Shear Wave Elastography of the Prostate: Initial Results and Pathology Correlation

R G Barr, MD, PhD[1,2], Richard Memo MD [2], Carl R. Schaub MD [2]

[1.] Radiology Consultants Inc., Youngstown OH, Northside Medical Center, Youngstown, Ohio [2.] Northeastern Ohio Medical College, Rootstown OH

BACKGROUND

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. However, among men diagnosed with the disease, 93% will survive for at least 5 years, and 72% for at least 10 years.

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 (for example, 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, about 20% of PC will present with PSA<4.0 ng/mL. 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%). TRUS guided prostate biopsies are then used to evaluate those patients identified as abnormal by this screening protocol. When sextant biopsies are employed, only 25% of these patients will have at least one positive biopsy, while the biopsy technique will fail to detect tumor in at least 25% of patients proven subsequently to have PC.

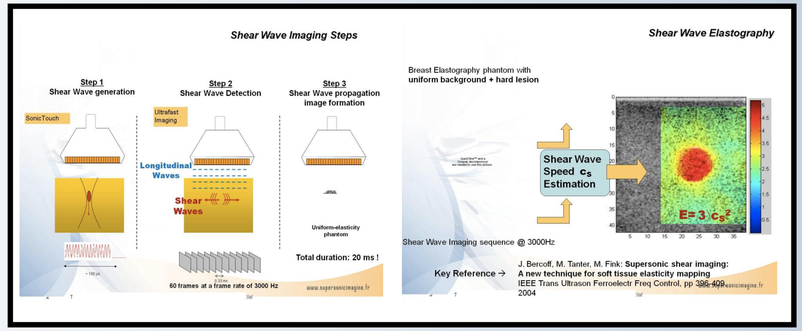
T2 Weighted MRI's and MR spectroscopy (MRS) are also used to diagnose PC. The weaknesses of MRI's are their low sensitivities and their inability to accurately detect tumors smaller than 1cm in diameter. MRS also has trouble detecting small tumors due to the relatively small effect on metabolites. Obviously the current set of imaging modalities are not sufficient to properly diagnose PC. One possible solution to this problem is arising in the form of elasticity imaging, or elastography.

PURPOSE AND HYPOTHESIS

To determine the specificity, sensitivity, PPV and NPV of Shear Wave Elastography in detecting prostate cancer. Correlate Imaging findings with pathology findings.

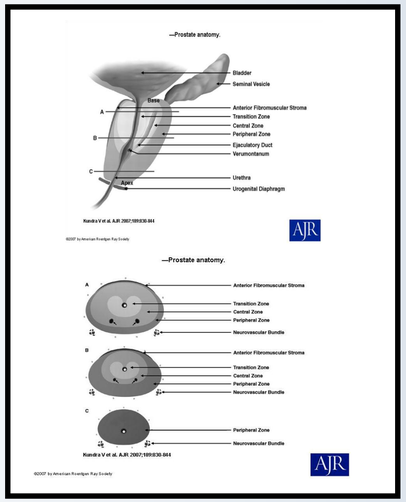
Shear Wave Elastography Principals

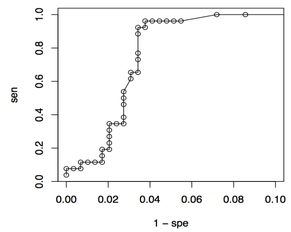
Elastography evaluates tissues on the basis of stiffness instead of echogenicity. This adds a new method of detecting pathology that could otherwise be missed by conventional ultrasound. Presently there are two types of ultrasound elastography, strain and shear wave. In this poster we will be discussing shear wave elastography (SWE). The parameter usually measured for tissue stiffness is Young's modulus, or simply the ratio of stress put on a material to the tissue deformation caused by the stress. Shear wave is a technique that uses a sonographic push pulse to generate a shear wave in the tissues. Shear wave velocity through the tissue is affected by the stiffness, with stiffer tissues allowing it to move faster. The shear wave speed Vs (m/s) or Young's Modulus (kPa) for each pixel is color coded and overlayed on the B-mode image.



