The Egyptian Journal of Radiology and Nuclear Medicine (2015) 46, 761–768

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

www.elsevier.com/locate/ejrnm
www.sciencedirect.com

ORIGINAL ARTICLE

Value of ultrasound elastography versus transrectal prostatic biopsy in prostatic cancer detection

Amr Abd El Fattah Hassan Gadalla [a,*], Sherif Fathy Abd El Rahman [a], Shady Elia Anis [b], Mohsen El-Sayed khalil [a]

[a] *Radiodiagnosis, Faculty of Medicine, Cairo University, Egypt*
[b] *Pathology, Faculty of Medicine, Cairo University, Egypt*

Received 27 February 2015; accepted 9 May 2015
Available online 27 May 2015

KEYWORDS

Prostatic cancer;
Transrectal biopsy;
Ultrasound elastography;
Strain ratio

Abstract *Objective:* To detect the impact of ultrasound elastography in diagnosis of prostatic cancer, and to evaluate its capability in differentiating benign from malignant lesions.
Materials and methods: Fifty patients with different prostatic lesions suspicious for malignancy were included. All patients had a conventional B-mode ultrasound examination and color Doppler imaging, and then real time ultrasound elastography was performed in the same session. Finally, the results were compared to the histo-pathological results of those lesions.
Results: The addition of Strain ratio parameter for evaluating the elastography images showed the highest sensitivity of 74.2%, specificity of 73.7% and accuracy of 74.0% at a best cutoff point of 5.5 between benign and malignant lesions.
Conclusion: Based on our results, prostate US combined with elastography can be a helpful tool for finding malignant lesions. Also it can help in targeting the biopsy site.

1. Introduction

Prostate cancer is the 2nd most common cancer worldwide for males, and the 5th most common cancer overall (1). Because there is no effective way of detecting prostate cancer with current imaging techniques, systematic ultrasound-guided biopsy is used to detect prostate cancer in patients with elevated prostate specific antigen (PSA) levels. However, sampling errors are common, and many patients have to repeat biopsies before cancer is detected (2). Ultrasound elastography was developed in the early nineties as an alternative ultrasonographic technique able to visualize tissue stiffness (3). Prostate carcinoma is significantly stiffer than normal prostate tissue. Using sonoelastography to target biopsy sites has the potential to allow prostate cancer detection with fewer biopsy cores than systematic biopsy (4). The principle of elastography is that tissue compression produces strain (displacement) within the tissue and that the strain is smaller in harder tissue than in softer

* Corresponding author.
E-mail addresses: dr_amr722@hotmail.com (A.A. El Fattah Hassan Gadalla), sfathy1977@hotmail.com (S.F.A. El Rahman), Shadyeliaanis76@yahoo.com (S.E. Anis), dr_mohsenkhalil@yahoo.com (M. El-Sayed khalil).
Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.

http://dx.doi.org/10.1016/j.ejrnm.2015.05.009

tissue. Therefore, by measuring the tissue strain induced by compression, we can estimate tissue hardness (5). In order to assess the Elastographic appearance of the prostate, Kamoi et al. proposed a subjective scoring system that takes into account both the grayscale appearance and the stiffness displayed by elastography. The key point in this scale is represented by the relationship between a hypoechoic lesion and a stiff prostatic area. Lesions scaled 3 and above are highly suggestive of malignancy (6). Strain ratio measurement is obtained by dividing the mean strain within the normal prostatic tissue by the mean strain from the lesion (7).

2. Patients and methods

2.1. Study population

2.1.1. Inclusion criteria

- The study was prospectively carried on 50 male patients with prostatic lesions (between June 2013 and February 2015). Male patients with abnormal digital rectal examination of the prostate and/ or value of PSA > 4 ng/ml were included in the study after obtaining informed consent. The study is IBR approved.

2.1.2. Exclusion criteria

- Patients with anal complications or rectal mass.
- Patients subjected to prostatic adenomectomy (TURP or open adenomectomy).
- Patients refusing the examination.
- Patients with bleeding tendency.

2.2. Equipment

- The study was performed on a digital ultrasound scanner (EUB-7500; Hitachi medical, Tokyo, Japan) with real time tissue elastography unit EZU-TE3, by placing a high frequency (7.5 MHz) endorectal end-fire transducer in close proximity to the prostate.

