

Quantitative Analysis of Ultrasound Tissue Diffusion Elastography in The Diagnosis of Benign and Malignant Prostate Lesions

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Purpose: This study aims to evaluate the value of quantitative analysis of ultrasound real-time tissue diffusion elastography in the diagnosis of benign and malignant prostate lesions.

Materials and Methods: From March 2010 to June 2013, 52 patients suspected with prostate cancer based on laboratory or clinical test results and underwent prostate biopsy in our hospital were enrolled into this study. The age of these patients ranged between 45-82 years, with an average age of 67.2 ± 6.8 years. All patients underwent transrectal real-time ultrasound elastography (TRTE) before biopsy. A total of 63 prostate nodules were detected, and the 11 elastic characteristic quantities of these nodules were quantitatively analyzed via tissue diffusion quantitative analysis. The results of ultrasonography were compared with the results of operation and pathology.

Result: Among these 11 characteristic quantities, which include the mean (MEAN) and standard deviation (SD), blue area ratio (AREA%), complexity (COMP), kurtosis (KURT), skewness (SKEW), contrast (CONT), equality (ENT), entropy (IDM), consistency (ASM) and correlation (CORR), except for COMP and CORR, the differences in other nine characteristic quantities between benign and malignant prostatic nodules were statistically significant ($P < 0.05$). Among these, the AREA% and MEAN had the highest correlation, which were 0.791 and -0.791, respectively. The Youden's index (sensitivity and specificity) of AREA% in the ROC curves was the highest, the cutoff value was 80.65% for the diagnosis of prostate cancer, sensitivity was 87.9%, and specificity was 96.6%.

Conclusion: Quantitative analysis of ultrasound real-time tissue diffusion elastography is helpful in the diagnosis of benign and malignant prostate lesions, provides a relatively accurate evaluation method in clinical practice, and has broad application prospects.

Keywords: ultrasound; elastography; prostate cancer; tissue dispersion quantitative analysis; biopsy

INTRODUCTION

Prostate cancer has become one of the major diseases that threatens the health of elderly men. In recent years, its incidence has increased annually in China. Furthermore, the missed diagnosis rate of digital rectal examination in the diagnosis of cancers is as high as 80%, hence, its value is very limited.⁽¹⁾ Prostate-specific antigen (PSA) detection and transrectal ultrasonography (TRUS) greatly improves the early diagnosis of prostate cancer, and are significantly better than digital rectal examination.⁽²⁾

However, 25-45% of prostate cancer patients present with normal PSA levels.⁽³⁾ At present, the conventional diagnosis of prostate nodules by TRUS is mainly according to the location, shape, envelope, internal echo and blood flow at the sites of the lesions; which has low sensitivity and specificity.⁽⁴⁾ In addition, cell density in prostate cancer is higher than in normal tissues, and this increase in cell density would lead to changes in tissue elasticity.⁽⁵⁾

Clinical pathology studies have shown that there are significant differences in the elastic coefficients of fat, breast, fibrotic tissue, non-invasive carcinogenesis and invasive cancerous tissue. Therefore, the degree of deformation of different tissues under different external forces will be different. The tissue elastography technique is based on this theory and receives the information of the tissue displacement after compression by echo, and displays it by color signal encoding after computer super-high speed processing. Real-time tissue elastography (RTE) is by means of exert internal pressure or external pressure on tissues with the probe. Under the conditions of elastic mechanics and biomechanics, these tissues generate a response such as the distribution of displacement, strain and velocity. According to differences in the elastic coefficient of tissues, the strains vary. Furthermore, the echo signals before and after compression were collected and analyzed. According to the displacement of different positions in the tissues, the deformation degree is calculated and displayed as images using grayscale or color coding.

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Table 1. Analysis of elastic characteristic quantity of benign and malignant lesions of prostate.

