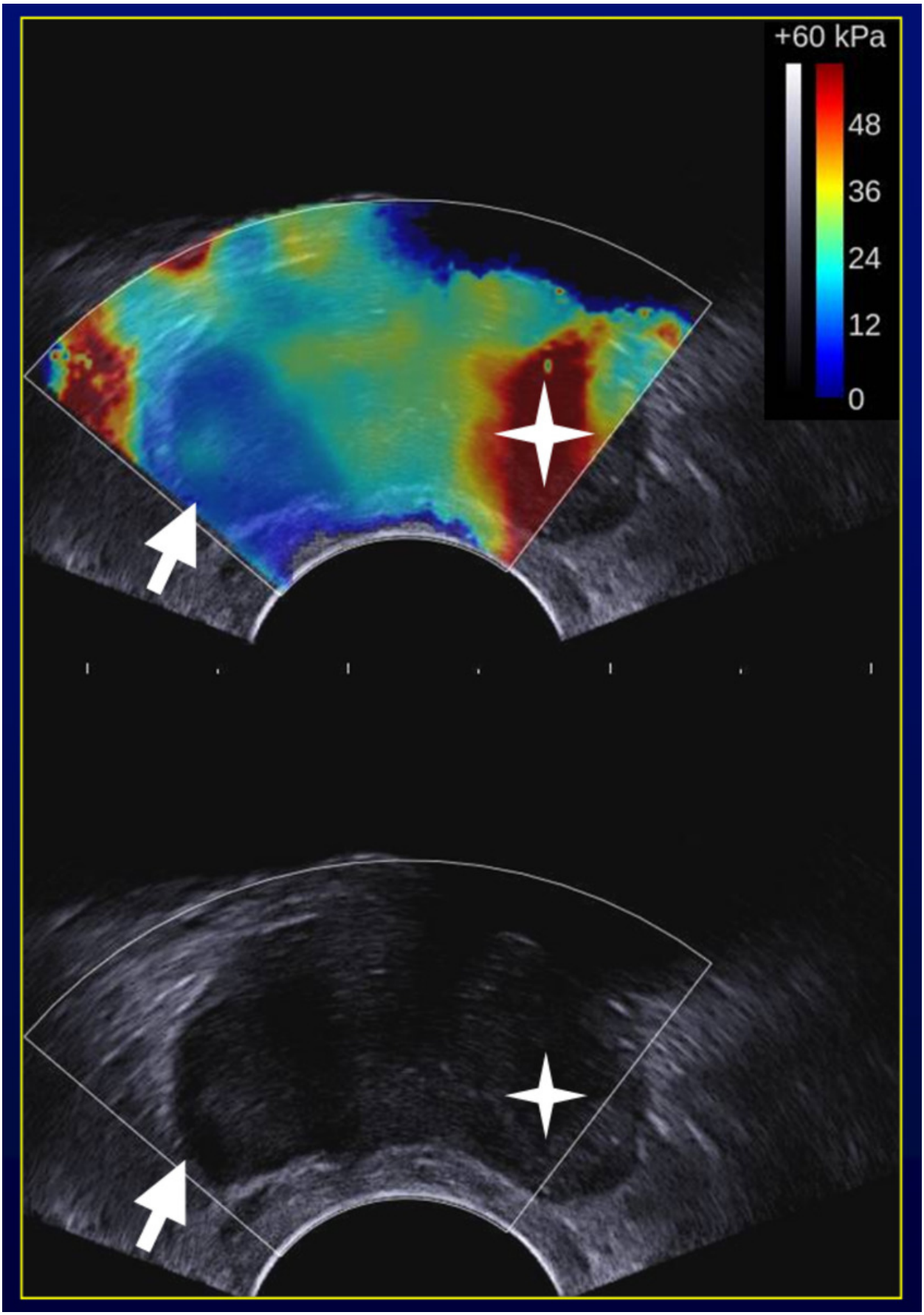
+60 kPa
48
36
24
12
0

Fig. 5: A poor visible nodule at B-mode imaging was reported on the right peripheral zone (straight arrow). It was benign at pathology. However, a stiff area was detected incidentally on the left peripheral zone. Pathology revealed a Gleason 7 adenocarcinoma.

Conclusion

Trans rectal quantitative Shear Wave Elastography is a feasible technique for prostate cancer evaluation. It provides additional information about stiffness of nodules localized in the peripheral zone, complementary to that of CEUS. These preliminary results are encouraging but a larger multicentric evaluation remains necessary.

References

Bercoff J, Tanter M, Fink M. Supersonic shear imaging: a new technique for soft tissue elasticity mapping. IEEE Trans Ultrason Ferroelectr Freq Control. 2004 Apr;51(4):396-409.

Athanasiou A, Tardivon A, Tanter M, Sigal-Zafrani B, Bercoff J, Deffieux T, Gennisson JL, Fink M, Neuenschwander S. Breast lesions: quantitative elastography with supersonic shear imaging--preliminary results. Radiology. 2010 Jul;256(1):297-303.

Personal Information

Transrectal Shear Wave Elastography of the Prostate: Initial Results and Potential Implications

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Background

Prostate cancer is the second-leading cause of cancer mortality in men in the United States. Current diagnosis relies on digital rectal exam (DRE), prostate specific antigen level (PSA), transrectal ultrasound (TRUS), and magnetic resonance imaging (MRI). These techniques have limitations, and PSA levels have a low positive predictive value for cancer. Shear wave elastography (SWE) has the potential to address these limitations and add to the current diagnostic workup [1, 2].

Aims

To determine if SWE of the prostate can lead to higher sensitivity and specificity in detecting cancer; To determine if SWE can increase the negative predictive value for prostate cancer screening and better direct image-guided biopsy.

Methods

Patients scheduled for TRUS biopsy with an elevated PSA and/or abnormal DRE were asked to participate in the IRB approved study. TRUS was performed with B-mode and color Doppler imaging. Nodules and other suspicious areas were noted by the radiologist. SWE was then performed using a SE12-3 probe on a SuperSonic Imagine (SSI) system. Afterwards, the urologist performed a DRE, scanned with B-mode ultrasound, and performed sextant biopsy based on standard clinical practice without knowledge of the SWE findings. Any abnormalities on B-mode alone were also biopsied per standard protocol. If abnormalities on SSI were not included in the original biopsy, additional samples of these areas were obtained after the completion of standard biopsy. The prostate was divided into sextants for analysis. SWE was deemed positive if the area was greater than 35 kPa, negative if less than 20 kPa, and borderline if 20-35 kPa. B-mode nodules were documented and correlated with SWE values. SWE and biopsy results were compared for each sextant. Biopsies were staged based on the Gleason score (scale of 2-10).

Results

A total of 32 patients participated in the study, providing 192 sextants. Average patient age was 64.2 years (range 53-79). Average PSA was 5.05 (range 0.21-18.6). A total of 14 foci of cancer were detected in 7 of the 32 patients (22%). 173/178 sextants were true negatives. 14/14 sextants were true positives. There were 5 false positives and 0 false negatives. This produced a sensitivity of 100%, specificity of 97%, positive predictive value of 74%, and negative predictive value of 100%.

Conclusions

Transrectal shear wave elastography of the prostate has the potential to become the primary imaging modality for detection of prostate cancer. With a high negative predictive value, this technique could eliminate a significant number of biopsies.

References

1 Bercoff J. "ShearWave Elastography." Supersonic Imagine White Paper. October 2008.
2 Correas JM, Khairoune A, Tissier AM, et al. "Trans-rectal quantitative shear wave elastography: application to prostate cancer – a feasibility study." Proceedings of the European Congress of Radiology, 2011.

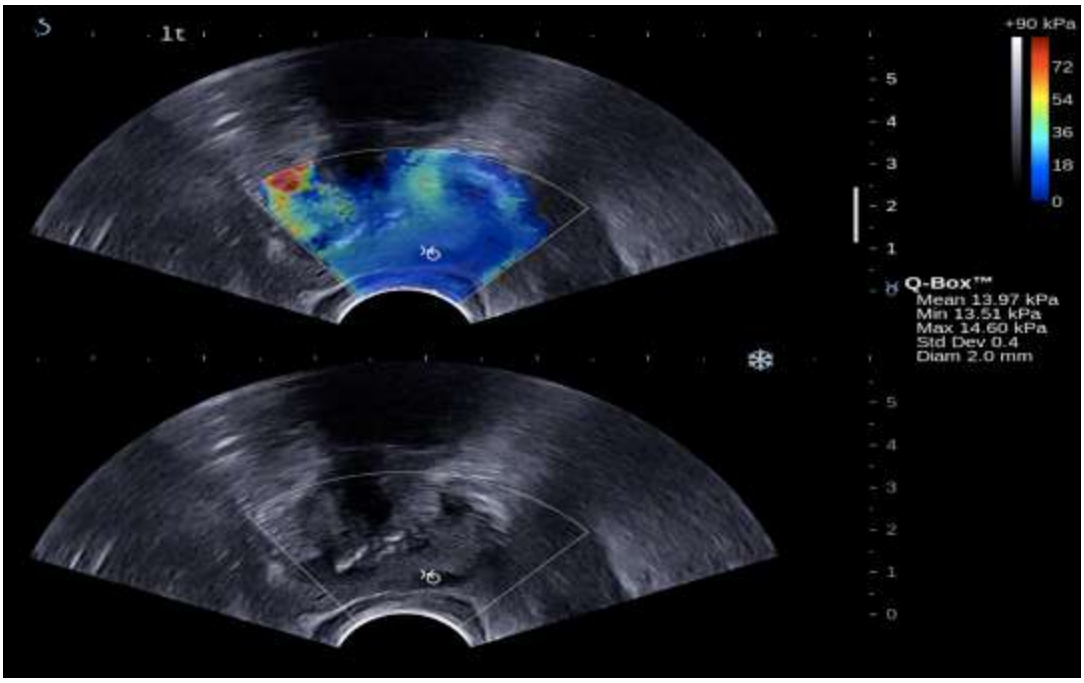

Figure 1. Benign prostate nodule

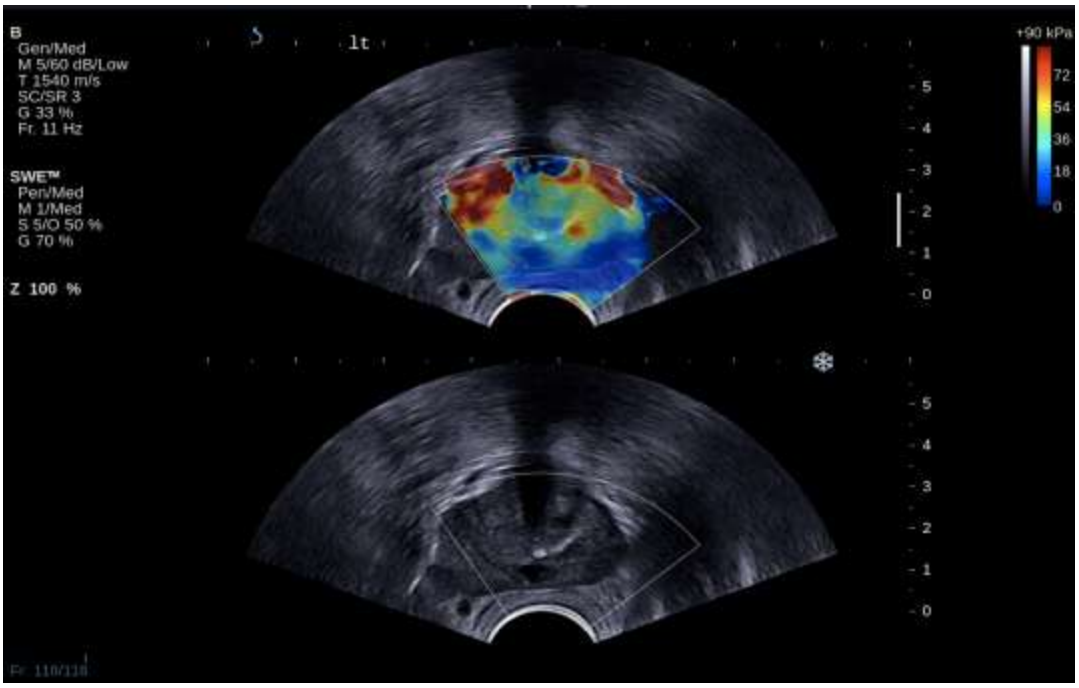

Figure 2. Adenocarcinoma (Gleason 6)

Quantitative Shear Wave Elastrography for Prostate Lesion Evaluation

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Purpose

The goal of this study was to evaluate Shear Wave Elastography (SWE) for prostate nodule evaluation.

Material & Methods

23 patients with increased PSA values were prospectively enrolled. The prostate was studied using transrectal ultrasound (TRUS) with colour Doppler US (CDUS), Contrast-enhanced US (CEUS), SWE and MRI. SWE measurements and ratios between nodules and adjacent parenchyma were calculated. Imaging findings were correlated to sextant prostate biopsies (n=12) and targeted biopsies on suspicious areas (n=2-6).

Results

10 patients exhibited significant prostate adenocarcinomas. Prostate cancer nodules exhibited higher stiffness (mean 55±45 kPa) than the adjacent peripheral gland (mean 18±9 kPa). The stiffness ratio between nodule and adjacent parenchyma was significantly higher for cancer (3.0±1.0) compared with benign nodules (1.0±0.20; $p< 0.01$). The ratio cutoff value of 1.5 allowed the best discrimination of the two populations. The Sensitivity (Se), Specificity (Spe), Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were calculated for each modality: CDUS, CEUS, SWE ratio (with 1.5 cutoff) and MRI. CDUS: Se= 50%; Spe= 76%; PPV= 50%; NPV= 76%. CEUS: Se= 67%; Spe= 81%; PPV= 67%; NPV= 81%. SWE ratio: Se= 90%; Spe= 100%; PPV= 100%; NPV= 94%. MRI: Se= 63%; Spe= 75%; PPV= 56%; NPV= 80%.

Conclusion

TRUS SWE has large potentials for the characterization of prostate cancer. These first results have to be confirmed by a larger-scale clinical investigation.

Role of Shear Wave Elastography (SWE) in Detection and Characterization of Focal Lesions of the Prostate

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[1]Kifissia, Greece, [2]Tirana, Albania

Purpose

To access the role of Shear wave Elastography (SWE) in the detection and characterization of focal lesions of the prostate.

Material & Methods

We prospectively examined 80 consecutive patients in a 6-month period with TRUS, SWE and TRUS-guided biopsies. The median patient age was 59 years (range 45-88 years), the median serum PSA level was 8,5 ng/ml (range 1,9-47 ng/ml) and the median prostate volume was 55 ml (range 25-180 ml). All examinations were performed on an Aixplorer/Supersonic system with an end-fire transrectal probe (SE 12-3).

Results

Prostate cancer (PRCA) was found in 32/80 patients (40%). A total number of 36 PRCAs were proved by TRUS-guided biopsies. The SWE findings were positive in 27 (75%) of PRCAs. In particular, 5 (18,5%) PRCAs were positive only on SWE, including 2 peripheral zone (PZ) and 3 transitional zone (TZ) lesions. The SWE findings were negative in 9 (25%) lesions, all in the PZ. SWE findings in these cases showed disagreement with tumor location or undetectable lesion. 7 of these lesions were judged as positive on TRUS.

Conclusion

SWE in conjunction with TRUS shows promising results in the detection of PRCA. Meticulous technique and strict protocol are necessary. SWE helps guiding needle biopsy and proving PRCA in atypical lesions in the PZ and the TZ.