2.3. Techniques

- First, prostatic lesions were evaluated by conventional B-mode ultrasound and color Doppler imaging. On the same session, real time US elastography examination was performed. The probe was applied to the prostate and was compressed and retracted at a fixed speed in a direction perpendicular to the diagnosis area. The probe was applied with light pressure and used the ''press indicator'', which is a column of numbers displayed on the side of the image that shows the current amount of compression with the probe, as a guide. Lesions were biopsied by using US guided interventional procedures by true cut needle biopsy (via 22-gauge spinal needle). Imaging findings were correlated with sextant prostate biopsies and targeted biopsies on suspicious areas.

3. Elastography analysis

- We chose a color map in which red and green indicate softer areas, while blue indicate harder areas. We set the Region of

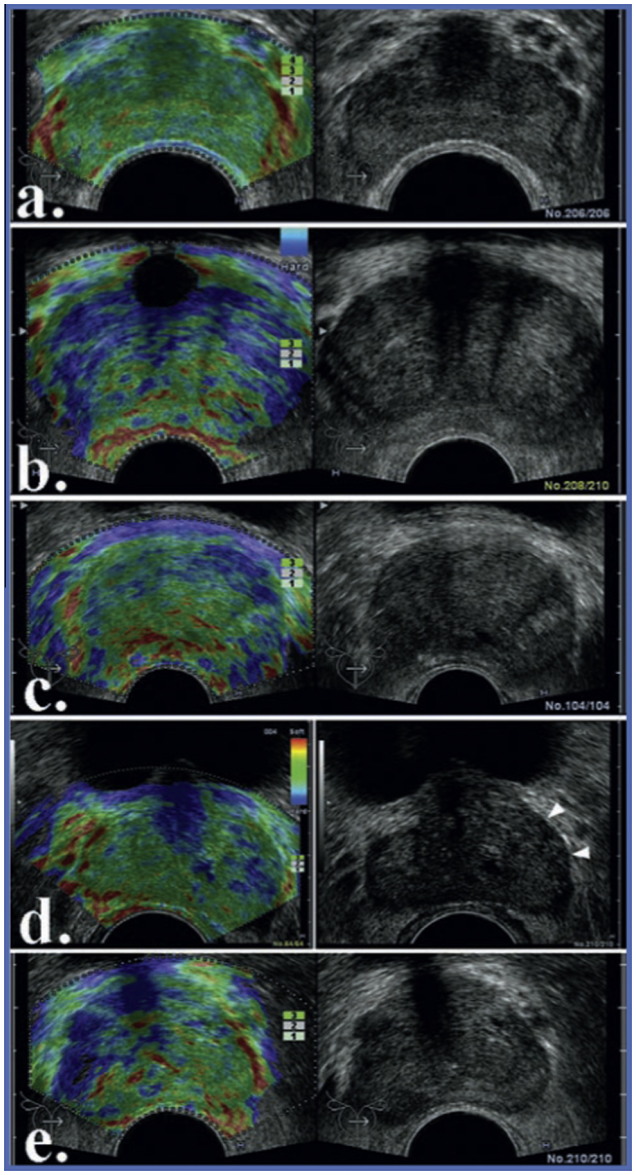

Fig. 1 Sonoelastographic scoring system proposed by Kamoi et al.: (a) score 1 – normal – homogeneous strain, the entire gland evenly shaded in green; (b) score 2 – probably normal – symmetric heterogeneous strain, the gland shows a symmetrical mosaic pattern of green and blue; (c) score 3 – indeterminate – focal asymmetric stiff lesion not related to hypoechoic area, the focal asymmetric lesion in blue, in the left lobe; (d) score 4 – probably carcinoma – hypoechoic lesion (bulging the contour of the left lobe, arrowheads) with stiffness in the center of the lesion and strain at the periphery; the peripheral part of lesion in green and the central part in blue; (e) score 5 – definitely carcinoma – stiffness in the entire hypoechoic lesion in the right lobe and in the surrounding area, the entire lesion in blue.