Group	Number of Lesions	MEAN	SD	AREA%	COMP	KURT	SKEW	CONT	ENT	IDM	ASM
Optimum	29	86.75 ± 30.49	38.56 ± 12.77	36.24 ± 27.52	25.83 ± 8.97	3.15 ± 1.11	0.65 ± 0.47	29.97 ± 5.57	3.18 ± 0.35	0.26 ± 0.08	0.00 ± 0.00
Malignant	33	18.18 ± 3.16	19.76 ± 12.67	91.09 ± 14.29	25.14 ± 17.64	6.60 ± 4.16	1.57 ± 0.77	24.87 ± 4.33	2.22 ± 0.62	0.57 ± 0.18	0.09 ± 0.14
F value		11.49	6.01	21.401	4.502	18.828	7.397	1.565	4.751	17.514	34.816
P value ^a		0.000	0.016	0.000	0.038	0.000	0.009	0.216	0.033	0.000	0.000

^a $P < 0.05$ was considered statistically significant.

In the present study, with postoperative puncture and pathological results as the gold standard, RTE and the quantitative analysis of tissue diffusion were applied in the differential diagnosis of benign and malignant prostate lesions to evaluate its diagnostic value.

MATERIALS AND METHODS

Research Data

This study was approved by the ethical committee. From March 2010 to June 2013, 52 patients suspected with prostate cancer based on laboratory or clinical test results and underwent prostate biopsy in our hospital were enrolled into this study. The age of these patients ranged between 45-82 years, with an average age of 67.2 ± 6.8 years. Exclusion criteria were: patients who received treatment for prostate disease before admission including transurethral resection of the prostate, particle implantation for prostate cancer, and prostate hormone therapy, patients with a prostate size exceeding the transrectal real-time ultrasound elastography (TRTE) range, and patients who underwent prostate puncture within one year. All patients underwent ultrasound-guided biopsy or surgery to obtain pathological results. There are two pathologists who both had experience over ten years and they were unaware of the clinical conditions and ultrasound performance of the patients. All patients agreed to participate in this study and provided a signed informed consent.

Instruments and Methods

The HiVision 900 color Doppler ultrasound diagnostic apparatus (Tokyo, Japan) was used for this study, with the EUP-V53W probe. The frequency ranged between 4-9 MHz. The patient was positioned in the left lateral position and underwent routine TRUS to detect the nodules and observe the morphology, envelope, internal echo and blood flow, and measure systolic velocity (Vs) and diastolic velocity (Vd) of the blood flow and resistance index (RI) within the lesions.

The mode was switched to elastic imaging, and the gray-scale map and elastic graph were simultaneously observed using the dual display function. The probe was adjusted to show the nodule at the center of the screen, pressure was manually exerted on the prostate using a transrectal probe, and elastic imaging was performed by steady small jitter until a stable and repeatable dynamic elastic graph was obtained. If nodules were not found by two-dimensional ultrasound, the mode was switched to elastic imaging after conventional TRUS; and the whole prostate was first observed. Then, the probe was laterally adjusted, and the bilateral internal prostate gland, transitional zone and the outer gland region were observed. The pressure value was displayed as a number within 1-5 in real-time. It was only when the elastic images were continuously displayed and the pressure values were within 4-5 that the test results could be

evaluated with valid results.

Quantitative Measurement of Tissue Diffusion

The image was analyzed using the random elastic tissue diffusion quantitative analysis software. The position of the sampling frame did not exceed the largest rectangular area of the scope of the lesion. Measurement was conducted three times, and the mean was calculated. Hence, 11 quantitative parameters of tissue diffusion were obtained, including the mean (MEAN) and standard deviation (SD), blue area ratio (AREA%), complexity (COMP), kurtosis (KURT), skewness (SKEW), contrast (CONT), equality (ENT), entropy (IDM), consistency (ASM) and correlation (CORR).

Statistical Analysis

Data were analyzed using statistical software SPSS 12.0. The 11 characteristic quantities of the elastic imaging of benign and malignant lesions of the prostate were tested for normal distribution. Data in normal distribution were compared using *t*-test, and data in non-normal distribution were compared using nonparametric *U*-test. $P < 0.05$ was considered statistically significant. The correlation between elastic characteristic quantities and pathological grades was analyzed using Spearman correlation analysis. The receiver operating characteristic curve (ROC) was drawn using significant characteristic quantities. Then, the sensitivity and specificity of each characteristic quantity in the diagnosis of prostate cancer was calculated.