Transrectal Ultrasound Quantitative Shear Wave Elastrography : Application to Prostate Nodule Characterization – A Feasibility Study

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Necker University Hospital, Paris, France

Purpose

The purpose of this study was to evaluate the feasibility of real time TransRectal UltraSound (TRUS) quantitative Shear Wave Elastography (SWE) imaging for prostate lesion characterization.

Method and Materials

31 patients presenting increased PSA values (4-10 ng/mL) were prospectively enrolled after signing an informed consent form. The prostate was studied using trans-rectal ultrasound (TRUS) with spatial compounded B-mode, Color Doppler UltraSound (CDUS), and SWE with an Aixplorer ultrasound system (Supersonic Imagine, Aix-en-Provence, France). Elasticity measurements in KiloPascal and ratios between nodules and adjacent parenchyma were calculated. Contrast-Enhanced US (CEUS) was performed using low MI pulse subtraction after injection of 4.8 ml of SonoVue® (Bracco, Milan, Italy). Imaging findings were correlated to sextant prostate biopsies (n=12) and targeted biopsies on suspicious areas (n=2-6) detected at SWE and CEUS. MRI with axial and coronal T2w acquisition, axial T1w acquisition, diffusion and dynamic contrast-enhanced MRI was also evaluated.

Results

Among the 39 nodules detected either at ultrasound imaging or at pathology, 14 were adenocarcinomas with Gleason score above 6 and 25 were adenomatous hyperplasia or focal prostatitis. Prostate cancer nodules exhibited higher stiffness (mean 58±48 kPa) than the adjacent peripheral gland (mean 20±10 kPa). The stiffness ratio between nodule and adjacent parenchyma was significantly higher for cancer (3.0±1.0) compared to benign nodules (1.0±0.20; $p < 0.01$). The ratio cutoff value of 1.5 allowed the best discrimination of the two populations. The Sensitivity (Se), Specificity (Spe), Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were calculated for each modality: CDUS, CEUS, SWE ratio (with 1.5 cutoff) and MRI. CDUS: Se= 55%; Spe= 76%; PPV= 55%; NPV= 76%. CEUS: Se= 70%; Spe= 80%; PPV= 70%; NPV= 80%. SWE ratio: Se= 85%; Spe= 90%; PPV= 85%; NPV= 90%. MRI: Se= 73%; Spe= 75%; PPV= 56%; NPV= 82%.

Conclusions

TRUS SWE has large potentials for the characterization of prostate nodules. These preliminary results must be confirmed by a multi centric clinical trial.

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Quantitative Shear Wave Elastography of the prostate: correlation to sextant and targeted biopsies

Poster No.: C-2349

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Type: Scientific Exhibit

Authors: J.-M. Correas[1], V. Vassiliu[2], A.-M. Tissier[2], A. KHAIROUNE[3], A. Méjean[2], O. Hélénon[4]; [1]Paris Cedex 15/FR, [2]Paris/FR, [3]Paris, Cedex 15/FR, [4]Paris, Cédex 15/FR

Keywords: Oncology, Ultrasound, Elastography, Biopsy, Tissue characterisation

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Purpose

Over the past two decades, prostate cancer diagnosis has become more common as a result of the aging population and the widespread use of screening tests. While prostate cancer specific mortality has declined over the past 4 years, prostate cancer is the second leading cause of cancer-related deaths in men. In addition, prostate cancer is the most commonly diagnosed malignancy in men with an estimated 790,000 cases in theUSAin 2010 and 217,730 new cases diagnosed every year in theUSA.

For over 30 years, the screening standard for prostate abnormalities has been the combination of digital rectal examination and the prostate specific antigen (PSA) test. An abnormal or rising serum PSA level, or an abnormal digital rectal examination, triggers further evaluation, typically with transrectal ultrasound TRUS-guided sextant biopsies. Prostate biopsy findings are also widely used to estimate the tumor volume (number of positive samples and length of tumor invasion) and aggressiveness (Gleason score).

These approaches have some limitations. First, using PSA as a screening tool leads to a substantial number of unnecessary biopsies in patients with no cancer or with indolent cancer that do not need immediate treatment. Currently, over-detection rates are estimated to be between 27% and 56% [1]. Second, a negative set of biopsies does not rule out the presence of cancer. Among the patients with negative 10- to 12-core biopsy schemes, 17-21.2% has cancer at repeated biopsy [2, 3]. Hence, a dilemma faces many urologists with patients with persistent abnormal PSA level and negative biopsies: when to repeat biopsy and when to stop biopsying [4]? Third, although PSA level and biopsy findings correlate positively with clinical stage, tumor volume and histologic grade, they are of limited value in predicting tumor burden and aggressiveness in individual patients [1]. To overcome these difficulties, it is possible to further increase the number of samples in order to improve prostate volume sampling. This approach can rule out prostate cancer and offers a better estimation of the tumor volume and Gleason score [5]. However, it is associated with increased cost and morbidity, as well as over diagnosing microscopic tumor foci that do not require treatment [6, 7].

Multi-parametric MRI (MP-MRI), combining T2-weighted imaging and functional sequences) has become a major modality for tumor detection/ localization [8-12], particularly in candidates to radical prostatectomy, with areas under the ROC curve > 0.9 [13, 14]. Interesting results have also been reported in more challenging populations such as patients with negative biopsy and elevated PSA levels [15]. However, MRI performance varies depending on which combination of positive features is selected for cancer diagnosis [16]. This further increases the inter-observer variability in interpreting multi-modality MRI, particularly for small lesions of limited Gleason score (# 6). MRI is also an expensive imaging technique with limited access and does not allow direct biopsy guidance. Other limiting factors include severe claustrophobia, a Pace-Maker, contra-indication to Gadolinium chelates …

The detection of prostate cancer using TRUS B-mode imaging is not significantly improved by the use of Color/Power Doppler, and its sensitivity and specificity remain low in between 40 to 50% [17]. Contrast-Enhanced Ultrasound (CEUS) is under evaluation and can sensitize prostate biopsy [18, 19]. However, the contrast ratio between cancer and normal peripheral zone is highly transient (a few seconds). TRUS identification of stiffness prostate tissue is another approach in order to improve conventional ultrasonography, as it is well known that prostate cancer is stiffer than normal prostate tissue.

The purpose of our study was to evaluate the performance of real time TRUS quantitative Shear Wave Elastography (SWE) for prostate lesion detection and characterization in correlation to pathology provided by systematic sextant and targeted biopsies.

Methods and Materials

69 patients presenting increased PSA values (4-15 ng/mL, 9.3±7.7) were prospectively enrolled after signing an informed consent form. The prostate was studied using trans-rectal ultrasound with spatial compounded B-mode, Color Doppler UltraSound (CDUS), and SWE with an Aixplorer ultrasound system (Supersonic Imagine,Aix-en-Provence,France). The prostate was entirely scanned from base to apex in SWE mode for the detection of stiff areas. Twelve elasticity measurements were taken at the level of systematic biopsy sites (in kPa). Additional elasticity measurements were performed for each nodule detected by either B-mode or SWE. Ratios between nodules and adjacent parenchyma were systematically calculated. SWE measurements were correlated to systematic posterior sextant biopsies (n=12) and targeted biopsies (n=2-7). A total of 737 median and paramedian sextant biopsies (with 133 positive cores) and 195 targeted biopsies (with 89 positive cores) on 75 nodules were performed.

SWE is using radiation force and shear wave propagation, and does not require manual compression, leading to a better reproducibility. It is a two-dimensional, real time, and quantitative trans-rectal imaging technique that provides elasticity maps of prostate tissues [20].

The trans-rectal transducer produces a localized radiation force deep in the tissue. This radiation force or push induces a shear wave, which then propagates from this focal point (Fig. 1). Several focal points are then generated almost simultaneously, in a line perpendicular to the surface of the patient's rectal wall (Fig. 2). This force creates a conical shear wave front, which sweeps the image plane, on both sides of the focal point. The progression of the shear wave is captured by the very rapid acquisition of ultrasound images (about 5000 images per second), called UltraFast Imaging (Fig. 3 and 4). The

acquisition takes only a few milliseconds, which is why this technique is not affected by patient or operator movement. UltraFast Imaging is necessary to capture the shear wave as it moves at a speed in the order of 1-10 m/s. A comparison of two consecutive ultrasound scans allows the measurement of displacements induced by the shear wave, and creation of a "movie" showing the propagation of the shear wave (Fig. 5). The shear ware propagation velocity is then calculated and the elasticity of the medium displayed in kilo Pascals (or m/sec) in a two-dimensional map, together with an anatomical B-mode image reference (Fig. 6).

Images for this section:

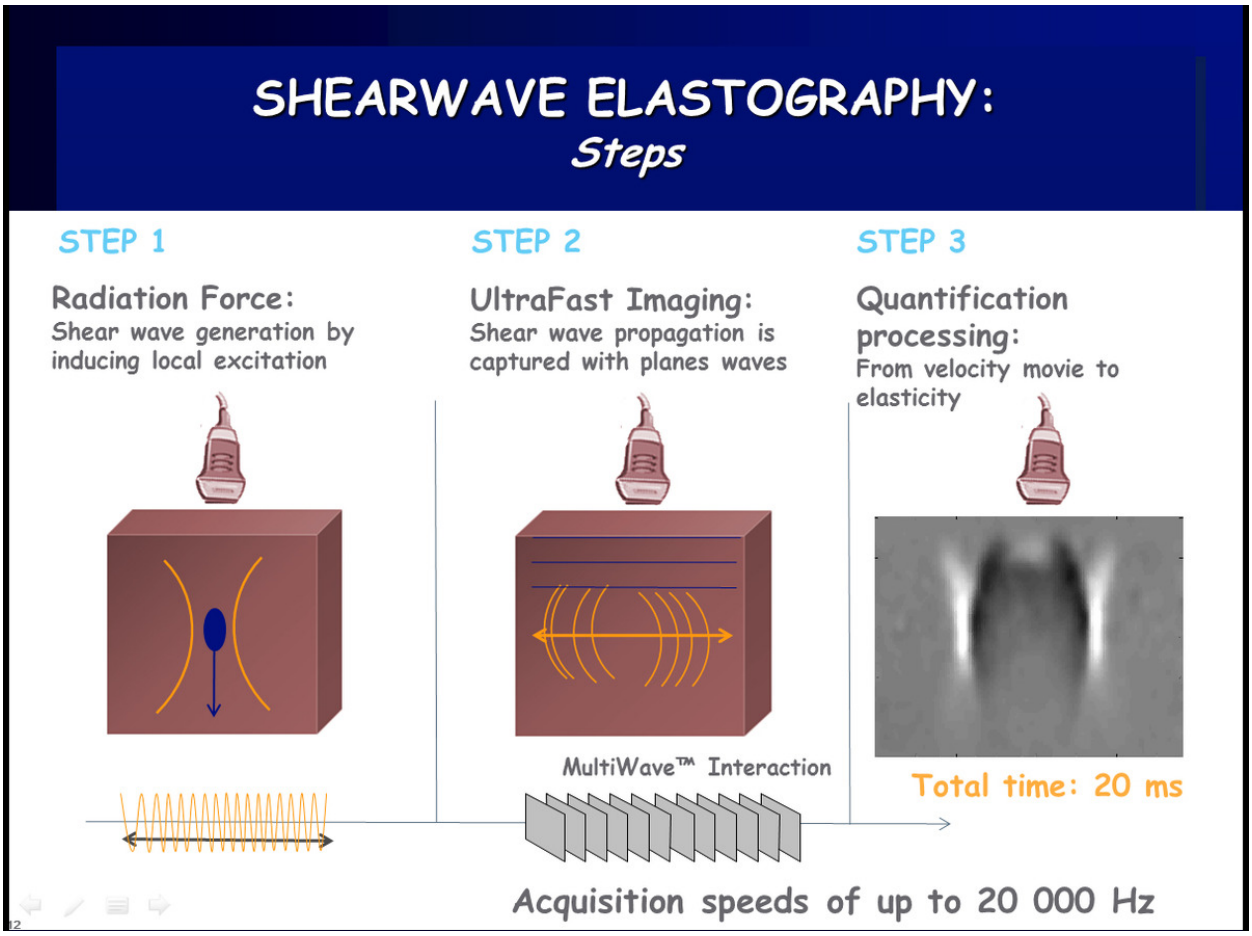

Fig. 1: SWE steps to measure tissue elasticity.

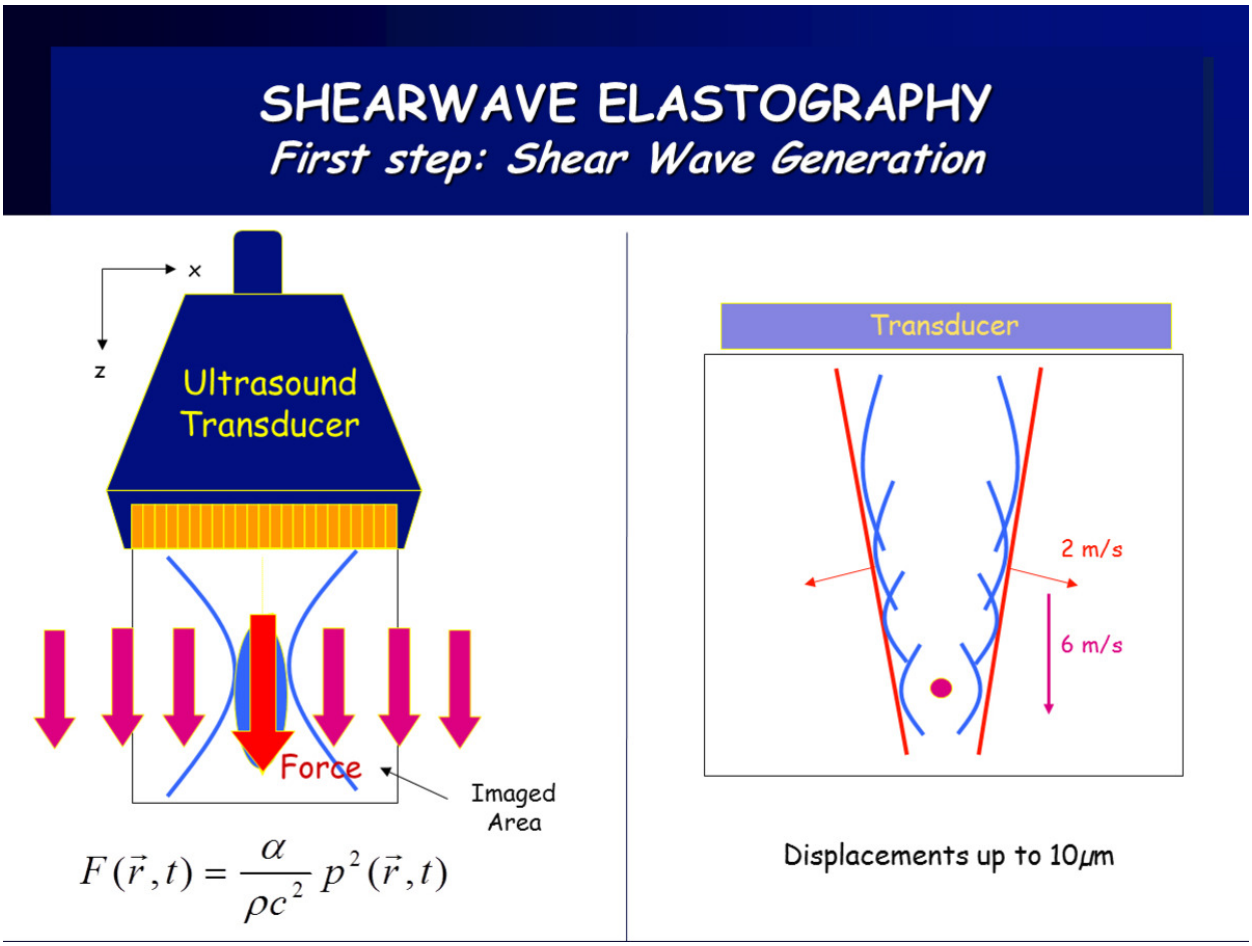

Fig. 2: Several focal points are generated almost simultaneously, in a line perpendicular to the surface of the patient's rectal wall to create a shear wave front.