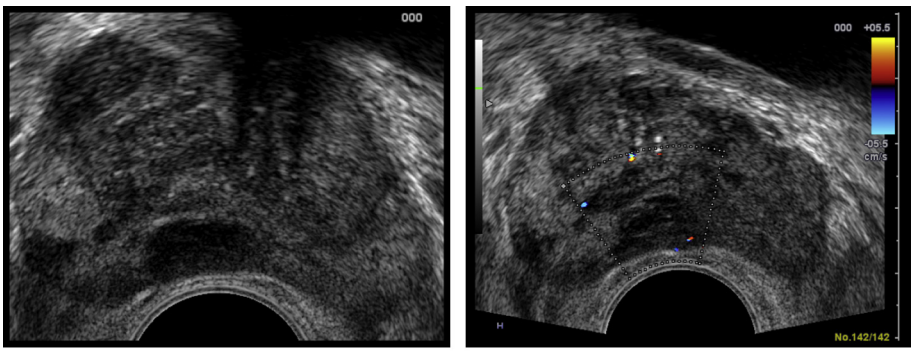

Fig. 2 (a) Transrectal ultrasound B-mode image shows multiple hypoechoic focal lesions in a 62-year-old male presented with prostatic enlargement symptoms, elevated PSA level (30.5 ng/mL) with enlarged hard prostate consistency by PR examination. (b) In color Doppler they appear hypovascular.

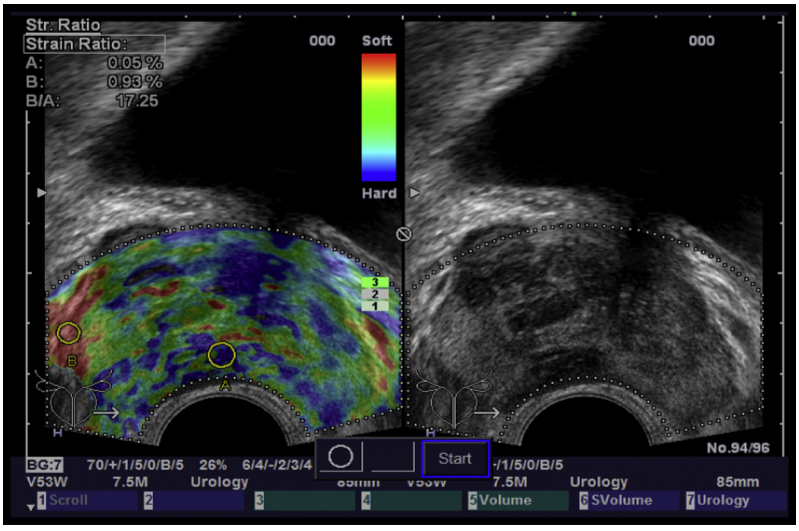

Fig. 3 The strain ratio (SR) calculation in the focal lesion (A) in relation to normal prostatic tissue (B). SR = B/A was 17.25 in this case indicating malignancy. By elastography, the scoring was 4 (strain at the periphery of the hypoechoic lesions with sparing of the center of the lesion, the peripheral part of lesion is green and the central part is blue, so mostly malignant). *TRUS guided biopsy was done revealed prostatic Adenocarcinoma* (*Gleason Score 4 + 4*).

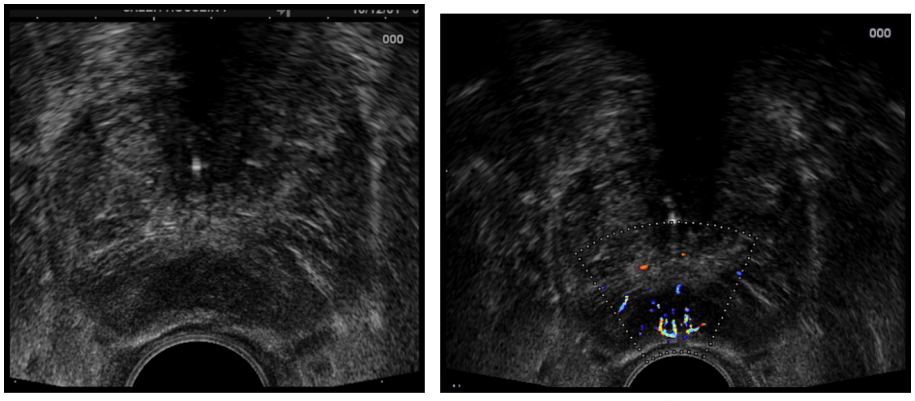

Fig. 4 (a) Transrectal ultrasound B-mode image shows the loss of normal architecture of the peripheral zone with an ill defined hypoechoic focal lesion in a 68-year-old male presented with prostatic enlargement symptoms, elevated PSA level (35 ng/mL) with enlarged hard prostate consistency by PR examination. (b) In color Doppler, it appears hypervascular.