RESULTS

Among the 52 patients in study group, a total of 63 prostate lesions were detected by TRTE. It was confirmed by biopsy that 20 lesions were malignant. Among these lesions, 12 nodules had a Gleason score of 2-6 points, two nodules had a Gleason score of 7 points, and six nodules had a Gleason score of 8-10 points. Furthermore, 43 nodules were benign lesions. Among these lesions, nine cases were combined with chronic inflammation of the prostate and one case was combined with grade II of prostatic intraepithelial neoplasm (PIN, **Figures 1-3**). Furthermore, the PSA levels of these included patients ranged between 0.38-100 ng/mL, with an average value of 39.9 ng/mL and a median value of 18.7 ng/mL. Among these patients, seven patients had a PSA level of < 4 ng/mL, 13 patients had a PSA level of > 4 ng/mL and < 10 ng/mL, and 32 patients had a PSA level of ≥ 10 ng/mL.

The 11 characteristic quantities of prostate lesions were determined to be not in the normal distribution. Nonparametric *U*-test analysis revealed that, except for COMP and CORR, differences in other nine characteristic quantities between benign and malignant prostatic nodules were statistically significant ($P < 0.05$). Correlation analysis revealed that AREA%, IDM, SKEW, KURT and ASM were positively correlated with the malignant

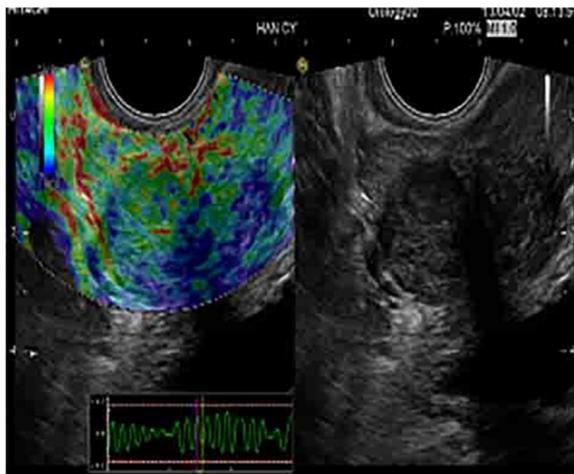


Figure 1. Different types of prostate pathological changes of color doppler ultrasound and ultrasound elasticity imaging. 1a Right low echo between inner and outer gland nodules,Inside, and high resistance arterial spectrum, TRUS malignant likely prompt. 1b The right between the inner and outer gland nodules,TRTE showed lesions subject for the green,with a little blue, score, level, a diagnosis of benign hyperplastic nodule. Confirmed by biopsy for prostate hyperplasia, interstitial small amounts of acute or chronic inflammatory cells infiltration.

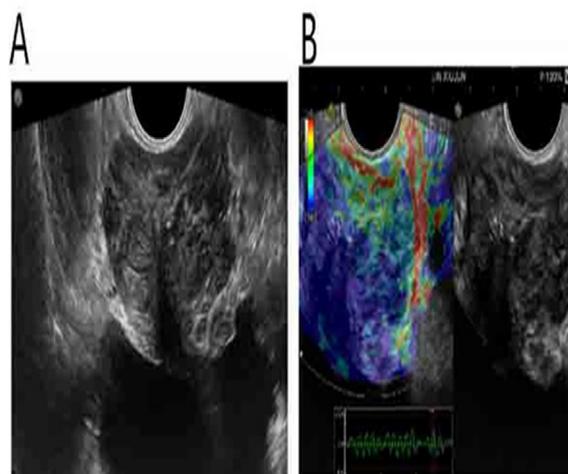


Figure 3. Different types of prostate pathological changes of color doppler ultrasound and ultrasound elasticity imaging. 3a The left side is no clear boundary between internal and external gland diffuse to reduce on the right side of the outer gland low echo nodules TRUS prompt malignant. 3b Lesions completely covered by blue, and the blue range is greater than the TRUS detected lesions area, involvement of bilateral internal and external gland, TRTE score level, a diagnosis of malignant, Confirmed by biopsy in poorly differentiated adenocarcinoma of prostate, Gleasonscore 5 + 4 = 9 points, both inner and outer gland needle puncture eight right carcinoma tissue.

