Shear Wave Elastography for Localization of Prostate Cancer Lesions and Assessment of Elasticity Thresholds: Implications for Targeted Biopsies and Active Surveillance Protocols

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Abbreviations and Acronyms

MRI = magnetic resonance imaging

PCa = prostate cancer

PSA = prostate specific antigen

SWE = shear wave elastography

TRUS = transrectal ultrasonography

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Purpose: Shear wave elastography allows the detection of cancer by using focused ultrasound pulses for locally deforming tissue. The differences in tissue elasticity and stiffness have been used increasingly in breast cancer imaging and help detect potential tumor lesions in the prostate. In this study we localized prostate cancer lesions using shear wave elastography before radical prostatectomy and assessed the examiner independent elasticity threshold for cancer foci detection.

Materials and Methods: Shear wave elastography scanning of the whole prostate was performed before radical prostatectomy in 60 consecutive patients with high, intermediate and low risk disease. Localization of suspected lesions and density threshold (kPa) were recorded in up to 12 areas and resulted in 703 different fields. Shear wave elastography findings were correlated with final pathology. Initially 381 areas were used to establish shear wave elastography cutoffs (development cohort 32 patients). Subsequently these cutoffs were validated in 322 areas (validation cohort 28 patients).

Results: Using shear wave elastography significant differences were recorded for the elasticity of benign tissue vs prostate cancer nodules at 42 kPa (range 29 to 71.3) vs 88 kPa (range 54 to 132) (all $p < 0.001$). Median cancer lesion diameter was 26 mm (range 18 to 41). Applying the most informative cutoff of 50 kPa to the validation cohort resulted in 80.9% and 69.1% sensitivity and specificity, respectively, and 74.2% accuracy for detecting cancer nodules based on final pathological finding. The corresponding positive and negative predictive values were 67.1% and 82.2%, respectively.

Conclusions: Shear wave elastography allows the identification of cancer foci based on shear wave elastography differences. Moreover, reliable cutoffs for this approach can be established, allowing examiner independent localization of prostate cancer foci.

Key Words: prostatic neoplasms, early detection of cancer, magnetic resonance imaging, elasticity imaging techniques, prostatectomy

THE diagnosis of prostate cancer relies on PSA testing and digital rectal examination. Prostate biopsy is still the gold standard for diagnosis.[1] Specifically at least 8 to 12 biopsy cores of the peripheral zone are recommended. However, these approaches potentially lead to under diagnosis. Patients with negative sextant biopsies may still have

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significant prostate cancer and patients not harboring cancer have to undergo biopsy as a result of insufficient selection tools.[2] Therefore, further options for evaluating PCa risk in individual patients are gaining popularity. MRI and biopsy techniques in particular are increasingly used for detection before radical prostatectomy and in active surveillance settings. However, MRI requires an interdisciplinary approach and special equipment, and is more time-consuming and costly than widely used TRUS imaging techniques.

Shear wave elastography is an ultrasound based, real-time method of visualizing cancer nodules. Specific differences in tissue elasticity and stiffness are increasingly used for detection and localization of breast malignancies, and may also help reveal tumor lesions in the prostate.[3,4] This approach is based on the fact that the structure of benign tissue in the prostate differs from that of cancerous tissue. Based on differences in elasticity, the stiffness of various tissue types may be an indicator of cancer. Accordingly, recent analyses demonstrated the ability of elastography to detect cancer nodules with good accuracy and its superiority compared to gray scale ultrasound.[5,6] Moreover SWE allows the calculation of elasticity ratios between benign and malignant tissue, which may result in a user independent imaging of the prostate. Based on these advantages of SWE, in this study we defined thresholds for PCa foci by comparing SWE with final pathological results (whole mount sections) in patients treated with radical prostatectomy to establish and validate cutoffs for benign and malignant tissue elasticity.