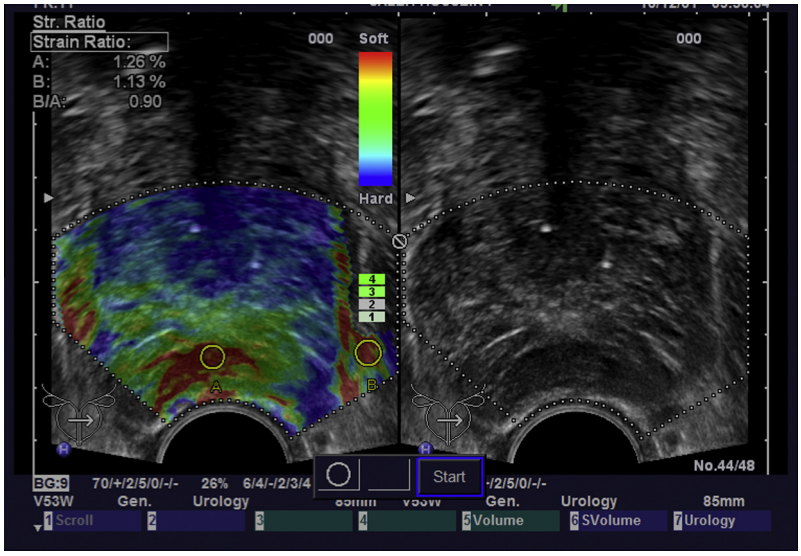

Fig. 5 The strain ratio (SR) calculation in the focal lesion (A) in relation to normal prostatic tissue (B). SR = B/A was 0.9 in this case indicating benign nature. By elastography, the scoring was 3(indeterminate – focal asymmetric stiff lesion not related to hypoechoic area, the focal asymmetric lesion is blue, in the left lobe). *TRUS guided biopsy was done revealed well differentiated Adenocarcinoma, Gleason Score 7 (3 + 4).*

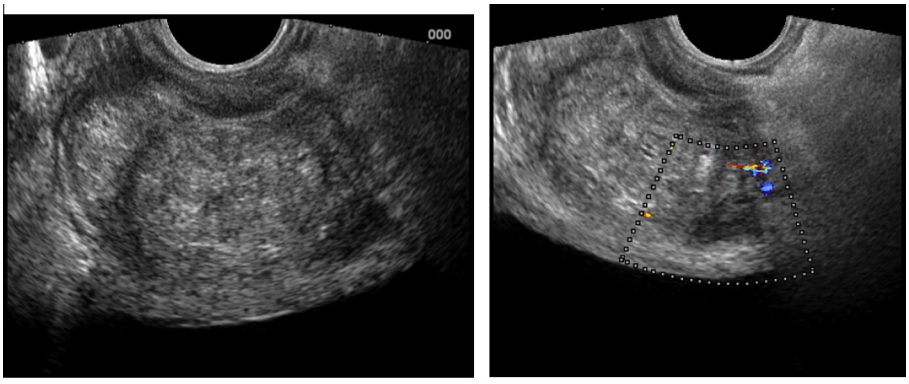

Fig. 6 (a) Transrectal ultrasound B-mode image shows irregular hypoechoic focal lesion in the right lobe of the peripheral zone causing focal capsular bulge in a 72-year-old male presented with prostatic enlargement symptoms, elevated PSA level (21.8 ng/mL) with enlarged hard prostate consistency by PR examination. (b) In color Doppler it appears hypovascular.

interest (ROI) to include a sufficient area of normal gland surrounding the lesion. In the qualitative (color coded) evaluation of the sonoelastographic images, lesion classification was performed on the basis of a 5-point scoring method (Fig. 1). *Score 1*: Homogeneous strain, the entire gland evenly shaded in green. *Score 2*: Symmetric heterogeneous strain, the gland shows a symmetrical mosaic pattern of green and blue. *Score 3*: Focal asymmetric lesion without strain, not related to hypoechoic lesion, the focal asymmetric lesion in blue. *Score 4*: Strain at the periphery of the hypoechoic lesion with sparing of the center of the lesion, the peripheral part of lesion in green and the central part in blue. *Score 5*: No strain in the entire hypoechoic lesion or in the surrounding area, the entire lesion in blue. Then the strain ratios of the lesions were calculated (Figs. 2–7).