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 tissue. The prostate has been described as having five lobes or four zones. Of greatest significance are the zones, as they differ significantly in types and frequency of pathology. These four zones are the peripheral zone, central zone, transitional zone and periurethral zone. The peripheral zone is disk-shaped, located antero-laterally, and occupies about 70% of the prostate. This is the zone in which 70-80% 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 about 25% of the prostate, and is rarely the site of PC. The transitional zone is made up of two 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 10-20% of PC arises in the transitional zone.





ROC for kPa measurements between malignant and benign prostate pathology. With a value of 37kPa as cut-off,the sensitivity is 96.2%the specificity is 96.2%, PPV is 69.4%, and NPV is 99.6%

MATERIALS AND 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 on a SuperSonic Imagine (SuperSonic Imagine, Aix en Provence, France) with a SE12-3 MHz probe including B-mode, color Doppler and SWI imaging. The SWE (Shear Wave™ Elastography) scale is set to a maximum of 90Kpa. In general, we need to use the SWE Penetration setting for most prostates that are enlarged. Imaging was performed in both the axial and transverse plane from seminal vesicles to the base of the gland. Usually the FOV of SWE is not wide enough to evaluate the entire prostate requiring us to scan the right and left lobes separately. Care is taken not to apply too much pressure. At each image plane we hold the probe steady and wait approximately 3-5 seconds (several frames) to obtain an appropriate image. Measurement of Young's Modulus (kPa) was made in every nodule and area with SWE velocity above baseline prostate tissue.

Nodules and other suspicious areas were noted by the radiologist. Afterwards, the urologist performed a DRE, performed a TRUS with a S2000 (Siemens Ultrasound, Mountain View, Ca) using a 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 biopsied per standard protocol. If abnormalities on 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. SWE was deemed positive if the area was greater than 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).

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. Average patient age was 64.2 years (range 53-79). Average PSA was 5.05 (range 0.21-18.6). A total of 26 foci of cancer were detected in 11 of the 53 patients (20.7%).

The central and transitional zones are complex, deep, and often contain calcifications that make interpretation difficult. The peripheral zone lends itself to excellent imaging. Therefore, we limit our interpretation to the peripheral zone which can become an issue in patients with a large prostate. The shear wave pulse penetrates 3-4 cm. In a large prostate this is usually not deep enough to measure the entire peripheral zone. Calcifications appear as hard nodules on SWE and can lead to false positive findings.

Based on the ROC curve a value of 37 kPa was used as the cut-off between benign and malignant. This produced a sensitivity of 96.2%, specificity of 96.2%, positive predictive value of 69.4%, and negative predictive value of 99.6%. 6/11 (55%) false positive were secondary to calcifications in benign tissue. The kPa of cancers ranged from 30 to 110 (ave. 58.0 +/-20.7).

There were 51 nodules noted on B-mode. Of these 6/51 (11.8%) were malignancies on pathology. 44/45 (97.8%) benign lesions were classified as benign on SWE, 6/6 (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 95.7%, PPV of 75%, and NPV of 100% in SWE predicting malignancy in nodules detected in B-mode.

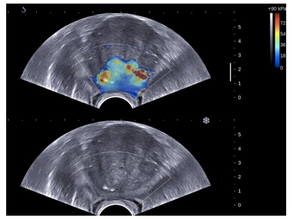
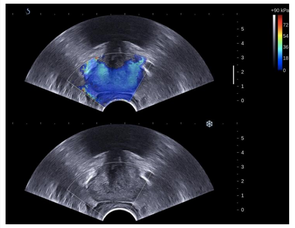
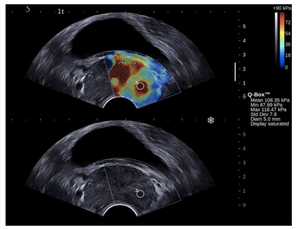


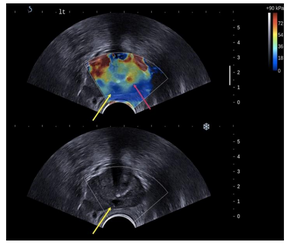
Image demonstrating the depth of penetration of the push pulse generating the shear wave. The image on the top is the Shearwave Image. The image on the bottom is the B-mode image. The measurement of the elasticity expressed as the Youngs Modulus, kPa, displayed on a color scale. In the areas without color in the FOV the shearwave is not generated and therefore the elasticity (stiffness) is not measured.