PATIENTS AND METHODS

A total of 60 consecutive selected patients scheduled to undergo open or robotic assisted radical prostatectomy were included in this study between December 2011 and June 2013. All patients had biopsy proven PCa before enrollment in our study. Prostate biopsy was usually performed when PSA exceeded 4 ng/ml or digital rectal examination findings were suspicious. The study cohort consisted of patients with D'Amico low, intermediate and high risk disease.

A single observer performed SWE examinations using the TRUS Aixplorer® System. All ultrasound procedures were performed in a standardized fashion with the patient in a left lateral decubitus position. During SWE the reaction of prostate tissue on acoustic push pulses through the ultrasound transducer was measured and stiffer areas were visualized (fig. 1). Compared to elastography, manually induced pressure by the examiner is not necessary.

The stiffness of the tissue was assessed in 12 areas in the prostate of each patient (the left and right part of the ventral and dorsal of the apex, mid gland and base of the prostate) (fig. 2). The stiffness of the tissue was measured

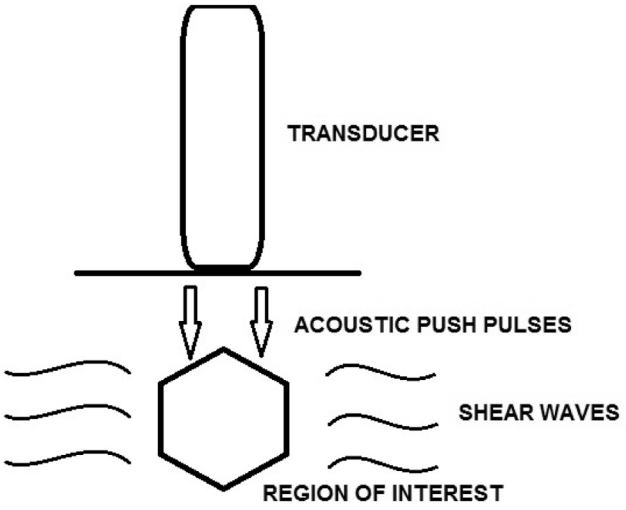

Figure 1. Principle of SWE. Transducer sends acoustic push pulses in tissue. Operator does not have to push.

in shear modulus (kPa) and visualized in a color scale from blue (soft tissue) to red (hard tissue). To establish reliable cutoffs the patients were randomized into a development or a validation cohort.

During TRUS and SWE, density cutoffs (kPa) and localization of suspected lesions in 703 areas were acquired. These cutoffs were compared to histopathological findings. Additionally, density ratios were assessed in 6 areas (right and left part of the apex, mid gland and base of every prostate) by measuring the ratio of the highest and the lowest density, resulting in a total of 344 areas. Data were collected in an institutional database (FileMaker® Pro 10) for further evaluation.

After surgery all SWE measurements were compared with histopathological results of the whole mount sections. Every prostate was sliced in 3 to 5 mm sections according to the Stanford protocol.[7] Tumor lesions were identified and marked on macroscopic photography of the prostate by an experienced uropathologist blinded to the SWE data (fig. 3). The diameter of the largest cancer focus was measured.

Baseline characteristics of the development cohort (32 patients, 381 areas) and validation cohort (28 patients, 322 areas) were compared using the chi-square likelihood test for categorical variables and the Wilcoxon test for continuous variables. Data from the development cohort were used to establish an elasticity and elasticity ratio cutoff. OR, IQR and AUC were assessed for several cutoff options (cutoff 45 kPa, 50 kPa, 55 kPa and 90 kPa, and ratio 2.0, 2.2, 2.4 and 2.6). These cutoffs were applied to the validation cohort. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated. Correlation between the number of positive areas and tumor volume was calculated using Spearman's rank correlation coefficient (r_s).

Positive areas in the elastogram with a stiffness greater than 50 kPa and greater than 100 kPa were correlated with the histopathological findings of the whole mount section of the prostate. In these analyses