4. Results

This study was prospectively carried on 50 patients, the mean age for all patients was 63.1 years (age range, 50–79 years), 19 patients with benign lesions had a mean age of 60.4 years (age range, 54–70 years), and 31 patients with malignant lesions had a mean age of 64.7 years (age range, 50–79 years). The median of the total PSA level for all patients was 31.8 ng/mL (range, 7.5–130 ng/mL). The median for prostatic volume was 63.0 mL (range, 43–145 mL). Conventional B-mode ultrasound examination and real-time ultrasound elastography were performed, 8 (16%) patients were categorized as Elastoscoring 2, 14 (28%) patients were categorized as Elastoscoring 3, 19 (38%) patients were categorized as Elastoscoring 4, and 9 (18%) patients were categorized as

Fig. 7 The strain ratio (SR) calculation in the focal lesion (A) in relation to normal prostatic tissue (B). SR = B/A was 35 in this case indicating malignancy. By elastography, the scoring was 4 (strain at the periphery of the hypoechoic lesion with sparing of the center of the lesion, the peripheral part of lesion is green and the central part is blue, so mostly carcinoma). *TRUS guided biopsy was done revealed Adenocarcinoma, Gleason Score 9 (4 + 5).*

Elastoscoring 5. Strain ratio was calculated (range, 0.49–50). According to elastography results, 28 out of 50 patients (56%) had prostatic cancer and 22 out of 50 patients (44%) had benign lesions. The final pathological diagnoses in our study revealed 31 out of 50 patients (62%) were positive for prostate carcinoma and 19 out of 50 patients (38%) were negative for prostate carcinoma. The pathological score for prostate cancer patients in our study revealed 9 patients out of 31 (29%) with Gleason score 2 + 2, 3 patients with Gleason score 2 + 3 (9.7%), 2 patients with Gleason score 3 + 3 (6.5%), 6 patients with Gleason score 3 + 4 (19.4%), 8 patients with Gleason score 4 + 4 (25.8%), 2 patients with Gleason score 4 + 5 (6.5%), and 1 patient with Gleason score 5 + 5 (3.2%). For statistical analysis we considered Elastoscoring categories of 1, 2, 3 as benign and that of 4 and 5 as malignant. On performing this, there were 14 cases out of 19 (73.7%) cases were benign (true negative) by sonoelastography compared to the pathology, and 23 cases out of 31 (74.2%) cases were malignant by sonoelastography compared to the pathology (true positive), 5 cases out of 19 (26.3%) are false positive, and 8 cases out of 31 are false negative (25.8%) as shown in Table 1. The prostate is divided into sex areas as follow: peripheral median, intra-adenomatous, peripheral right, peripheral left, apex and anterior. Each area is evaluated by elastography, and 300 systematic cores were taken in addition to 100 cores from suspicious areas. Evaluation of sensitivity, specificity, PPV, NPV and accuracy

Table 1 Description of different parameters.

	Description (n = 50)	
Age range, mean ± SD	50–79	63.1 ± 7.6
Median, IQR	62.5	56.8–68.3
Elastography scoring n (%)		
2	8	16.0
3	14	28.0
4	19	38.0
5	9	18.0
Elastography results n (%)		
Malignant	28	56.0
Non-malignant	22	44.0
Pathology n (%)		
Malignant	31	62.0
Non-Malignant	19	38.0
Pathology score (n = 31) n (%)		
2 + 2	9	29.0
2 + 3	3	9.7
3 + 3	2	6.5
3 + 4	6	19.4
4 + 4	8	25.8
4 + 5	2	6.5
5 + 5	1	3.2
Prostatic volume range, mean ± SD	43–145	75.2 ± 27.2
Median, IQR	63.0	57.8–91.8
PSA level range, mean ± SD	7.5–130	43.2 ± 36.5
Median, IQR	31.8	10.0–74.0
Strain ratio range, mean ± SD	0.49–50	16.0 ± 15.6
Median, IQR	9.5	3.3–30.4

SD = standard deviation, IQR interquartile range.