degree of lesions; and the correlation coefficients were 0.791, 0.754, 0.581, 0.488 and 0.398, respectively. Furthermore, the correlation with AREA% was the highest. MEAN, ENT, SD and CONT were negatively correlated with the malignant degree of lesions, and the correlation coefficients were -0.791, -0.721, -0.600 and -0.466, respectively. Furthermore, correlation with MEAN was the highest (Table 1).

The ROC for the diagnosis of prostate cancer was drawn using the 11 characteristic quantities of elastic imaging. The Youden's index (sensitivity and specificity) of AREA% was the highest, the area under the curve (AUC) was 0.961, the diagnostic cutoff value was 80.65%, sensitivity was 87.9%, and specificity was 96.6%. Based on the Youden's index (from high to low), the diagnostic efficiencies of the other eight character-

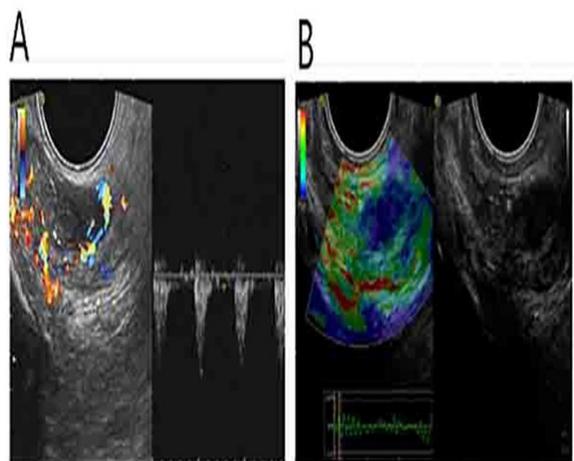


Figure 2. Different types of prostate pathological changes of color doppler ultrasound and ultrasound elasticity imaging. 2a The left outer gland low echo nodules, inside, and high resistance arterial spectrum TRUS malignant likely prompt. 2b The left outer gland nodules is almost covered by blue, blue and lesion area roughly the same score level a diagnosis of malignant. Confirmed by biopsy for moderately differentiated adenocarcinoma of prostate, Gleason score 3 + 3 = 6 points.

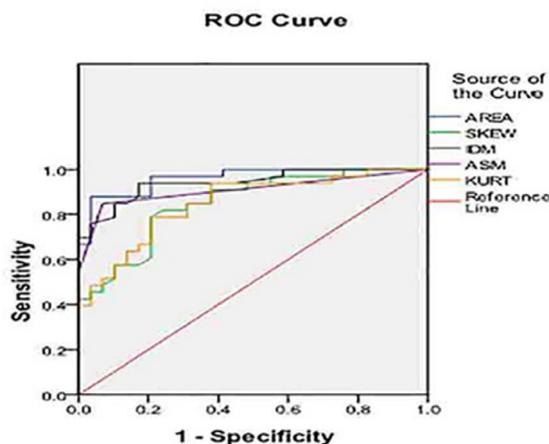


Figure 4. Positive correlation characteristics of benign and malignant lesions of the prostate diagnostic value of ROC curve.