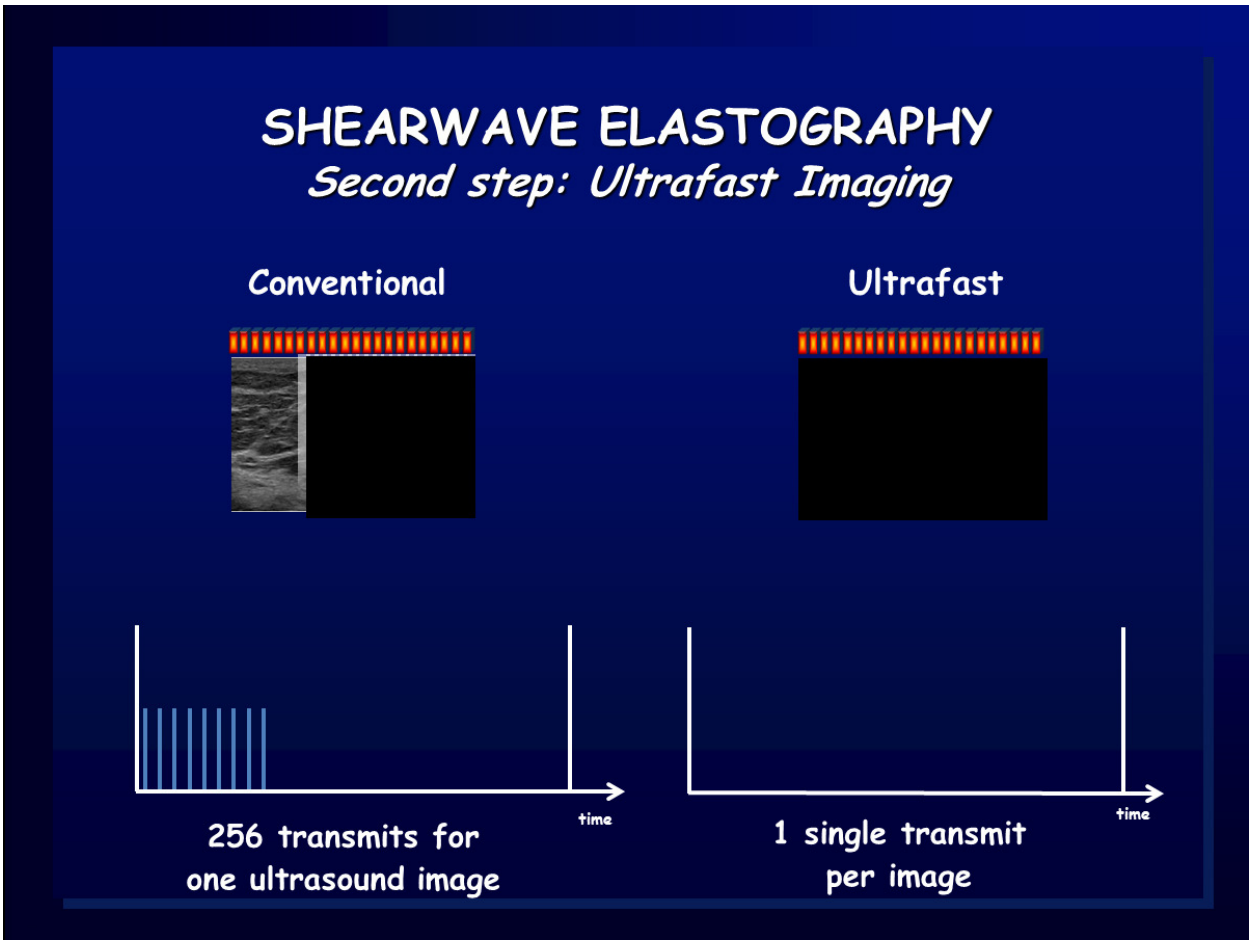

Fig. 3: Conventional Imaging (left) versus Ultrafast Imaging (right): beginning of the conventional B-mode acquisition. Conventional Imaging acquires images line by line.

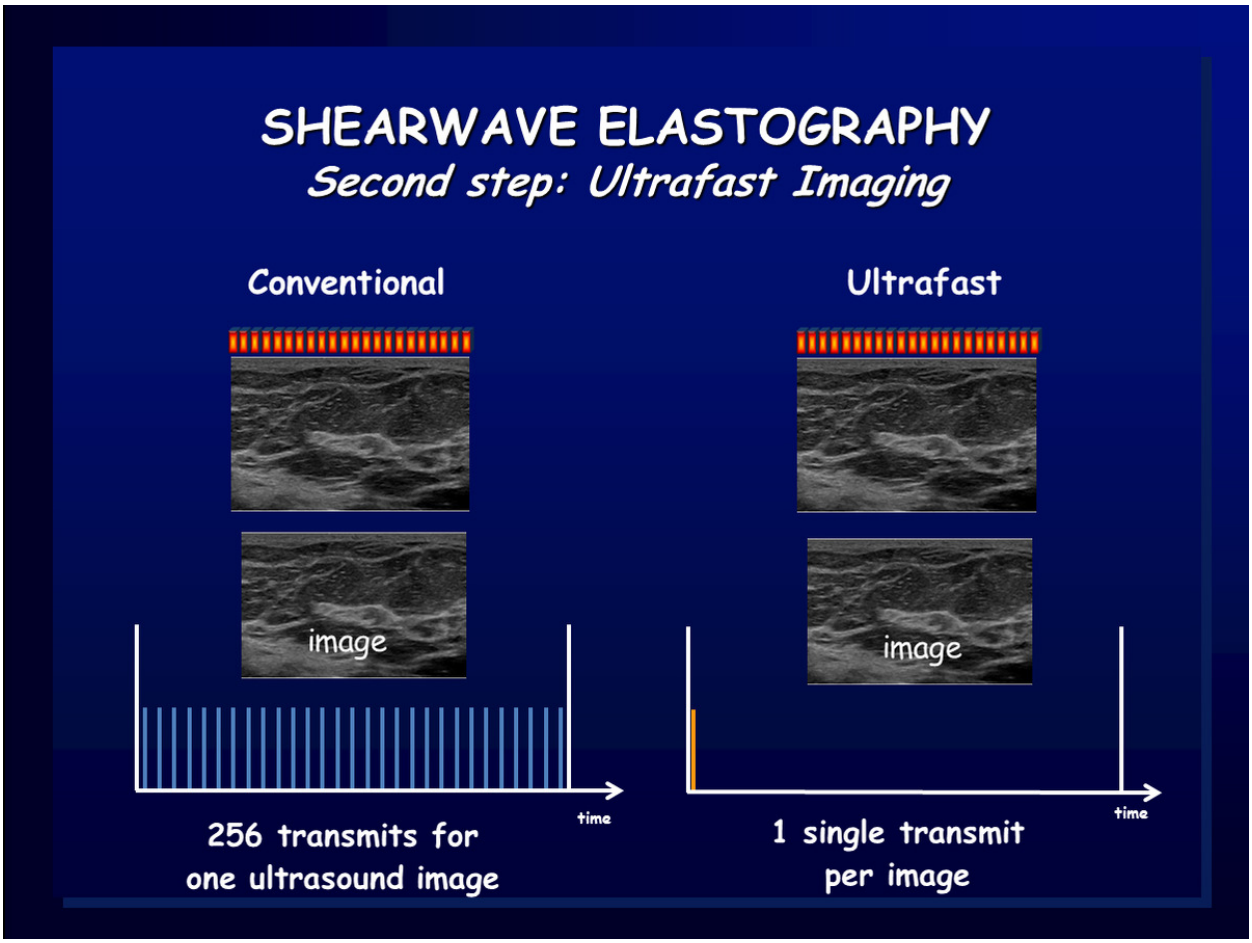

Fig. 4: Conventional Imaging (left) versus Ultrafast Imaging (right): while conventional B-mode acquisition is performed line by line, UltraFast Imaging acquires the whole image in one shot.

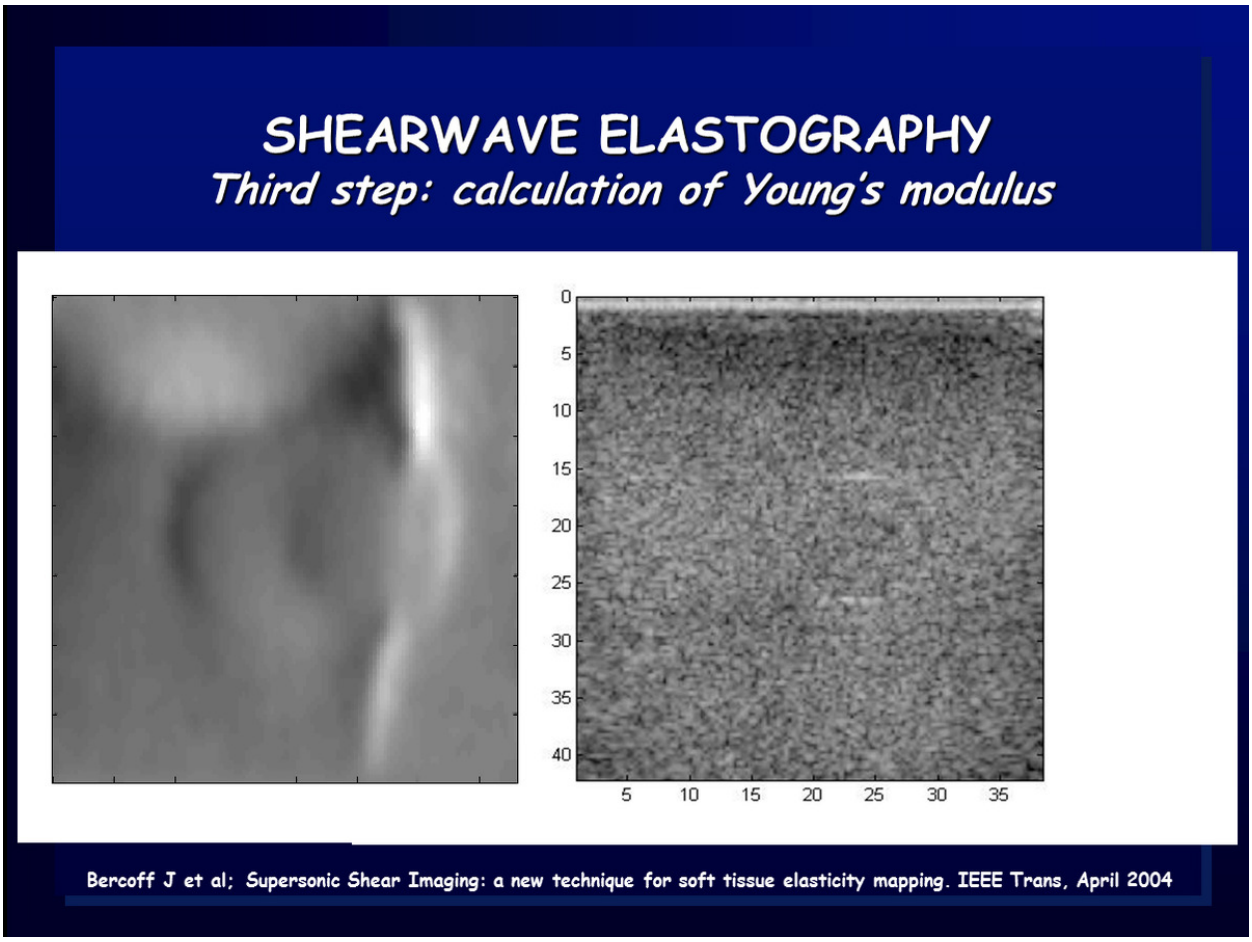

Fig. 5: Shear Wave propagating in an homogeneous medium with a hard inclusion. The Shear wave travels faster in the hard inclusion. The shear wave propagates in a few milliseconds in the medium and is captured thanks to UltraFast Imaging.

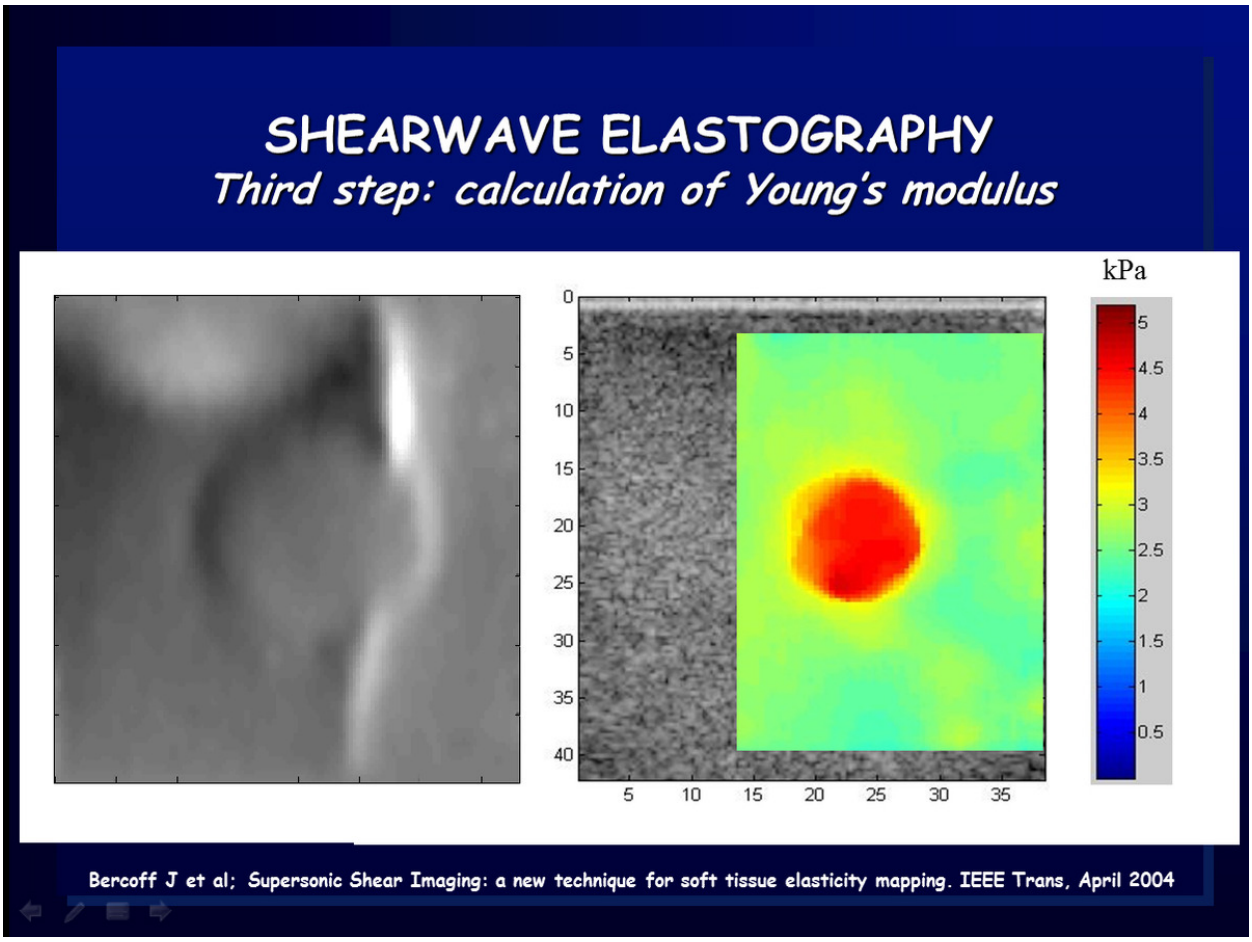

Fig. 6: The shear ware propagation speed is then estimated from this movie and the elasticity of the medium is then displayed in kiloPascals in a two-dimensional map, together with an anatomic reference gray scale image.

