Performance characteristics of transrectal shear wave elastography (SWE) imaging in the evaluation of clinically localised prostate cancer: a prospective study

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Introduction

Prostate cancer (PCa) accounts for the second most frequently diagnosed male cancer worldwide . Screening studies focusing on PCa detection by prostate-specific antigen (PSA) and digital rectal examination (DRE) as primary methods demonstrate that these approaches result in unnecessary biopsies, misdiagnosis and over-treatment of patients, in particularly those with insignificant PCa.

We and others have previously reported SWE for detecting and phenotyping PCa, and demonstrated strong diagnostic performance of this methodology. Nevertheless, to date there have been no large-scale prospective studies that have tested the diagnostic accuracy of SWE compared with radical prostatectomy histology as reference standard.

Accordingly, this prospective study aimed to:

1. Determine the diagnostic accuracy of transrectal SWE compared with the final pathology of radical prostatectomy.
2. Determine the reliability of transrectal SWE with respect to accurately characterise phenotyping various grades of PCa including establishing and validating cut-offs for benign and significant PCa.

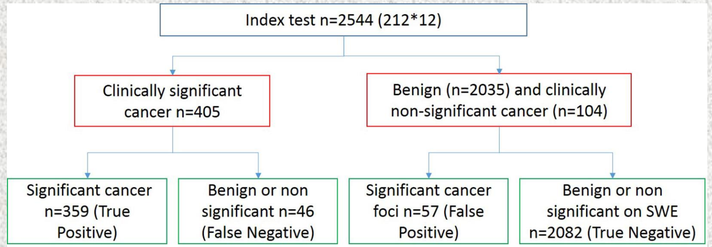
Materials and Methods

This was a prospective protocol-driven diagnostic accuracy study. 212 consecutive men undergoing laparoscopic radical prostatectomy (LRP) for clinically localised PCa were recruited into the study. Quantitative stiffness data of the prostate gland was obtained in each patient using an endocavitary transrectal transducer before LRP and compared with detailed histopathological examination of radical prostatectomy specimen using 3-D printing mold based technology ensuring improved image-histology orientation. Receiver operator characteristic curves (ROC) were assessed between the groups.

Results

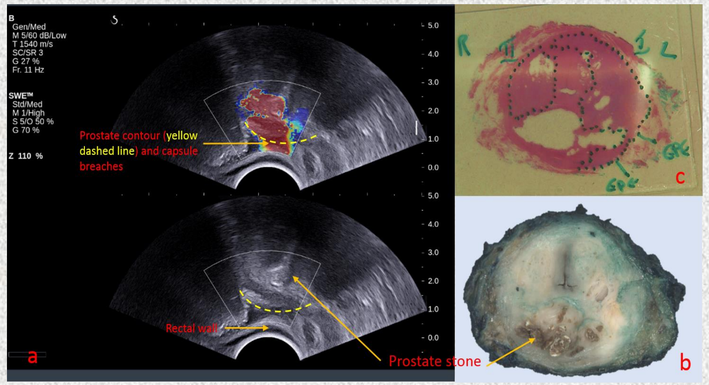
(a) Total cancer numbers		Size (mm) <5	5~10	>10	Total
Gleason Score	3+3	32	35	14	81
	3+4	18	77	201	296
	4+3	4	12	44	60
	3+5	0	0	7	7
	4+4	0	0	4	4
	4+5 or more	3	2	58	62
	Total	55	127	327	509
(b) Number of SWE identified cancer		**Size (mm)** <5	5~10	>10	Total
Gleason Score	3+3	9	18	12	39
	3+4	5	62	182	249
	4+3	2	5	41	48
	3+5	0	0	7	7
	4+4	0	0	4	4
	4+5 or more	1	2	56	59
	Total	17	87	302	406
(c) Stiffness of SWE identified cancer (kPa)		**Size (mm)** <5	5~10	>10	mean
Gleason Score	3+3	88.6	87.9	100.4	91.9
	3+4	118.5	100.8	102.5	102.4
	4+3	120.3	122.5	108.4	110.4
	3+5	N/A	N/A	113.7	113.7
	4+4	N/A	N/A	135.2	135.2
	4+5 or more	85.6	132.5	127.2	126.7
	mean	95.9	100.1	108.5	106.3
(d) Sensitivity of SWE for different sizes and grades		**Size (mm)** <5	5~10	>10	Total
Gleason Score	3+3	28.1%	51.4%	85.7%	48.1%
	3+4	27.8%	80.5%	90.5%	84.1%
	4+3	50.0%	41.7%	93.2%	80.0%
	3+5	N/A	N/A	100%	100%
	4+4	N/A	N/A	100%	100%
	4+5 or more	33.3%	100%	96.6%	95.2%
	Total	30.9%	68.5%	92.4%	79.8%