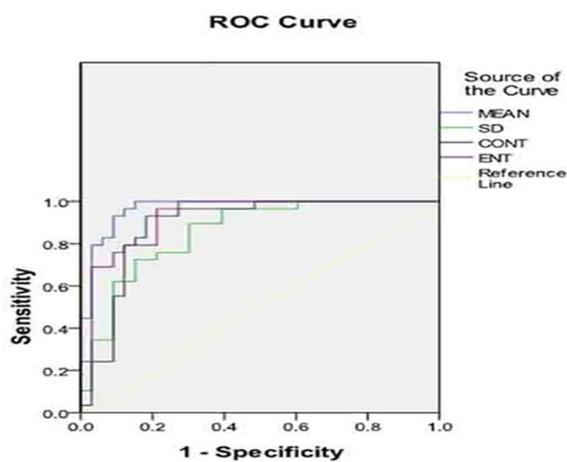


Figure 5. Negative correlation characteristics of benign and malignant lesions of the prostate diagnostic value of ROC curve.

istic quantities were MEAN, ASM, IDM, ENT, CONT, SD, SKEW and KURT, respectively; and the cutoff values were 45.15, 0.005, 0.315, 2.695, 16.65, 23.25, 0.93 and 3.75, respectively. Furthermore, the sensitivities were 87.9%, 93.1%, 84.8%, 93.9%, 96.6%, 93.1%, 89.7% and 78.8%, respectively; and the specificities were 96.6%, 90.9%, 93.1%, 82.8%, 78.8%, 81.8%, 69.7% and 79.3%, respectively (**Figures 4 and 5**).

DISCUSSION

Since 1991, real-time tissue diffusion elastography was proposed, and was gradually developed and applied. At present, it has gradually become mature in the diagnosis of breast and thyroid diseases. In the past, the diagnosis method of prostate elasticity was Kamoi 5-grade scoring.⁽⁶⁾ Its principle is to exert internal pressure such as heart beat and respiration or external pressure on tissues with the probe. Under the conditions of elastic mechanics and biomechanics, these tissues generate a response such as the distribution of displacement, strain and velocity. According to differences in the elastic coefficient which is stress/strain of tissues, the strains vary. Furthermore, the echo signals before and after compression were collected and analyzed. According to the displacement of different positions in the tissues, the deformation degree is calculated and displayed as images using grayscale or color coding. In recent years, TRTE transforms the migration amplitude of echo signals before and after compression into real-time color images, and describes the soft, medium hard and hard textures as red, green and blue colors, respectively. The large change in the displacement of tissues after compression is shown as red, the small change in the displacement of tissues after the compression is shown as blue, and the medium change in the displacement of tissues after the compression is shown as green. The elasticity of different tissues is encoded using color, which reflects its relative hardness.⁽⁷⁻⁹⁾ Kamoi K et al. confirmed that the above methods were helpful in improving the diagnostic rate of prostate lesions.⁽⁷⁾ On this basis, Hitachi has developed the tissue diffusion quantitative analysis software, which obtains 11 elastic characteristic quantities through the measurement of the strain histogram, for the quantitative evaluation of

tissue flexibility. The core of this method is the characteristic quantity extraction, grading and analysis of the degree of tissue diffusion in real-time tissue elastography.⁽¹⁰⁾ In this study, this technique was used for the quantitative evaluation of prostate gland lesions. Results revealed that among the 11 elastic characteristic quantities, except for COMP and CORR, differences in other nine characteristic quantities between benign and malignant prostatic nodules were statistically significant ($P < 0.05$). Among these, AREA% and MEAN had the highest correlation, the Youden's index of AREA% was the highest, and the cutoff value in the diagnosis of prostate cancer was 80.65%. In this study, the AREA% was lower than this cut-off value in two cases of malignant lesions, and the clinical stages of these two cases were highly differentiated adenocarcinoma. From the pathological perspective, due to the retention of the lumen, highly differentiated adenocarcinoma is very similar to normal prostate glands.⁽¹¹⁻¹³⁾ Therefore, in further studies, the relationship between the degree of differentiation of prostate cancer and the hardness of cancer tissues should be examined, in order to provide a more accurate preoperative assessment in clinical practice. However, this study had some limitations. First, sample size needs to be enlarged in the future study. Second, the external pressure on tissues with the probe have subjectivity.

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CONFLICT ON INTEREST

The authors have no conflicts of interest to declare.

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