Results

Significant prostate cancers were detected in 34 patients (core size # 2 mm, Gleason score # 6).

Among the 75 nodules, 35 corresponded to adenocarcinomas while 40 were adenomyomatous hyperplasia or focal prostatitis.

Prostate cancer nodules exhibited higher stiffness (mean 51±45 kPa) than the adjacent peripheral gland (mean 22±11 kPa) (Fig. 7).

The stiffness ratio between nodule and adjacent parenchyma was significantly higher for cancer (4.0±1.9) compared to benign nodules (1.5±0.9; $p < 0.002$), (Fig. 8).

The cut-off values for highest NPV were for stiffness values, 35kPa and for elasticity ratio, 1.5. SWE performance; Sensitivity (Se), Specificity (Spe), Positive Predictive Value (PPV), Negative Predictive Value (NPV), Accuracy (Acc) and ROC Area Under the Curve (ROC AUC), were calculated for both the SWE values and SWE ratios with these ratios maximizing the NPV. Table 1 summarizes the results.

	Se	**Spe**	**PPV**	**NPV**	**Accuracy**	**ROC AUC**
SWE values (cut-off : 35KPa)	63%	91%	91%	91%	86%	0.77
SWE ratio (cut-off: 1.5)	97%	70%	70%	97%	83%	0.93

Table 1: SWE Values and Ratios Sensitivity (Se), Specificity (Spe), Positive Predictive Value (PPV), Negative Predictive Value (NPV), Accuracy (Acc) and ROC Area Under the Curve (ROC AUC)

The ROC curves are also displayed in Fig. 9 and 10 for SWE Values and Ratios.

The following cases illustrate SWE potentials for prostate cancer detection and characterization (Fig. 11-15).

Figure 11 shows normal prostate tissue. The elasticity is color-coded using a scale ranging from blue (softest tissue) to red (hardest tissue). In patients presenting with no abnormalities, the peripheral zone had normal values of elasticity ranging from 10 to 30 kPa, while the transitional zone exhibited heterogeneous encoding with very stiff values over >30kPa.

Figure 12 is an example of a false negative case at SWE. A nodule was detected in the peripheral zone at both conventional B-mode (hypoechoic) and color Doppler US (moderately vascular). Elasticity in the lesion was around 20 kPa, comparable to the value found in the surrounding normal peripheral zone (SWE Ratio = 1). The nodule was biopsied and pathology confirmed the presence of an adenocarcinoma with a Gleason score of 7.

Figure 13 shows the case of a patient with an hypoechoic nodule developed at prostate base within the anterior peripheral zone. It exhibited a strongly elevated stiffness with values over 100KPa, compared to an average value of 15kPa for the adjacent normal prostate peripheral parenchyma. The nodule was biopsied and pathology confirmed the presence of a Gleason 7 adenocarcinoma.

Figure 14 gives an example of a benign nodule in the peripheral zone corresponding to focal chronic prostatitis. Both stiffness nodule and normal surrounding peripheral zone tissue are soft (values < 15 kPa, ratio = 0.70).

Figure 15 shows the case of a nodule located in the paramedian peripheral zone only detected using SWE. It exhibited an elevated stiffness (52 kPa), compared to the adjacent normal peripheral gland (14 kPa). The stiffness ratio was also strongly increased (>4). The targeted biopsies confirmed the presence of a Gleason 7 adenocarcinoma.

Images for this section:

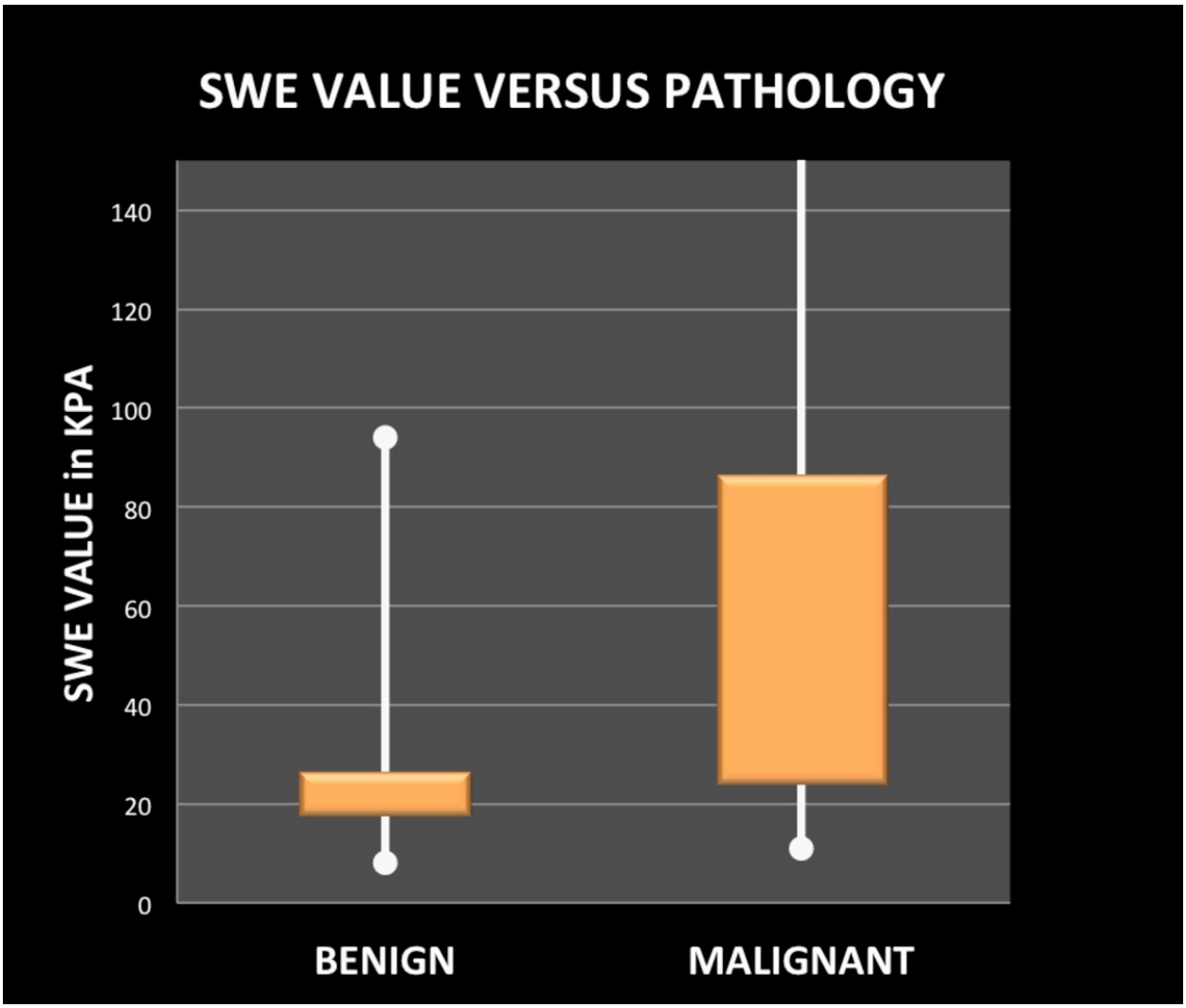

Fig. 7: Box plot of SWE Values versus pathology (from biopsy cores)

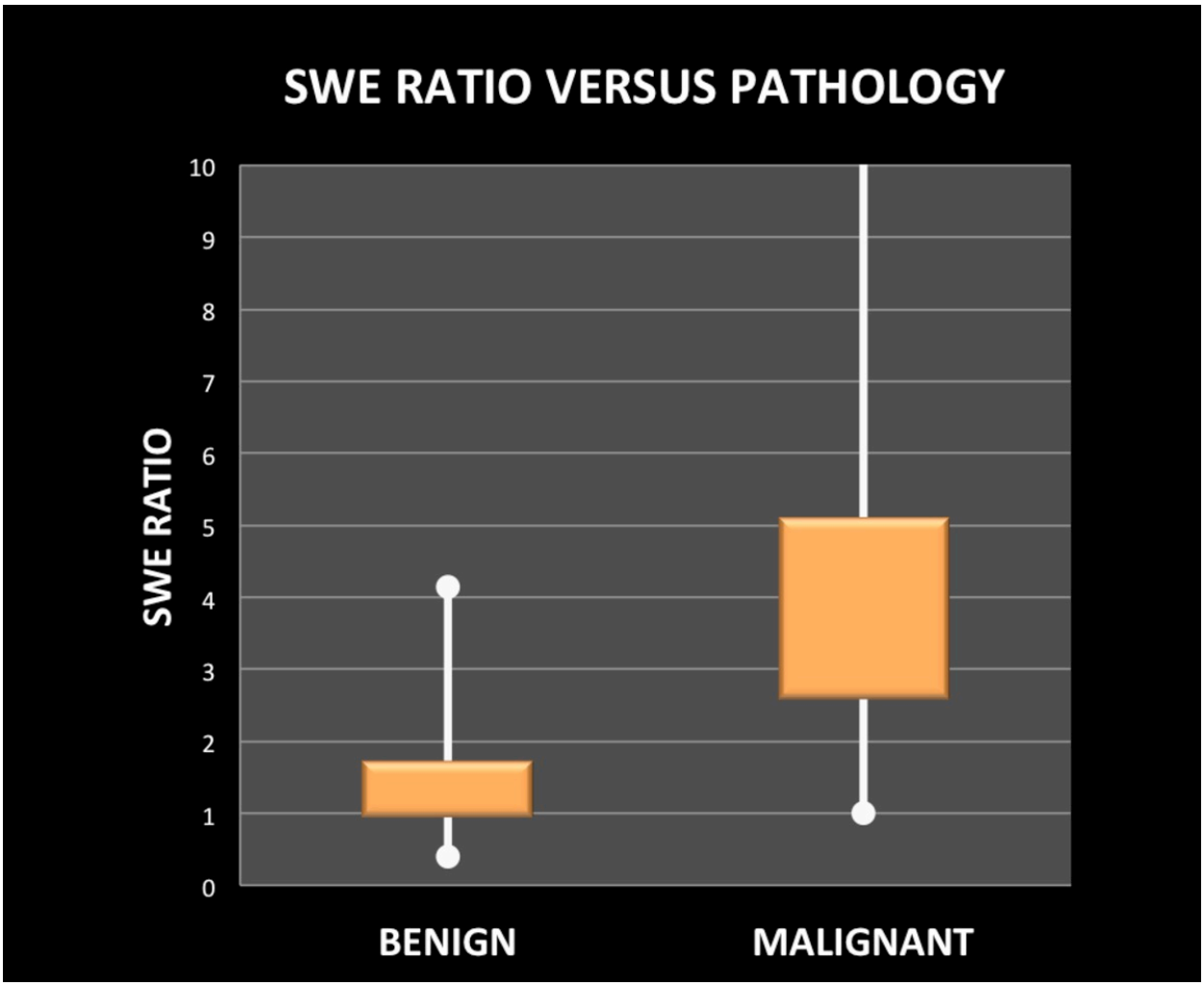

Fig. 8: Box plot of SWE Ratios versus pathology (from biopsy cores)

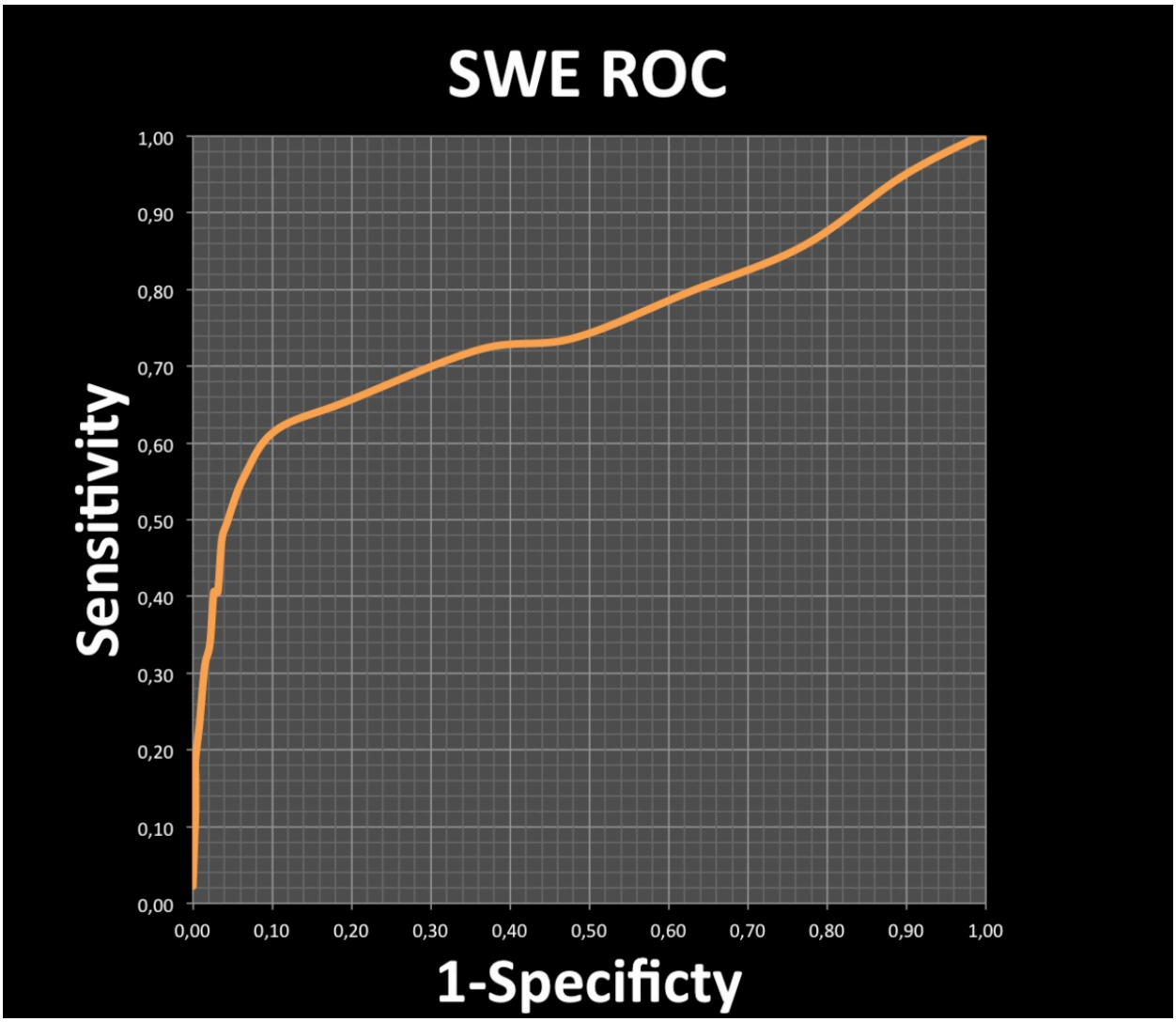

Fig. 9: ROC curve for SWE Values (AUC = 0.77)