In tumour-level analyses, 509 cancer foci from total of 2544 regions (12 regions from 212 patients) were marked from the whole-mount pathology. The cancer distribution map was shown in **A**. 10.8% (55/509), 25% (127/509) and 64.2% (327/509) of cancer foci were <5mm, 5-10mm and > 10mm in size respectively. GS 3+4 was the most common cancer accounting for 58.2% (296/509) of all the cancer foci. **B** illustrated that SWE identified cancer on the distribution map using 82.6 kPa as a cut-off value. Stiffness of the identified cancers are displayed in **C**. As such, after considering the size of all cancers, there were no significant differences for tissue stiffness across differing sizes of cancer foci. However, the mean value of Young's modulus of GS 6 to 9 increased from 91.9kPa (GS 3+3) to 126.7kPa (GS 4+5), respectively. The mean value for all lesions was 106.3kPa. **D** showed that sensitivity for SWE to detect <5mm cancers was much lower than 5-10mm and > 10mm Cancers (30.9% vs 68.5% and 92.4%), only 9 of 32 GS6 and <5mm cancers were found by SWE.



Diagnostic accuracy of SWE for significant cancers		
Sensitivity	TP/(TP+FN)	88.6% (95% CI* 85.1%-91.6%)
Specificity	TN/(TN+FP)	97.3% (95% CI 96.6-98.0%)
Positive predictive value (PPV)	TP/(TP+FP)	86.3% (95% CI 83.0-89.1%)
Negative predictive value (NPV)	TN/(TN+FN)	97.8% (95% CI 97.2-98.3%)
Accuracy (ACC)	(TP+TN)/(TP+TN+FP+FN)	96.0% (95% CI 95.1-96.7%)

The above figure presented diagnostic results of clinically significant cancer, while demonstrating SWE outcomes for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) compared with histopathology results. Sensitivity, specificity, PPV and NPV of SWE for clinically significant cancer were 88.6% (95% CI 85.1%-91.6%), 97.3% (CI 96.6-98.0%), 86.3% (CI 83.0-89.1%) and 97.8% (CI 97.2-98.3%), respectively ($p<0.05$).



This representative figure demonstrated a 70 years old patient's ultrasound and pathology images. MRI was negative, biopsy showed GS 3+3, SWE was as high as 300kPa and suggested prostate capsular breach in peripheral area. LRP pathology images confirmed cancer with extraprostatic extension (EPE) and GS 4+5.

Discussion

Observations of the present study illustrated that TRUS SWE demonstrated strong diagnostic performance in clinically localised PCa. We showed that transrectal SWE could identify PCa coupled with an ability to distinguish between clinically significant and low-risk PCa. We also demonstrated that tissue stiffness measurements (Young's modulus) estimated from 12 different regions of the prostate gland using a cut-off value (82.6kPa) identified significant differences between benign and malignant tissue. The cut-off value was based on internal validation using ten-fold cross validation method. Particularly, we found that significant lesions (GS≥7) demonstrate higher Young's moduli compared with benign and non-significant lesions (GS≤6). Lastly, TRUS SWE also showed strong performance to predict cancer stage and status of surgical margins. These data represented a significant contribution to the body of knowledge associated with utilising transrectal B-Mode ultrasonography for screening PCa.

Conclusions

The TRUS SWE imaging demonstrated a high reliability and accurately distinguished PCa from benign tissues while identifying a cut-off stiffness value. Moreover, SWE technology provided a high reliability in distinguishing PCa based on their phenotypes (grades of PCa). At last, the technology has also shown good diagnostic performance in the detection of margin status and stage of the disease.

References

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