Table 2 Percentage distribution of different anatomical prostatic zones among the proved prostatic cancer patients, total cases and total biopsy cores.

Cores	N	% out of total malignant (n = 31) (%)	% out of total cases (n = 50) (%)	% out of total cores (n = 300) (%)
Peripheral right	6	19.4	12.0	2.0
Peripheral left	5	16.1	10.0	1.7
Peripheral median	9	29.0	18.0	3.0
Apex	3	9.7	6.0	1.0
Intra-adenomatous	7	22.6	14.0	2.3
Anterior	1	3.2	2.0	0.3

Table 3 Sensitivity, Specificity, PPV, NPV and Accuracy of elastography at each core separately and for targeted cores from suspicious areas.

	Sensitivity (%)	Specificity	PPV (%)	NPV (%)	Accuracy (%)
Peripheral right	100.0	50.0	21.4	100.0	56.0
Peripheral left	60.0	44.4	10.7	90.9	46.0
Peripheral median	88.9	51.2	28.6	95.5	58.0
Apex	33.3	42.6	3.6	90.9	42.0
Intra-adenomatous	57.1	44.2	14.3	86.4	46.0
Anterior	100.0	44.9	3.6	100.0	46.0
Sum of cores	74.2	46.1	13.7	93.9	49.0
Targeted cores	86.4	87.8	91.1	81.8	87.0

Table 4 Comparison of pathology result regarding different parameters.

	Pathology		*P* value
	Malignant ($n = 31$)	Non-Malignant ($n = 19$)	
Elastography results n (%)			
Malignant	23, 74.2%	5, 26.3%	0.001
Non-Malignant	8, 25.8%	14, 73.7%	
Age			
Range	50.0–79.0	54.0–70.0	0.053
Mean ± SD	64.7 ± 8.4	60.4 ± 5.0	NS
Median	64.0	60.0	
Prostatic volume			
Range	43.0–145.0	52.0–80.0	0.003
Mean ± SD	84.2 ± 31.0	60.4 ± 7.2	S
Median	67.0	58.5	
PSA level			
Range	12.0–130.0	7.5–14.0	< 0.001
Mean ± SD	63.7 ± 32.1	9.8 ± 1.8	S
Median	63.5	9.5	
Strain ratio			
Range	0.9–50.0	0.5–19.0	< 0.001
Mean ± SD	22.4 ± 16.3	5.5 ± 5.6	S
Median	21.0	3.3	

Mann Whitney test.

Table 5 Comparison of elastography result regarding different parameters.

	Elastography results		*P* value
	Malignant ($n = 28$)	Non-Malignant ($n = 22$)	
Age			
Range	55.0–79.0	50.0–70.0	0.002
Mean ± SD	66.1 ± 7.5	59.2 ± 5.8	S
Median	64.5	59.0	
Prostatic volume			
Range	43.0–103.0	52.0–145.0	0.891
Mean ± SD	68.7 ± 15.9	83.4 ± 35.7	NS
Median	64.0	60.0	
PSA level			
Range	9.0–130.0	7.5–102.0	0.062
Mean ± SD	47.8 ± 34.8	37.3 ± 38.5	NS
Median	40.5	10.5	

Mann Whitney test.

was calculated for each core separately as well for targeted cores from suspicious areas as shown in Tables 2 and 3.

The malignancy detected by elastography was significantly associated with true malignancy in the pathology results. The mean age for malignant lesions was slightly higher than that for benign lesions and this difference was statistically insignificant (*P* value 0.053). It was found that the median PSA level for malignant lesions was 63.5 ng/mL and 9.5 ng/mL for non-malignant lesions. This difference was statistically significant (*P* value < 0.001). It was found that the median prostatic volume for malignant lesions was 67 mL and 58.5 mL for non-malignant lesions .This difference was statistically significant (*P* value 0.003). It was found that the median strain ratio was 21.0 for malignant lesions and 3.3 for non-malignant lesions, and this difference was statistically significant (*P* value < 0.001) as shown in Table 4. According to elastography results, there was a significant difference between malignant and non-malignant lesions regarding age while there was no significant difference between malignant and non-malignant lesions regarding prostatic volume and PSA level as shown in Table 5. Strain ratio showed significant proportionate strong correlation with pathological Gleason score. It also showed significant proportionate moderate correlation with age and PSA level while no significant correlation between the strain ratio and prostatic volume as shown in Table 6. Roc curve analysis revealed that strain ratio was a significant discriminant factor in predicting prostate malignancy (*P* value < 0.001) with area under curve (AUC) 0.828 and 95% confidence interval (0.717 – 0.938). Screening analysis of elastography in the prediction of malignancy using strain ratio revealed, the most accurate cutoff point of strain ratio as presented by ROC curve analysis was ⩾ 5.5 with sensitivity 74.2%, Specificity 73.7%, PPV 82.1%, NPV 63.6% and accuracy 74.0% as shown in Tables 7 and 8.