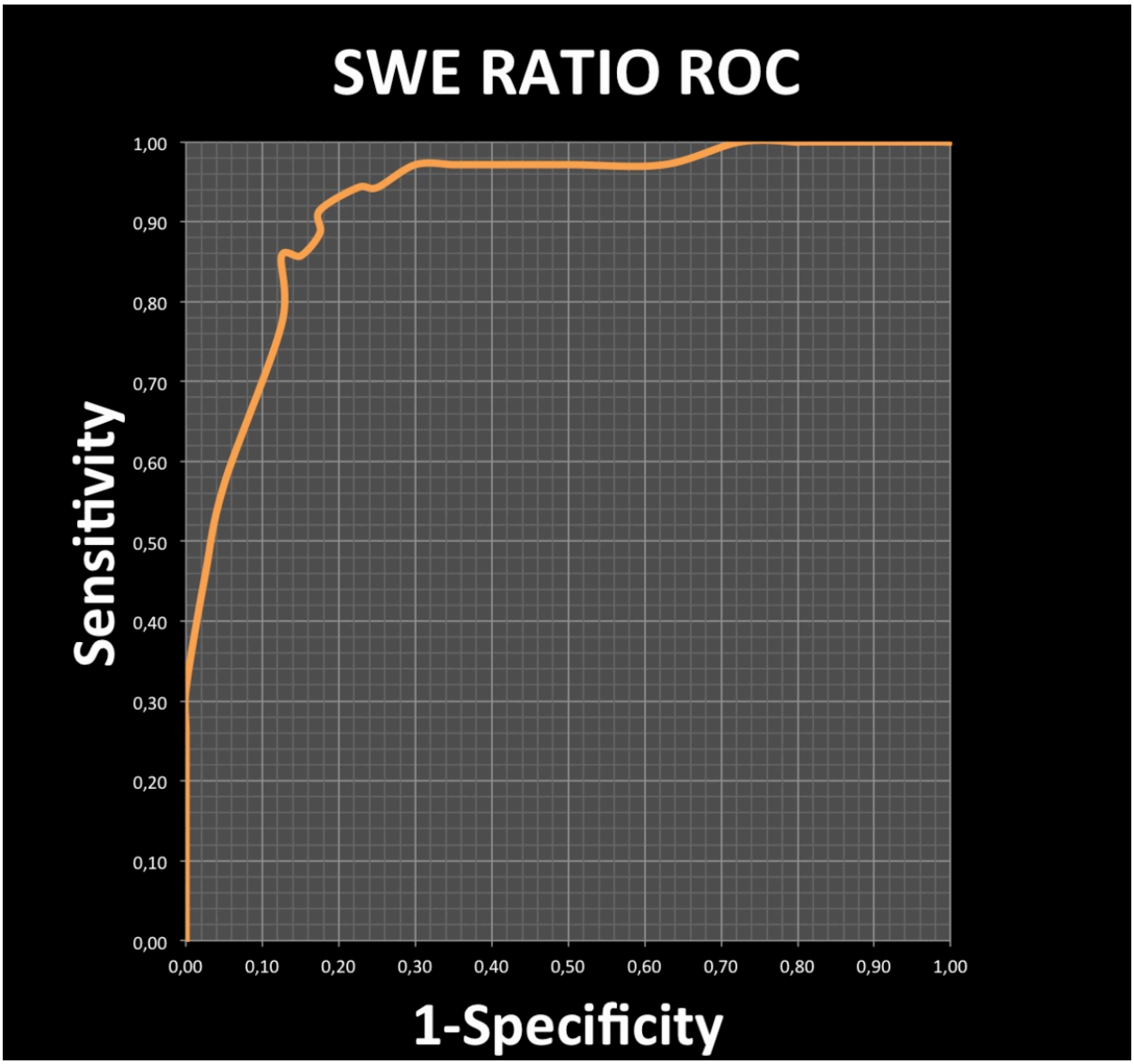

Fig. 10: ROC curve for SWE Ratios (AUC = 0.93)

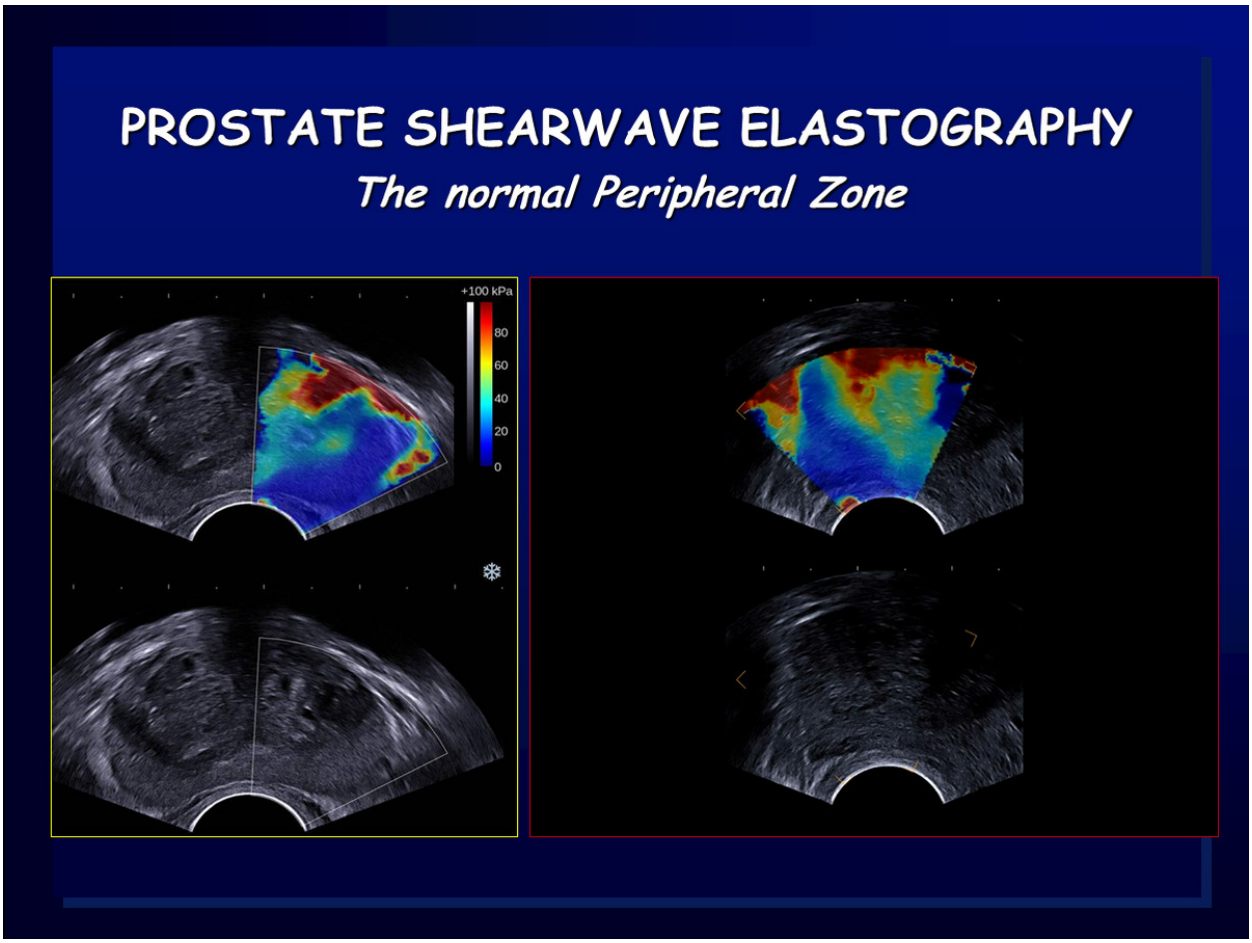

Fig. 11: SWE image of mid section of the prostate, transverse view. The elasticity is color-coded using a scale ranging from blue (softest tissue) to red (hardest tissue). In patients presenting with no abnormalities, the peripheral zone had normal values of elasticity ranging from 10 to 30 kPa, while the transitional zone exhibited heterogeneous encoding with very stiff values over >30kPa.

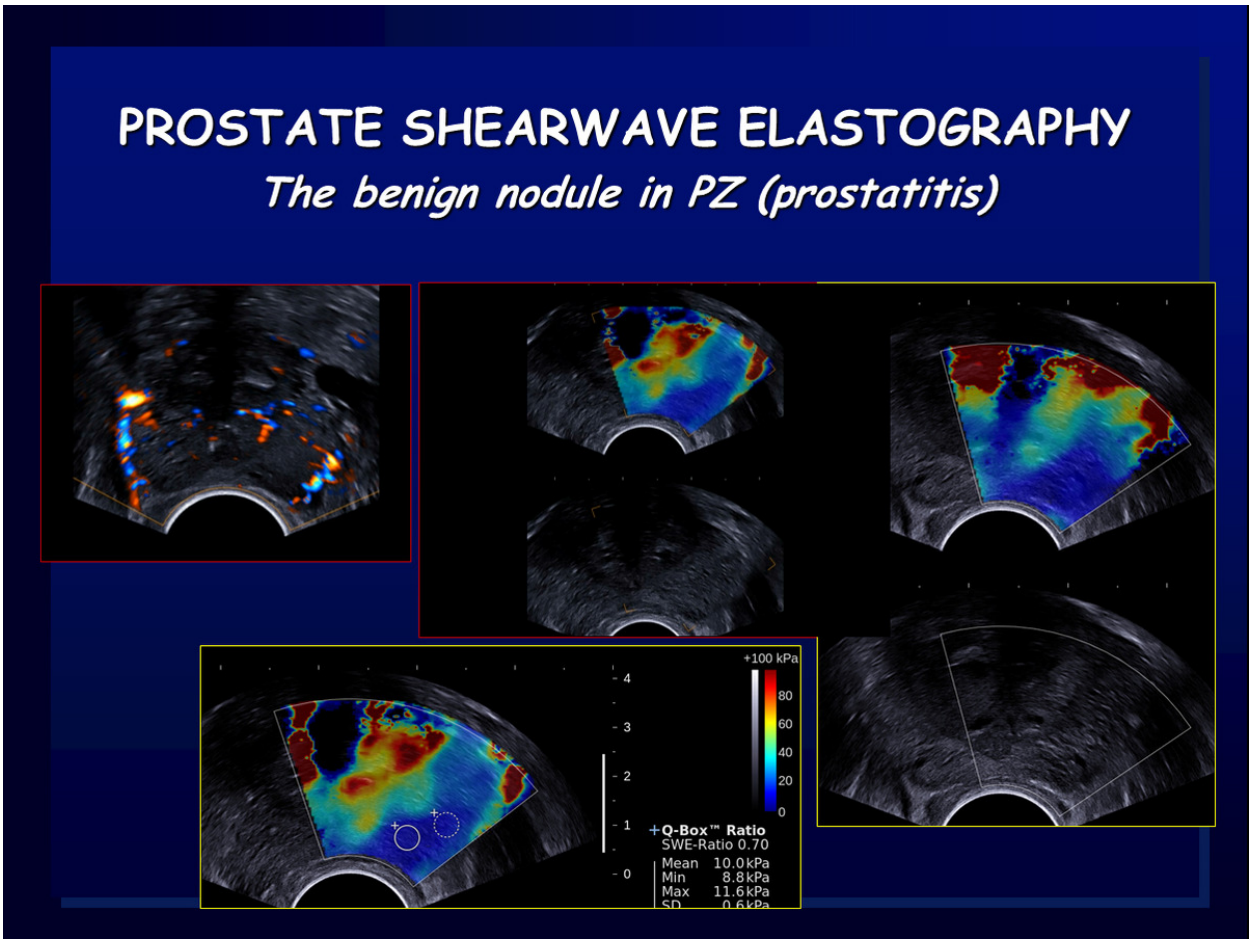

Fig. 12: Example of a false negative case using SWE. A nodule was detected in the peripheral zone at both conventional B-mode (hypoechoic) and color Doppler US (moderately vascular). Elasticity in the lesion was around 20 kPa, comparable to the value found in the surrounding normal peripheral zone (SWE Ratio = 1). The nodule was biopsied and pathology confirmed the presence of an adenocarcinoma with a Gleason score of 7.

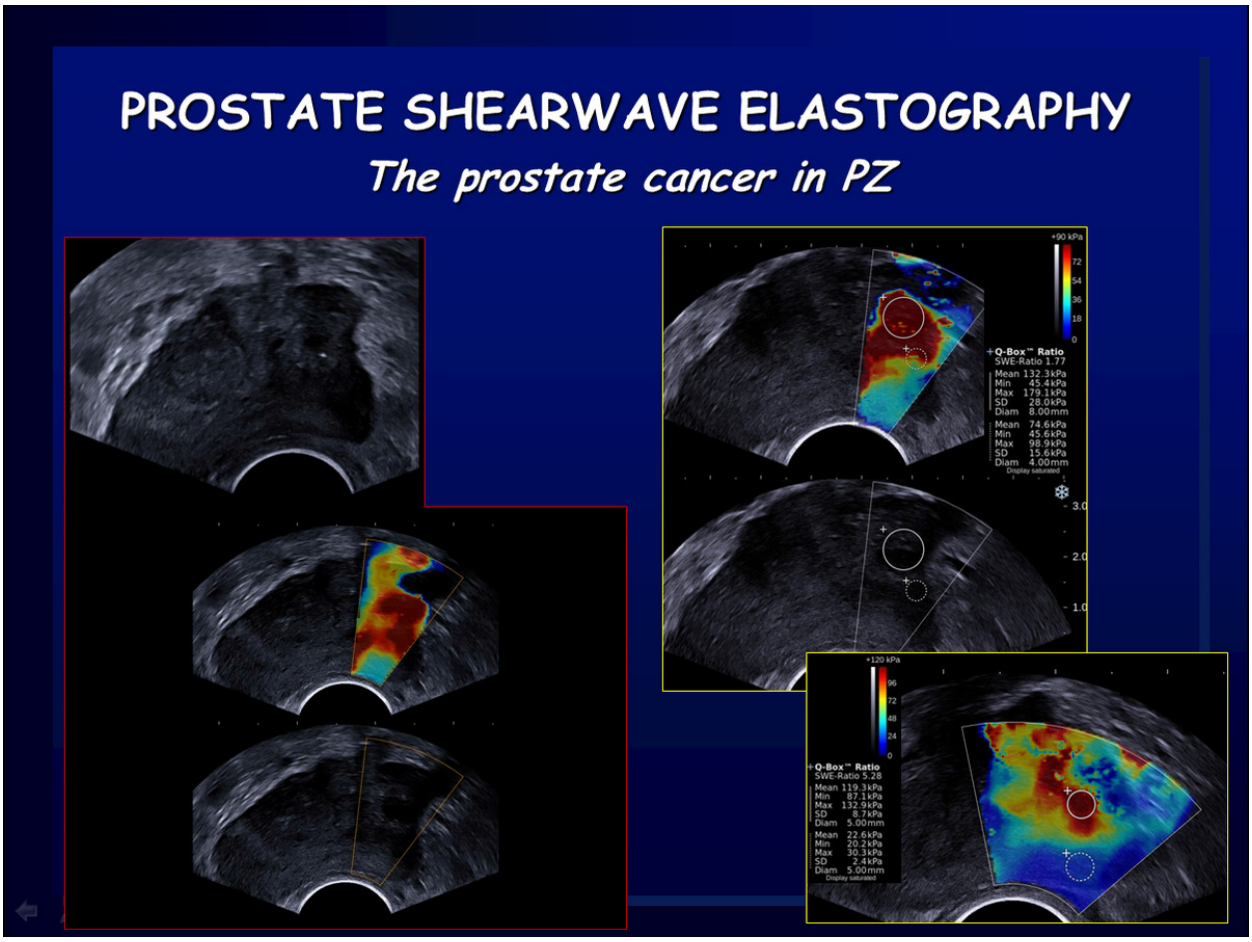

Fig. 13: Patient with an hypoechoic nodule developed at prostate base within the anterior peripheral zone. It exhibited a strongly elevated stiffness with values over 100KPa, compared to an average value of 15kPa for the adjacent normal prostate peripheral parenchyma. The nodule was biopsied and pathology confirmed the presence of a Gleason 7 adenocarcinoma.