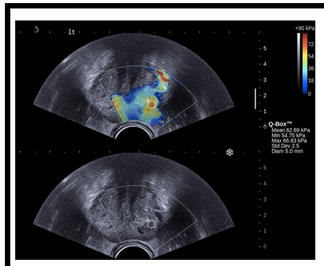
A prostate gland of a patient who recently had an elevation of PSA from 8 to 12.3. While increased PSA may be cause for concern, elastic imaging revealed a benign prostate gland. Note the homogenous blue reading, indicative of uniform low stiffness (< 20kPa) and likely ruling out carcinoma.



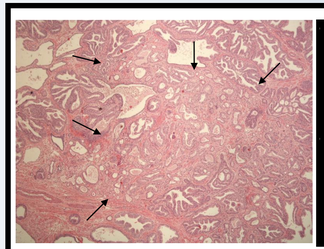
True positive for Gleason 6 carcinoma. This patient presented with a low PSA but firm left side on digital rectal exam. B-mode imaging and Color Doppler produced no findings. SWE presented in this image. Note the posterior high stiffness lesion on the left side. This lesion read at a high stiffness (119kPa)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

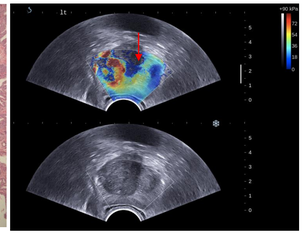


Comparison of US and SWE. This patient presented with a hypoechoic nodule on US (black lesion with arrow). SWE was performed and the nodule was found to be of low stiffness (<20kPa). Note the blue area with the yellow arrow. However, another lesion was found with a high stiffness (75kPa) and was found upon biopsy to be a Gleason grade 7 prostate cancer. Note the red lesion with the red arrow. This highlights the clinical advantages of Elasticity Imaging.



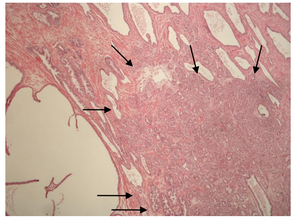
False positive on SWE. This patient had a high (67kPa) stiffness nodule noted on SWE. Note the posterior yellow-orange area circled. It was found upon biopsy to be inflamed prostatic tissue with focal calcifications. SWE correctly coded the califications as hard and therefore not distinuishable from PC, highlighting a weakness of SWE in PC detection.

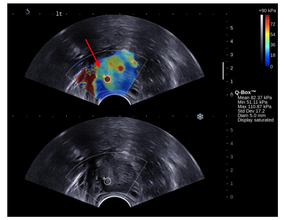




58yo WM presents with a PSA of 2.8. Sextant biopsy confirms PC. Patient underwent a total prostatectomy where a 5mm adenocarcinoma of the left mid gland was found. Gleason 7

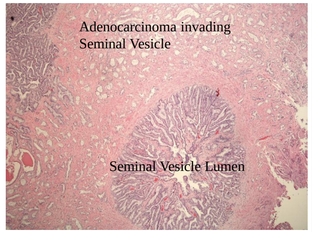
Histology slide on the left and SWE image on the right. The 5mm PC (black arrows) corresponds to an area which has a value of 38 kPa(red arrow).