5. Discussion

False results, both positive and negative, may occur during sonoelastography for prostate cancer, with a sizeable influence

Table 6 Correlation of strain ratio with other parameters.

	Strain ratio	
	r	*P* value
Age	0.459	0.001 S
Prostatic volume	0.011	0.939 NS
PSA level	0.409	0.003 S
Pathology score	0.872	<0.001 S

r = Spearman correlation coefficient, NS = non-significant, S = significant.

ROC curve analysis to explore the discriminant ability of strain ratio in predicting malignancy.

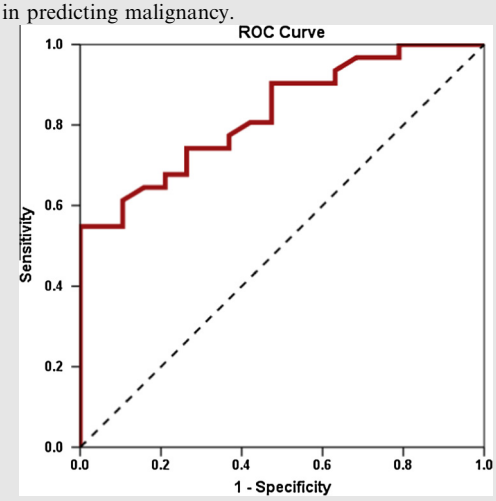

Table 7 ROC curve analysis revealed that SR was a significant discriminant factor in predicting prostate malignancy (*P* value <0.001) with AUC 0.828 and 95% confidence interval (0.717–0.938).

Tested variable	AUC	95% CI	*P* value
Strain ratio	0.828	0.717–0.938	<0.001

Table 8 The most accurate cutoff point of strain ratio as presented by ROC curve analysis was ⩾ 5.5 with sensitivity 74.2%, Specificity 73.7%, PPV 82.1%, NPV 63.6% and accuracy 74.0%.

Tested variable	Cutoff point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Strain ratio	⩾5.5	74.2	73.7	82.1	63.6	74.0

on sensitivity and specificity (8). Prostate volume above 80 cc or a large transitional zone places part of the prostate out of the range of sonoelastography. Large calcification in the peripheral gland as a consequence of prostatitis induces hard areas in the parenchyma. Multifocal tumors with individual focus diameter less than 3–5 mm are difficult to depict. Very large tumors, involving the whole gland, do not produce focal stiff areas. On the other hand, positive elastography with negative biopsy has been reported in the benign hypertrophy patients (9). The majority of false positive results are associated with chronic inflammation and atrophy in the basal area of the gland (10). The main limitations of the method are related to the variability induced by manual operation of the probe and examiner experience. The effect of these limitations may be reduced by using automated balloon pulsation and verifying the accuracy of vibration on the automated scale (11). In our study, screening analysis of elastography in prediction of malignancy using pathology as a gold standard revealed, the most accurate cutoff point of strain ratio as presented by ROC curve analysis was ⩾5.5 with sensitivity 74.2%, Specificity 73.7%, PPV 82.1%, NPV 63.6% and accuracy 74.0%. The study done by Salomon et al. (12) reported sensitivity (75.4%), specificity (76.6%), PPV (87.8%), NPV (59%), and accuracy (76%) and the study done Barr et al. (13) reported sensitivity of 100%, specificity of 95.6%, PPV of 75%, and NPV of 100%. In our study, we found that the strain ratio of 5.5 as the cutoff point, between malignant and benign lesions could be identified accurately which is close to the cutoff point 3.05 in the previous study done by Zhai et al. (14) and far away from the cutoff point 17.44 in the study done by Zhang et al. (15). In our study we found also that the strain ratio had significant proportionate strong correlation with the pathological Gleason score. The studies done by Sumura et al. (16) and Zhang et al. (15) reported the strong relationship between the Gleason scores and the elastographic findings.