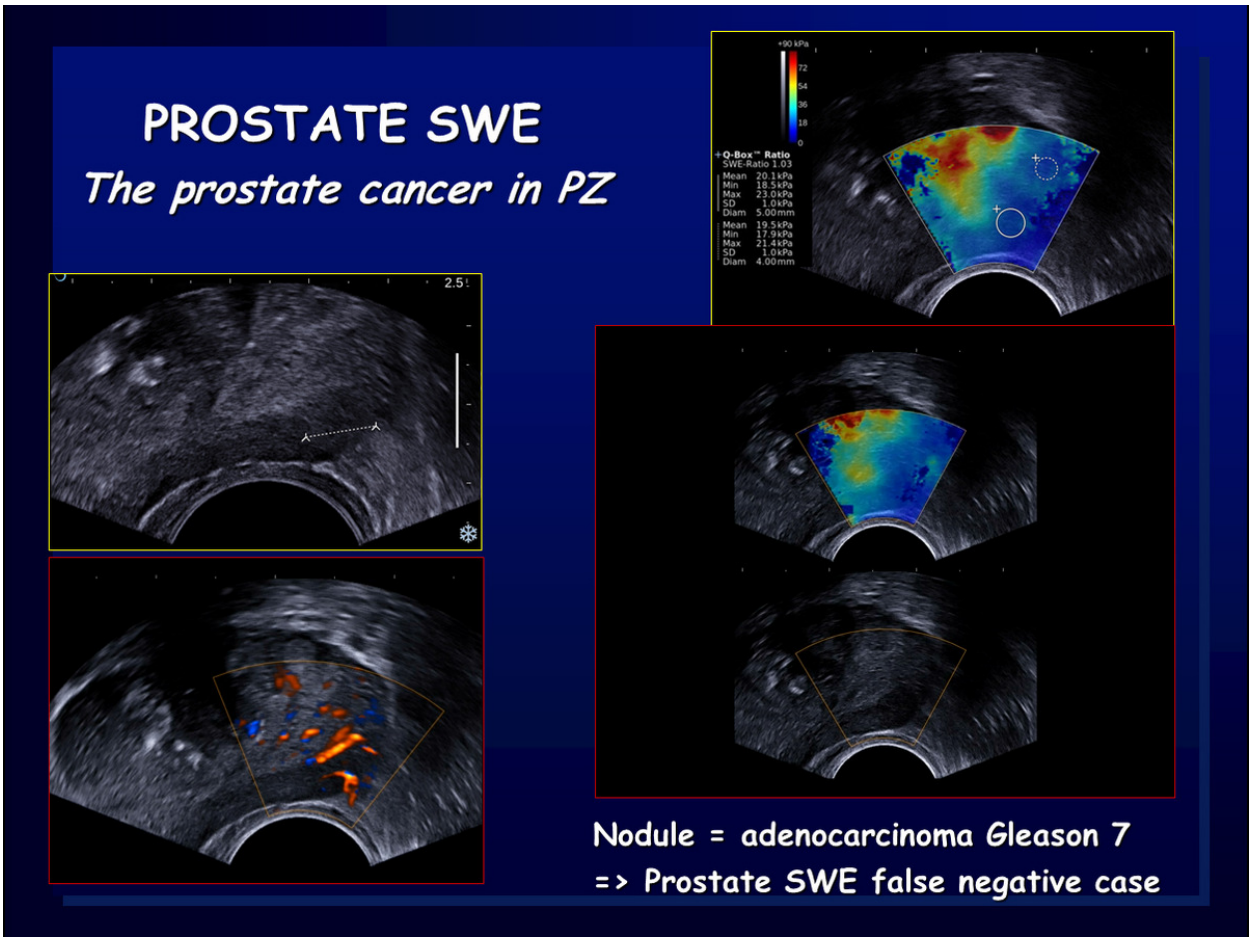

Fig. 14: Benign nodule in the peripheral zone corresponding to focal chronic prostatitis. Both stiffness nodule and normal surrounding peripheral zone tissue are soft (values < 15 kPa, ratio = 0.70).

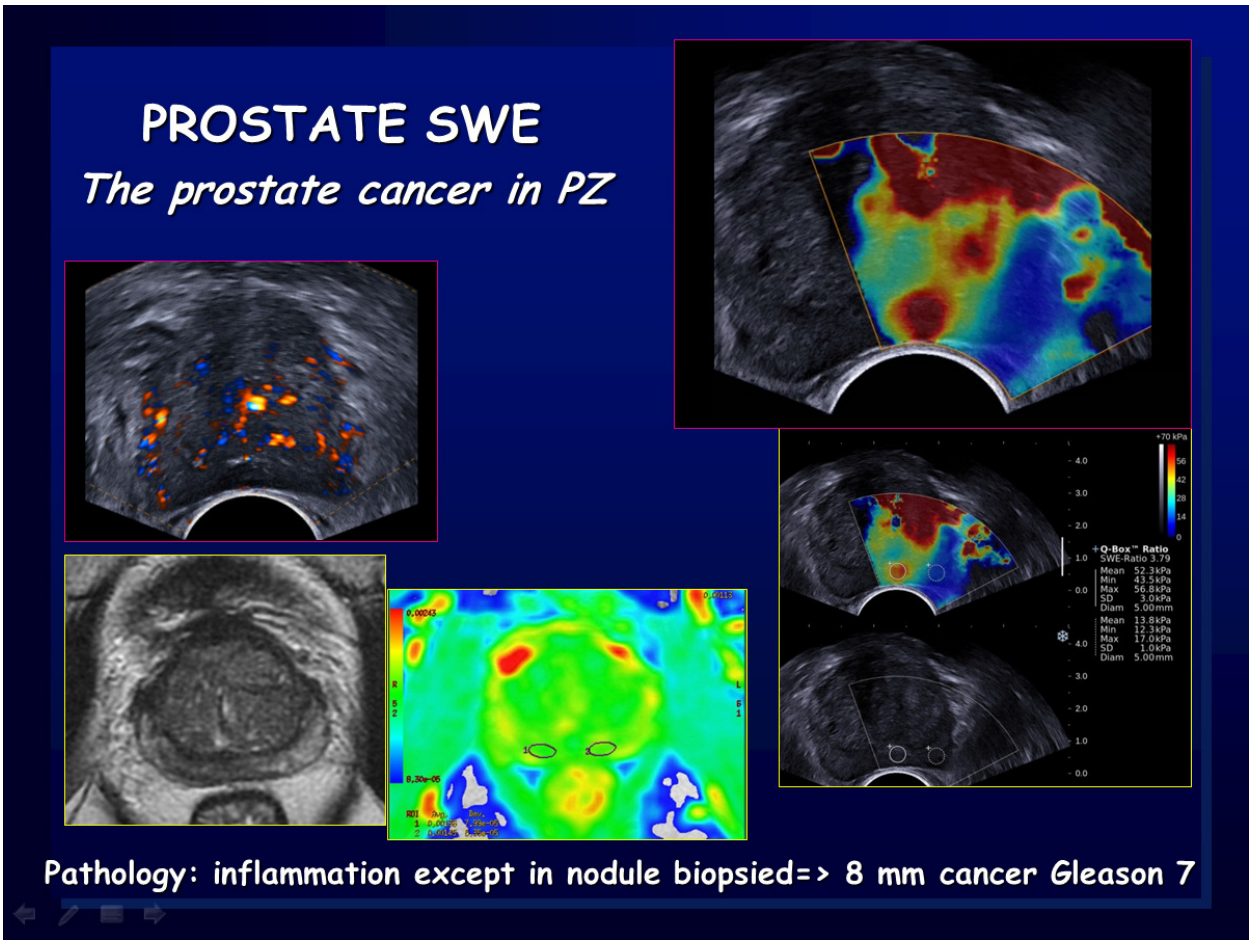

Fig. 15: Nodule located in the paramedian peripheral zone only detected using SWE. It exhibited an elevated stiffness (52 kPa), compared to the adjacent normal peripheral gland (14 kPa). The stiffness ratio was also strongly increased (>4). The targeted biopsies confirmed the presence of a Gleason 7 adenocarcinoma.

Conclusion

SWE is a new ultrasound imaging technique that can be used to study tissue elasticity.

This technology delivers new capabilities to clinicians:

• A quantitative information on human tissue properties through the estimation of elasticity in kPa;

• The ability to visualize the elasticity of small lesions;

• An additional diagnostic imaging method that can be added to routine prostate TRUS for cancer detection and targeted biopsies.

Multi centric clinical trials remain necessary to confirm these preliminary data.

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Personal Information

Conflict of Interest:

- Toshiba MS: expert, member of the advisory board
- Philips US: expert, member of the advisory board
- SuperSonic Imagine: expert
- General Electric US: expert
- Bracco SA: principal investigator of BR1-127 protocol

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Shear Wave Ultrasound Elastography of the Prostate

Initial Results

Richard G. Barr, MD, PhD,† Richard Memo, MD,*‡ and Carl R. Schaub, MD**

Purpose: This prospective study was to evaluate shear wave elastography (SWE) in the detection of prostate cancer (PC).

Methods: Patients scheduled for a transrectal ultrasound (TRUS) biopsy of the prostate because of elevated prostate-specific antigen levels or abnormal digital rectal examination result underwent a standard TRUS and SWE. A second TRUS examination and sextant biopsy by a second physician blinded to SWE results was then performed. Pathologic result was reviewed, and sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated.

Results: A total of 53 patients (318 sextants) participated in the study. Mean age was 64.2 years (range, 53–79 years). A total of 26 foci of PC were detected in 11 patients (20.7%). On the basis of the receiver operating characteristic curve, a value of 37 kPa was used as the cutoff between benign and malignant. This produced a sensitivity of 96.2% (25/26), a specificity of 96.2% (281/292), a PPV of 69.4% (25/36), and an NPV of 99.6% (281/282). Six (55%) of 11 false-positive samples were secondary to benign calcifications. The Young modulus of PC ranged from 30 to 110 kPa (mean [SD], 58.0 [20.7] kPa). At the patient level, if a cutoff of 40 kPa was used, all PCs would have been detected, and the positive biopsy rate would be 11 (50%) of 22 compared to 11 (20.8%) of 53 without SWE—a 140% increase in the positive biopsy rate.

Conclusions: Shear wave elastography has a high sensitivity, specificity, PPV, and NPV for the detection of PC. With a high PPV, patients with elevated prostate-specific antigen levels or abnormal results in the digital rectal examination and negative SWE may not require biopsy. This could significantly reduce the negative biopsy rate in PC detection.

Key Words: elastography, prostate cancer, transrectal ultrasound, shear wave imaging, PSA

(*Ultrasound Quarterly* 2012;28:13–20)

Prostate cancer (PC), usually adenocarcinoma of the prostate, is the commonest malignancy in American men (excluding skin cancers) and is second only to lung cancer as a cause of cancer-related death.[1] However, among men diagnosed with the disease, 93% will survive for at least 5 years and 72% will survive for at least 10 years.[1]

Prostate-specific antigen (PSA), measured in serum, has been used as a screening test for PC, with PSA levels above 4.0 ng/mL considered abnormal. In addition to adenocarcinoma, a variety of benign diseases of the prostate (eg, acute prostatitis and benign prostatic hypertrophy) as well as prostatic instrumentation will elevate PSA levels, so false-positive PSA results are common. On the other hand, approximately 20% of PC will present with PSA level less than 4.0 ng/mL.[2,3] A commonly used screening protocol for PC combines serum PSA measurement with digital rectal examination (DRE). The positive predictive value (PPV) of this combination is quoted as 60.6%, an improvement over DRE alone (PPV, 31.4%) or PSA alone (PPV, 42.1%).[3,4] Transrectal ultrasound (TRUS)–guided prostate biopsies are then used to evaluate those patients identified as having abnormal levels by this screening protocol. When sextant biopsies are used, only 25% of these patients will have at least 1 positive biopsy, whereas the biopsy technique will fail to detect tumor in at least 25% of patients proven subsequently to have PC.[5,6]

T2-weighted magnetic resonance imaging and magnetic resonance spectroscopy are also used to diagnose PC. The weaknesses of magnetic resonance imaging are their low sensitivities and their inability to accurately detect tumors smaller than 1 cm in diameter.[7,8] Magnetic resonance spectroscopy also has trouble detecting small tumors owing to their relatively small effect on metabolites.[9] The current set of imaging modalities is not sufficient to properly diagnose PC. One possible solution to this problem is arising in the form of elasticity imaging—or elastography.

Contrast-enhanced ultrasound is also being evaluated for detection and characterization of PC.[10]

Previous studies using strain elastography have demonstrated sensitivity and specificities of 55% to 70%, PPV of 57% to 85%, and negative predictive value (NPV) of 72% to 87%.[11–13] Preliminary studies with shear wave elastography have shown it to possess high sensitivity, high specificity, and high NPV (all >90%) when compared to the current modalities.[14] This high NPV will especially allow patients with high PSA levels but negative elastic examinations to be monitored and spared the usual sextant biopsy.

Elastography Principles

Elastography evaluates tissue stiffness instead of echogenicity. This adds a new method of detecting any pathologic abnormality that could otherwise be missed by conventional ultrasound.[12] Presently, there are 2 types of ultrasound elastography: strain and shear wave. This study used shear wave elastography (SWE). Tissue stiffness is expressed as Young

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Dr Memo and Dr Schaub have no conflict of interest to declare.
Portions of this study are not approved by the US Food and Drug Administration (FDA). Quantification with shear wave imaging is not presently approved by the FDA. The use of shear wave imaging of the prostate is approved by the FDA without quantification.
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modulus or simply the ratio of stress put on a material to the tissue deformation caused by the stress.[15] Shear wave is a technique that uses a sonographic push pulse to generate a shear wave in the tissues. Shear wave velocity (V_s) through the tissue is affected by the stiffness, with stiffer tissues allowing it to move faster (Fig. 1).[16,17] The shear wave speed V_s (m/s) or Young modulus (kPa) for each pixel is color coded and overlaid on the B-mode image. A detailed discussion of the differences of strain and shear wave elastography imaging can be found elsewhere.[18]

Prostate Anatomy

The prostate lies in the anterior pelvis and surrounds the middle portion of the male urethra, termed the *prostatic urethra*. It is composed of glandular (exocrine) and stromal tissues. The prostate has been described as having 5 lobes or 4 zones (Fig. 2).[20] Of greatest significance are the zones because they differ significantly in types and frequency of pathologic abnormalities. These 4 zones are the peripheral zone, central zone, transitional zone, and periurethral zone. The peripheral zone is disk-shaped, located anterolaterally, and occupies approximately 70% of the prostate. This is the zone in which 70% to 80% of PC arises, making it a prime target for prostatic surveillance. The central zone is wedge shaped and is located between the urethra and the peripheral zone. It occupies approximately 25% of the prostate and is rarely the site of PC. The transitional zone is made up of 2 separate lobes adjacent to the anterior prostatic urethra. It comprises only 5% of the prostate but is significant because this is the area in which benign prostatic hypertrophy arises in a majority of men later in life. The remaining 10% to 20% of PC arises in the transitional zone.[20]

METHODS

This prospective study was performed under local institutional review board supervision and was in compliance with the Health Insurance Portability and Accountability Act of 1996. Patients scheduled for TRUS biopsy because of an elevated PSA level and/or abnormal DRE result were asked to participate in this study. Transrectal ultrasound was performed on an Aixplorer (SuperSonic Imagine, Aix en Provence, France) with an SE12-3 MHz probe including B-mode, color Doppler, and SWE imaging. The SWE scale is set to a maximum value of 90 kPa. In general, the SWE penetration setting was required because the prostates were enlarged. Imaging was performed in both the axial and transverse planes from seminal vesicles to the apex of the gland. Usually, the field of view of the SWE is not wide enough to evaluate the entire prostate, requiring the right and left lobes be imaged separately. The least amount of pressure on the prostate as possible while maintaining contact with the probe was used in all cases. At each imaging plane, the probe was held steady for approximately 3 to 5 seconds (several frames) to obtain a stabilized image. Measurement of the Young modulus (kPa) was made in every nodule and area with SWE velocity above the baseline prostate tissue. Images were stored digitally.