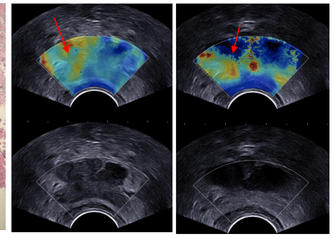




62 yo WM with a family history of PC, PSA 7.9. Sextant biopsy confirms PC in the mid right peripheral zone. Patient underwent total prostatectomy.

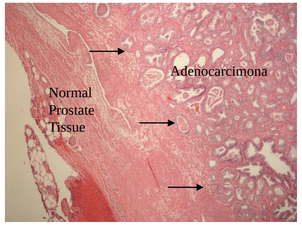
Histology at total prostatectomy confirms Gleason 7 PC (black arrows). On SWE the PC has a kPa value of 82 (red arrows).

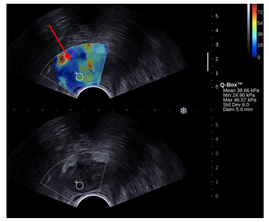




45 yo BM with a PSA of 6.6. PC of right base at sextant biopsy. Patient underwent total prostatectomy

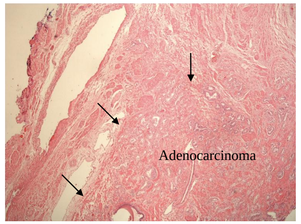
Histology at total prostatectomy confirms Gleason 7 PC at right base extending into right seminal vesicle. On SWE the PC is identified with a kPa of 63 with extension into the right seminal vesicle with a kPa value of 72 (red arrows)

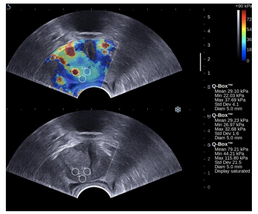




59 yo WM with a PSA of 4.3. Sextant biopsy confirms PC in the right base. Patient underwent total prostatectomy

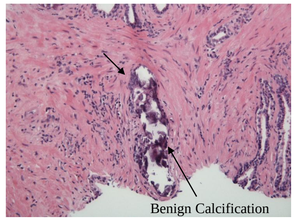
Histology at total prostatectomy confirms PC Gleason 7 (black arrows). On SWE the PC had a kPa value of 39 (red arrow)

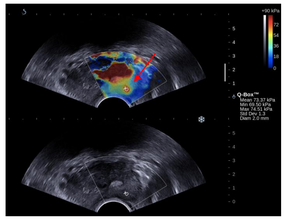




54 yo with a PSA of 5.8, DRE unremarkable. Sextant biopsy positive for PC. Patient underwent a total prostatectomy.

Histology at total prostatectomy confirms PC Gleason 7 (black arrows). On SWE the cancer has a kPa of 79.





58 yo WM with a PSA or 3.4, DRE large gland without nodule. Patient underwent sextant biopsy

False positive on SWE. This patient had a stiff (73kPa) and echogenic lesion that suggested malignancy (red arrow). Upon biopsy it was found to be benign prostatic tissue that had calcifications on the sextant biopsy. This highlights a current limitation to SWE.

CONCLUSIONS

ShearWave™ elastography is a very promising technique for the detection and targeted biopsy of prostate cancer. Additional studies are needed before it can become part of the standard protocol in prostate cancer treatment. Of particular interest is its high negative predictive value that may reduce the need for invasive procedures such as biopsies. At present, only 25-30% of patients have a positive biopsy. Preliminary results suggest that patients with an elevated PSA and a normal SWE may not require a biopsy leading to a significantly higher positive biopsy rate. In our preliminary study the positive biopsy rate without SWE was 11/53 (20.7%). Using SWE with a cut-off of 37kPa would have improved the biopsy rate to 10/17 (58.8%), although one cancer would have been missed. If a cut-off of 30 kPa was used all cancers would have been detected and the biopsy rate would be 11/21 (52.4%). The ability to detect and guide biopsies of areas suspicious for cancer will also help to improve prostate cancer detection rates.

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.

Shear Wave Imaging without quantification is FDA approved in the USA
Quantification tool available outside of USA