6. Conclusion

Based on our results, prostate US elastography can be a helpful tool for finding malignant lesions. Also it can help in targeting the biopsy site; however, better evaluation by bigger study is advised.

Conflict of interest

We have no conflict of interest to declare or any financial support for production of the manuscript.

Acknowledgment

Our sincere thanks and love to all our professors and colleagues in the Radiology and pathology departments, faculty of Medicine, Cairo University, for their support.

References

(1) Ferlay J, Shin HR, Bray F, et al. Globocan 2008 v1.2, Cancer incidence and mortality worldwide: IARC Cancer Base No. 10 [Internet]. Lyon, France. International Agency for Research on Cancer; 2010.
(2) Aigner F, Pallwein L, Junker D, et al. Value of real-time elastography targeted biopsy for prostate cancer detection in men with prostate specific antigen 1.25 ng/ml or greater and 4.00 ng/ml or less. J Urol 2010;184:913–7.
(3) Nelson ED, Slotoroff CB, Gomella LG, Halpern EJ. Targeted biopsy of the prostate: the impact of color Doppler imaging and

elastography on prostate cancer detection and Gleason score. Urology 2007;70:1136–40.
(4) Pallwein L, Aigner F, Faschingbauer R, et al. Is real–time elastography targeted biopsy able to enhance prostate cancer detection? Analysis of detection rate based on an elasticity scoring system. In: Eighth International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity, Sept. 14–17, Vlissingen, the Netherlands; 2009.
(5) Itoh A, Ueno E, Tohno E, et al. Clinical application of US elastography for diagnosis. Radiology 2006;239:341–50.
(6) Kamoi K, Okihara K, Ochiai A, et al. The utility of transrectal real-time elastography in the diagnosis of prostate cancer. Ultrasound Med Biol 2008;34:1025–32.
(7) Dowell B. Real time tissue elastography. Ultrasound 2008;16:123–7.
(8) Pelzer A, Heinzelbecker J, Kirchner M, Stroebel P, Michel SM. Limitations of real-time elastography in the detection of prostate cancer. Important facts for future studies. J Urol 2010;183(Suppl):e780.
(9) Miyagawa T, Tsutsumi M, Matsumura T, et al. Real-time elastography for the diagnosis of prostate cancer: evaluation of elastographic moving images. Jpn J Clin Oncol 2009;39:394–8.
(10) Pallwein L, Aigner F, Pinggera G, Mitterberger M, Frauscher F. Bartsch G – Is real-time elastography targeted biopsy able to enhance prostate cancer detection? Value of an elasticity-scoring system, American Urological Association Annual Meeting, May 17–22. USA: Orlando; 2008.
(11) Giurgiu CR, Dudea SM, Coman I. Elastography in the early detection of prostate cancer. J. Radiother Med Oncol 2010;16:89–93.
(12) Salomon G, Köllerman J, Thederan I, et al. Evaluation of Prostate cancer detection with ultrasound real-time elastography: a comparison with step section pathological analysis after radical prostatectomy. Eur Urol 2008;54:1354–62.
(13) Richard G. Barr, MD, PhD, Richard Memo, MD, and Carl R. Schaub, MD, "Shear Wave Ultrasound Elastography of the Prostate, Ultrasound Quarterly Vol. 28, Number 1, March; 2012.
(14) Zhai L, Madden J, Foo WC, et al. Acoustic radiation force impulse imaging of human prostates ex vivo. Ultrasound Med Biol 2010;36:576–88.
(15) Zhang Yan, Tang Jie, Li Yan-mi, et al. Differentiation of prostate cancer from benign lesions using strain index of transrectal real-time tissue elastography. Euro J Radiol 2012;81:857–62.
(16) Sumura M, Shigeno K, Hyuga T, et al. Initial evaluation of prostate cancer with real-time elastography based on step-section pathologic analysis after radical prostatectomy: a preliminary study. Int J Urol 2007;14(9):811–6.