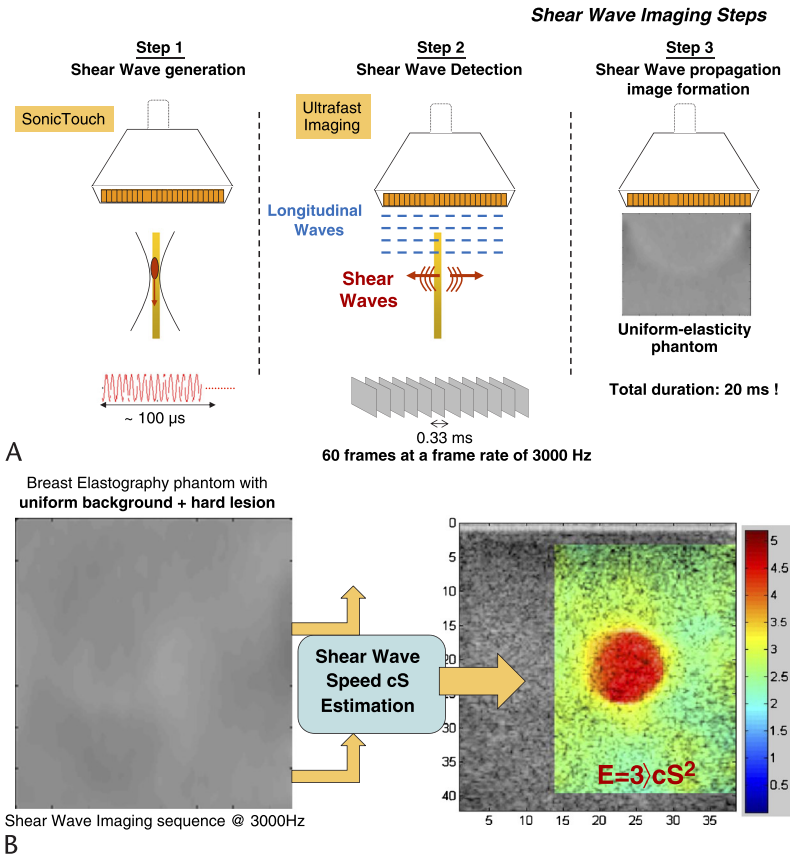

FIGURE 1. A, Technique for SWE. Step 1: The sonographic push pulse being released and propagating a shear wave through the tissue. Step 2: Ultrafast imaging being used to pick up longitudinal wave echoes coming back from the tissue. Step 3: An "elastic map," or phantom, being made based on how fast the echoes came back. The stiffer the tissue the faster the shear wave propagates through them. B, A sample elastic phantom of breast tissue. Note the obvious red foci in the middle of the image. It represents a tumor, which has a higher stiffness value and thus a faster shear wave velocity.

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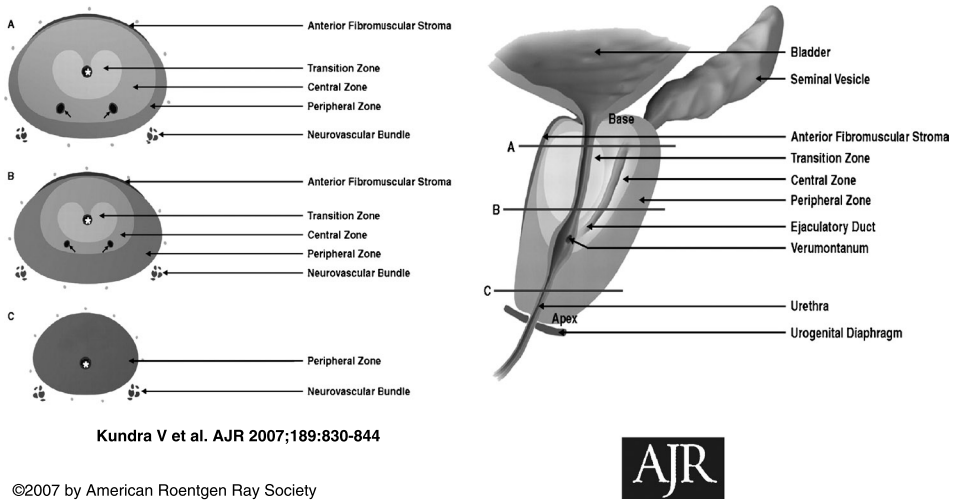

FIGURE 2. Anatomy of the prostate gland. Note the 3 zones and their spatial relationship to one another. The transition zone surrounds the urethra and is the least posterior. It is also the site of BPH, which is why urination is compromised. The peripheral zone is the most posterior and is the thus the easiest to image with elastography. This is useful considering it is a high rate of pathology. Reprinted from Kundra et al[19] by permission of American Roentgen Ray Society.

Nodules and other suspicious areas were noted by the radiologist. Afterward, the urologist performed a DRE, performed a TRUS with S2000 (Siemens Ultrasound, Mountain View, Calif) using an EC 9-4 probe with B-mode ultrasound, and performed sextant biopsy based on standard clinical practice without knowledge of the SWE findings. Prostate volume was calculated using the volume measurement on the ultrasound unit. Any abnormalities on B-mode alone were also examined by biopsy per standard protocol. If abnormalities on the SWE were not included in the original biopsy, additional samples of these areas were obtained after the completion of standard biopsy.

The prostate was divided into sextants for analysis. The central and transitional zones are complex, deep, and often contain calcifications that make interpretation difficult. The peripheral zone lends itself to excellent shear wave imaging. Therefore, we limit our interpretation to the peripheral zone. Nodules identified on B-mode were documented and correlated with SWE values. The SWE and biopsy results were compared for each sextant. Biopsies were staged based on the Gleason score (scale of 2–10). The receiver operating characteristic (ROC) curve was generated using the Young modulus and the pathologic result (benign or malignant). The highest Young modulus value in the sextant was used.

In patients undergoing total prostatectomy, the specimens were sliced in the plane of imaging for correlation with imaging findings.

RESULTS

A total of 53 patients participated in the study, providing 318 sextants. Mean patient age was 64.2 years (range, 53–79 years). Mean PSA level was 5.05 ng/mL (range, 0.21–18.6 ng/mL). A total of 26 foci of cancer were detected in 11 (20.7%) of the 53 patients. Of the 11 patients with cancer, 5 have undergone total prostatectomy for which histologic result was available for comparison.

Pathologic results also included 242 benign prostate tissues, 21 with atypia, 13 with acute prostatitis, and 16 with chronic prostatitis. The results are summarized in Table 1.

The ROC curve of the Young modulus for benign lesions (benign, atypia, acute, and chronic inflammation) and malignant lesions is presented in Figure 3. On the basis of the ROC curve, a value of 37 kPa was used as the cutoff between benign and malignant. This produced a sensitivity of 96.2% (25/26), specificity of 96.2% (281/292), PPV of 69.4% (25/36), and NPV of 99.6% (281/282). Of 11 false-positive samples, 6 (55%) were secondary to calcifications noted on B-mode in benign tissue. The Young modulus of cancers ranged from 30 to 110 kPa, with a mean (SD) value of 58.0 (20.7) kPa. Benign lesions had Young modulus ranging from 9 to 107 kPa, with a mean (SD) value of 21.5 (11.5) kPa.

The Young modulus values of PC were statistically significant compared to each of the benign categories: cancer versus benign ($P < 0.0001$), cancer versus atypia ($P < 0.0001$), cancer versus acute inflammation ($P < 0.0001$), and cancer versus chronic inflammation ($P < 0.0001$). The Young modulus values between benign lesions were all statistically nonsignificant: benign versus atypia ($P = 0.818$), benign versus acute inflammation ($P = 0.606$), benign versus chronic inflammation ($P = 0.0509$), and acute inflammation versus chronic inflammation ($P = 0.096$).

TABLE 1. Summary of Results

n	Pathologic Result	Minimum kPa	Maximum kPa	Mean kPa	SD
242	Benign	9	107	21.2	11.8
21	Atypia	14	38	20.6	5.3
26	Cancer	30	110	58.0	20.7
13	Acute inflammation	9	28	19.5	5.5
16	Chronic inflammation	13	63	27.3	15.5

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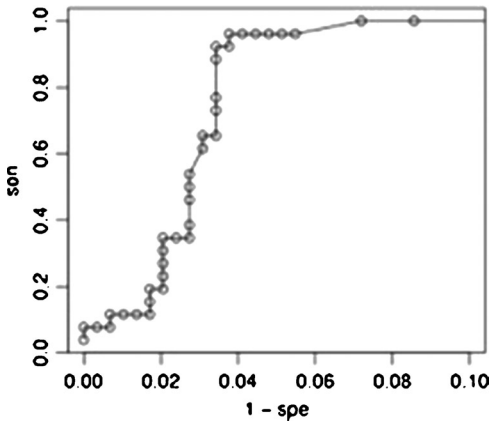

FIGURE 3. The ROC curve for kPa measurements between malignant and benign prostate pathology. With a value of 37 kPa as cutoff, the sensitivity is 96.2%, the specificity is 96.2%, PPV is 69.4%, and NPV is 99.6%.

There were 51 nodules noted on B-mode imaging. Of these, 6 (11.8%) were malignancies on pathology. Of 45 benign lesions, 43 (95.6%) were classified as benign on SWE, and all 6 (100%) malignant lesions were classified as malignant on SWE. There were 2 false-positives, both benign lesions with calcifications. This corresponds to a sensitivity of 100%, specificity of 95.6%, PPV of 75%, and NPV of 100% in SWE predicting malignancy in nodules detected in B-mode imaging.

At the sextant level, to obtain a 100% sensitivity, a cutoff value of 30 kPa is required. At the patient level (patient with cancer of 30 kPa also had 2 other PC foci with 40 kPa), if a cutoff of 40 kPa was used, all cancers would have been detected, and the positive biopsy rate would be 11 (50%) of 22 compared to 11 (20.8%) of 53 without SWE—a 140% increase in the positive biopsy rate.

The shear wave pulse penetrates 3 to 4 cm. In a large prostate, this may not penetrate deep enough to measure the entire peripheral zone (Fig. 4).

Figure 5 is a benign prostate gland in a 74-year-old black man who presented with a PSA level of 12.3 ng/mL. Five years earlier, his PSA level was 8.0 ng/mL. Result from the DRE was unremarkable. Sextant biopsy was negative for disease. B-mode ultrasound was negative for disease, with a prostate volume of 26 mL. On SWE, the peripheral zone is blue, corresponding to a low (<20 kPa) Young modulus throughout.

A selected image from a 65-year-old white man who presents with a PSA level of 4.6 ng/mL is presented in Figure 6. Firmness on the left side of the gland was present on DRE. No abnormality is identified on B-mode or Color Doppler imaging. On SWE, there is a lesion with a high Young modulus of 119 kPa (red). Image-guided biopsy confirms PC with Gleason grade 6.

Figure 7 is a selected image from a 54-year-old white man with a hypoechoic nodule in the peripheral zone. Note that the nodule has a low Young modulus of less than 20 kPa consistent with a benign etiology. However, there is an area of

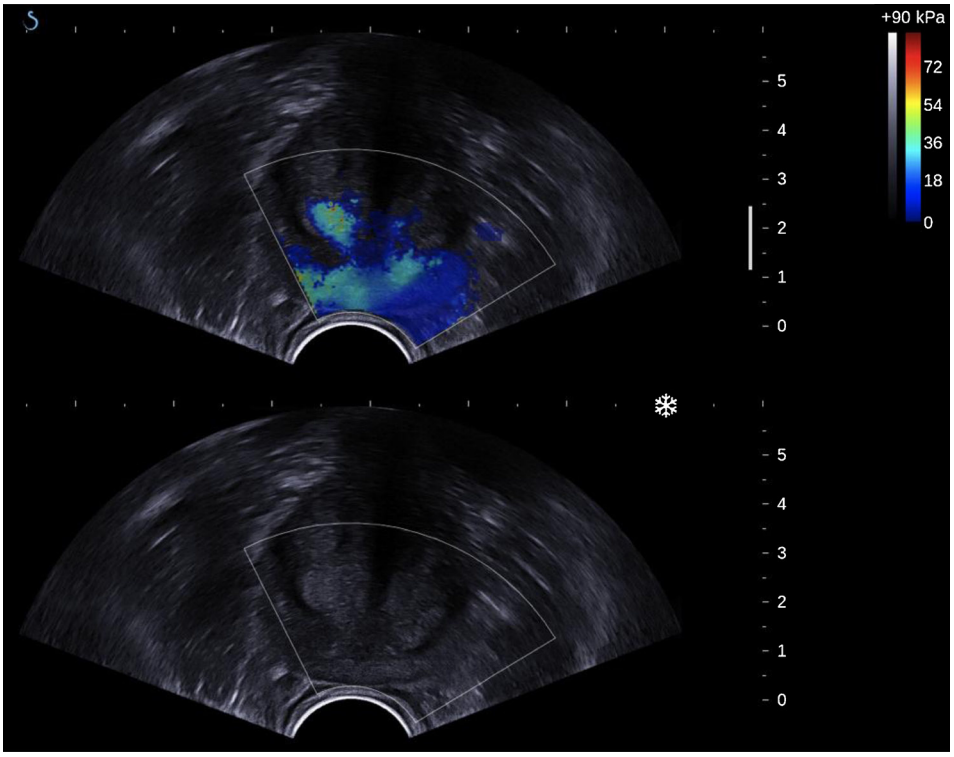

FIGURE 4. Image demonstrating the depth of penetration of the push pulse generating the shear wave. The image on the top is the shear wave image. The image on the bottom is the B-mode image. Measurement of elasticity is expressed as the Young modulus (kPa) displayed on a color scale. In the areas without color in the field of view, the shear wave is not generated, and therefore, the elasticity (stiffness) is not measured.

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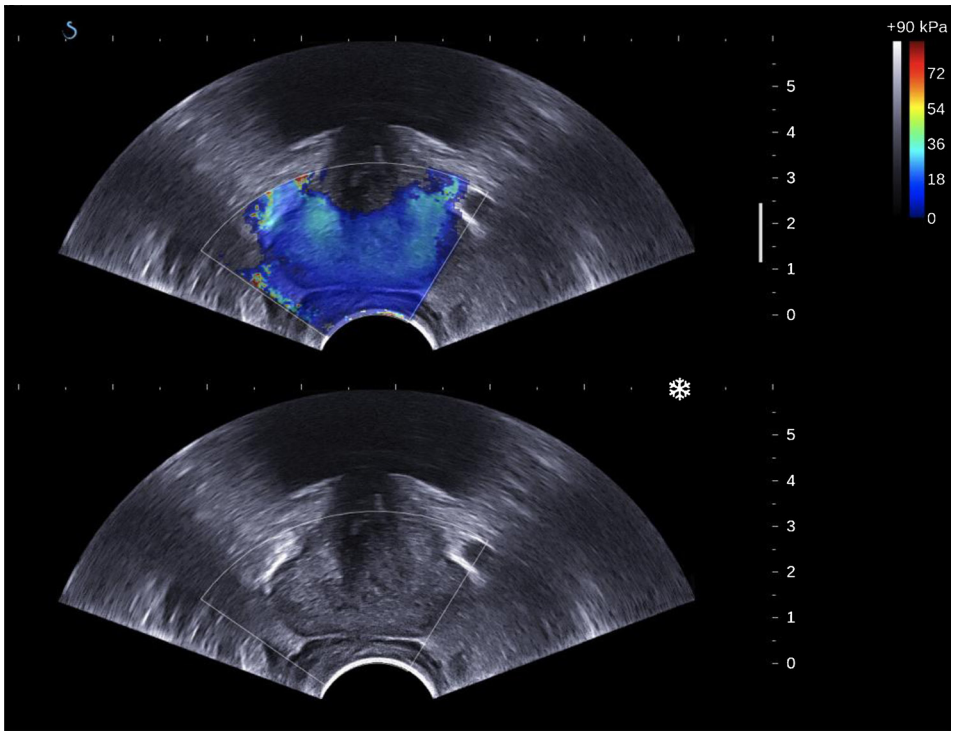

FIGURE 5. A prostate gland of a patient who recently had an elevation of PSA from 8 to 12.3 ng/mL. While increased PSA may be cause for concern, elastic imaging revealed a benign prostate gland. Note the homogenous blue reading, indicative of uniform low stiffness (< 20 kPa) and likely ruling out carcinoma.

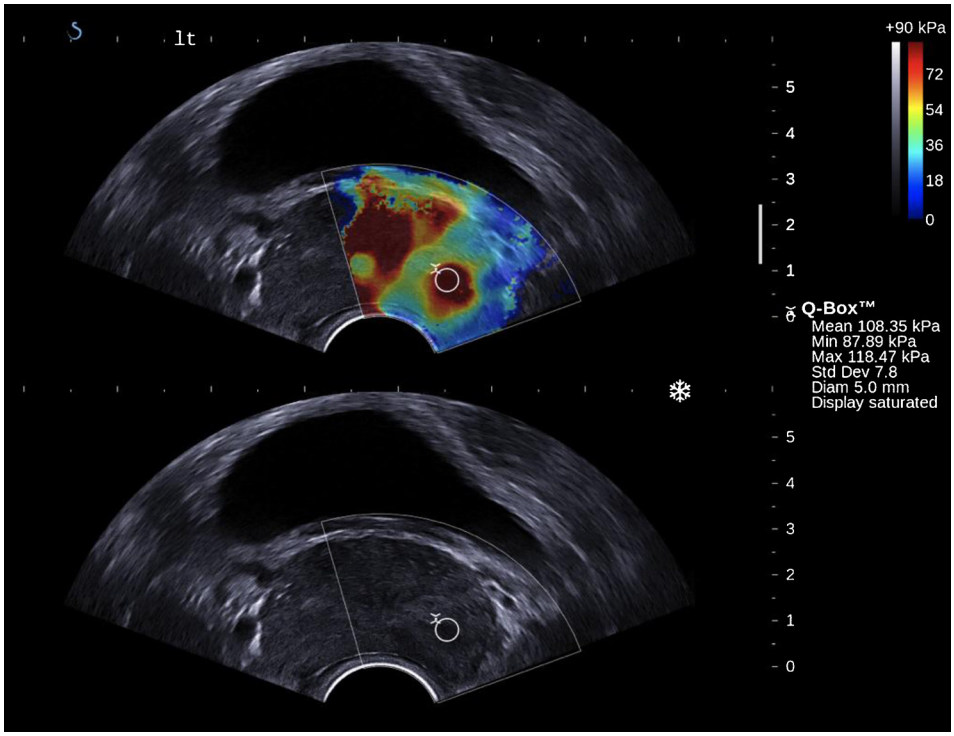

FIGURE 6. True positive for Gleason 6 carcinoma. This patient presented with a low PSA but firm left side on digital rectal exam. B-mode imaging and color Doppler produced no findings. Shear wave elastography presented this image. Note the posterior high stiffness lesion on the left side. This lesion read at a high stiffness (119 kPa) and was confirmed on biopsy to be a Gleason 6 carcinoma.

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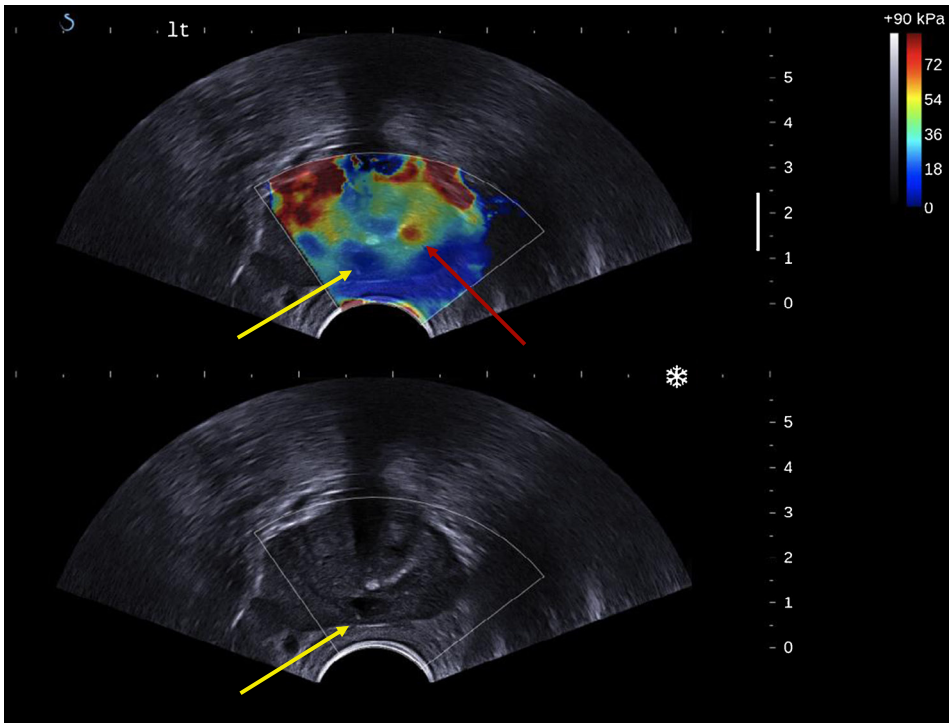

FIGURE 7. Comparison of ultrasound and SWE. This patient presented with a hypoechoic nodule on ultrasound (black lesion with arrow). Shear wave elastography was preformed, and the nodule was found to be of low stiffness (<20 kPa). Note the blue area with a yellow arrow. However, another lesion was found with a high stiffness (75 kPa) and was found on biopsy to be PC with Gleason grade 7. Note the red lesion with a red arrow.

high Young modulus of 75 kPa (red), suggestive of a malignancy. On image-guided biopsy, the hypoechoic nodule was benign, whereas the red area was PC with Gleason grade 7. This highlights the clinical strength of elastic imaging. Malignant lesions can be differentiated from benign prostatic hypertrophy or prostatitis quite easily, because often, their stiffness differs by a factor of 3 and can reach a factor of 10 in extreme cases. Elastography can also be used to guide biopsy of the prostate similar to B-mode imaging.

Calcifications appear as hard nodules on SWE and can lead to false-positive findings (Figs. 8 and 9). Figure 8 is an image from a 68-year-old white man showing an area with a high Young modulus of 73 kPa, suggestive of a malignant lesion. Small echogenic foci consistent with calcifications were noted on B-mode imaging. SWE–guided biopsy of the suspicious area confirms a benign prostatic tissue with focal calcifications. Figure 9 is a selected SWE image from a 56-year-old white man with a focal area of high Young modulus of 67 kPa. SWE–guided biopsy of the lesion revealed acute and chronic inflammation with focal calcifications.

Shear wave elastography can also be used to evaluate for extracapsular extension of tumor. Extracapsular extension of a PC into the seminal vesicles is presented in Figure 10 with the associated pathology on total prostatectomy. The area with a

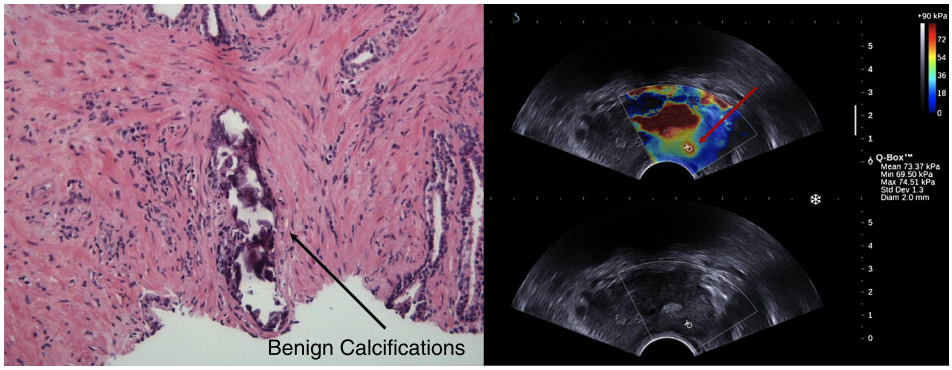

FIGURE 8. False-positive on SWE. This patient had a stiff (73 kPa) and echogenic lesion that suggested malignancy. Note the posterior red lesion circled. Upon biopsy, it was found to be benign prostatic tissue that had been calcified. This highlights a current limitation to SWE.

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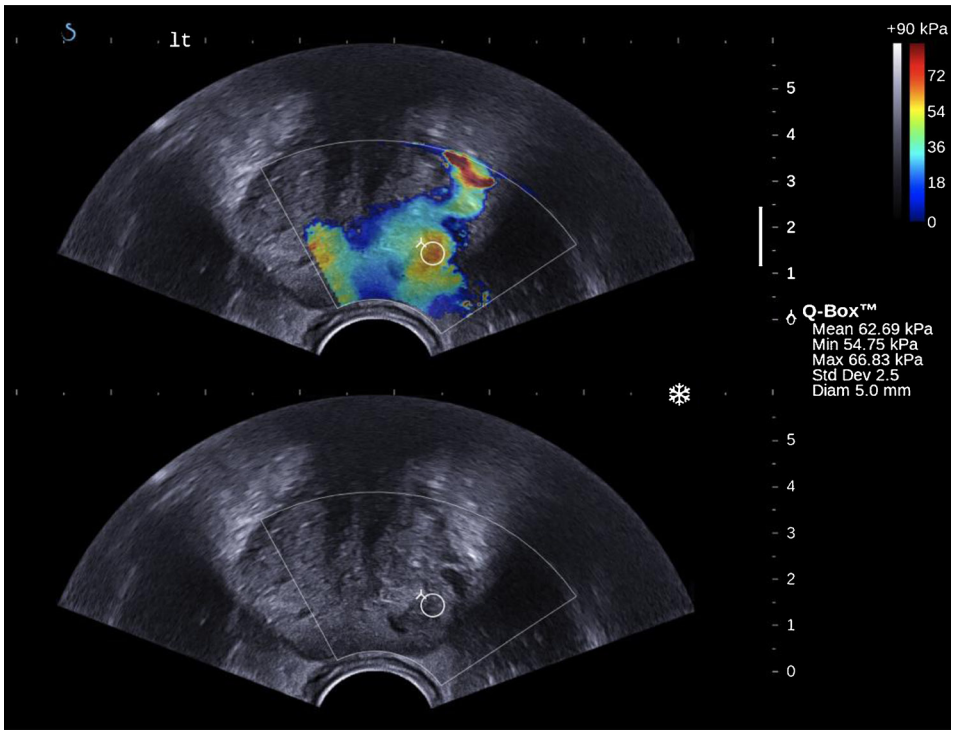

FIGURE 9. False-positive on SWE. This patient had a high (67 kPa) stiffness nodule noted on SWE. Note the posterior yellow-orange area circled. It was found on biopsy to be an inflamed prostatic tissue with focal calcifications, again highlighting a weakness of SWE.

high Young modulus is observed to extend beyond the prostate capsule and into the seminal vesicles on SWE, which was confirmed on surgical pathology.

DISCUSSION

Shear wave elastography is a very promising technique for the detection and biopsy of PC. Additional studies are needed before it can become part of the standard protocol in PC treatment. Of particular interest is its high negative predictive value that may reduce the need for invasive procedures such as biopsies. At present, only 25% to 30% of patients have a positive biopsy. In our study, there was a 20.8% positive biopsy rate. If SWE was used, the biopsy rate could have been decreased by 52.6%, yielding a biopsy rate of 50.0%. Further study needs to be performed to determine whether eliminating calcifications from biopsy is appropriate, which would have improved the biopsy rate to 68.8%. The ability to detect and guide biopsies of areas suspicious for cancer will also help to improve PC detection rates.

This study is limited by relatively small number of cases. Our cutoff value of 37 kPa needs to be validated in a larger

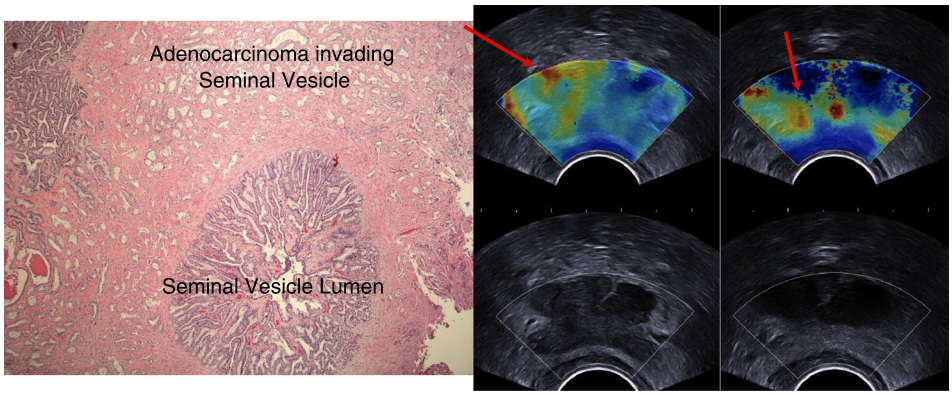

FIGURE 10. A 45-year-old black man with a PSA level of 6.6 ng/mL. On SWE, the PC is identified with a Young modulus of 63 kPa with extension into the right seminal vesicle with a Young modulus of 72 kPa (red arrows). At sextant biopsy, PC was confirmed in the right base. The patient underwent total prostatectomy. Histology at total prostatectomy confirms PC with Gleason grade 7 at the right base extending into the right seminal vesicle.

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multicenter trial. A larger number of cases is required to determine whether the Young modulus is correlated to the tumor grade. Our initial results suggest that shear wave elastography may be more sensitive and specific in diagnosing PC than strain elastography.

Transrectal SWE of the prostate has the potential to become the primary imaging modality for detection of PC. The US Preventive Services Task Force recently advised not to recommend PSA screening because of possible complications of the low positive biopsy rate.[21] Their concern is that the risk of complications negated any benefit of detecting PC. The addition of SWE imaging to PSA and DRE PC screening has the potential to improve the risk/benefit ratio favoring screening.

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