Doppler Spectral Waveform Parameters at Neurovascular Bundle Vessels in Patients with Prostate Biopsy

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Abstract

Introduction and Objectives: There is a need to improve prescreening determination of prostate cancer to better select patients who need biopsy. Such a strategy properly implemented, will decrease the number of negative biopsies for prostate cancer and in turn better balance the risks and morbidity for patients recommended for biopsy. The aim of study is to investigate Doppler spectral waveform parameters of neurovascular bundle (NVB) vessels and determine differences between benign and malignant pathologies.

Patients and Methods: We performed a prospective analysis involving 292 patients who received prostate biopsy for elevated prostate-specific antigen (PSA) values or abnormal digital rectal examination, as well as 174 patients with symptomatic benign prostatic hyperplasia. Doppler spectral waveform (DSW) parameters (peak-systolic velocity [PSV], end-diastolic velocity [EDV], and resistive index [RI]) were measured at bilateral NVB vessels through Doppler transrectal ultrasound at the right lateral decubitus position, compared, and analyzed among patients with benign versus malignant histology for each side.

Results: Overall, both PSV and EDV at malignant sides were significantly higher than those at benign sides, as well as lower RI (all p -values <0.05 , unpaired t -test). In subgroup analysis with 93 patients of serum PSA between 10 and 20 ng/mL and 56 patients with one-side malignancy, higher EDV and lower RI were significantly associated with malignancies (all $p < 0.05$). The values of PSV and EDV rather than RI might be influenced by the patients' position and RI by the prostate volume.

Conclusions: In this study, DSW parameters (mainly EDV and RI) at NVB vessels were significantly associated with prostate cancer, particularly in patients with serum PSA of 10–20 ng/mL. It should be in caution that the patients' position and prostate volume may influence the Doppler signal as demonstrated in the current study. These findings can provide more diagnostic information before prostate biopsy.

Introduction

PROSTATE CANCER continues as the second leading male malignancy contributing to mortalities in the western countries.¹ A total of 238,590 estimated new prostate cancer cases and 29,720 deaths from prostate cancer occur in the United States in 2013.¹ Despite the utility of prostate-specific antigen (PSA) screening and the technical advances in prostate biopsy, more than half of these patients were diagnosed at advanced or metastatic disease in Taiwan.² Although there might be many contributing factors, one possible issue is that many aged men or urologists may fear prostate biopsy-related complications, such as hemorrhage or sepsis if the prostate cancer diagnosis is not assured before biopsy. There is a need to improve prescreening determination of prostate

cancer to better select patients who need biopsy. Such a strategy properly implemented, will decrease the number of negative biopsies for prostate cancer and in turn better balance the risks and morbidity for patients recommended for biopsy.

Several researchers have attempted to develop some innovative imaging techniques to improve prostate cancer detection, such as Doppler-related techniques,^{3–7} ultrasonic elastography,⁸ and magnetic resonance imaging of the prostate.⁹ Doppler techniques have been applied in perfusion studies of the prostate gland for the last two decades.¹⁰ Some studies have demonstrated that Doppler targeted biopsy can detect as many cancers as systematic biopsy with fewer than half the number of biopsy cores in combination with contrast enhancement and medication.¹¹ The blood supply of the

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prostate mainly derives from the inferior vesical artery whose branches enter the prostate mainly at each neurovascular bundle (NVB) site.¹² Therefore, the aim of this study is to investigate the Doppler spectral waveform (DSW) parameters of NVB vessels before prostate biopsy and to determine the differences between benign and malignant pathologies, which might provide some additional information to patients or urologists before prostate biopsy is conducted.

Patients and Methods

Study protocol and data collection were approved by the institutional review board (ER-99-246). We used a prospective cohort study design. Men who had received transrectal ultrasound of the prostate (TRUS) at our hospital from January 2007 to January 2010, were enrolled in our study. Men who had either rising or elevated PSA (>3.5 ng/mL) or abnormal digital rectal examination (DRE) were recommended for transrectal ultrasound-guided biopsy of the prostate. Men who received TRUS examination for symptomatic benign prostatic hyperplasia (BPH) were also enrolled into this study as references.

The ultrasound machine used for TRUS was the HAWK 2102 EXL scanner equipped with a type 8808 transducer (B-K Medical, Copenhagen, Denmark). Before measuring DSW parameters, patients received the conventional 2D gray-scale TRUS, according to the same procedures described as previously.¹³ Briefly, all the patients were examined in the right lateral decubitus position. The volume of the whole prostate or transitional zone (TZ) were according to the following ellipsoid formula, $0.52 \times td \times apd \times ccd$, where *td* represented the transverse diameter of the prostate or adenoma; *apd*, the anteroposterior diameter of the prostate or adenoma; and *ccd*, the craniocaudal diameter of the prostate or adenoma. TZ index means TZ volume divided by total prostate volume.

Subsequently, DSW parameters were measured to determine the prostatic blood flow. The prostatic vasculatures at bilateral NVB sites were analyzed in the largest transverse section of the prostate (Fig. 1) in accordance with reports by Leventis and colleagues¹⁴ and Neumaier and colleagues¹⁵ The arteries at the NVB sites were examined at the point just be-

fore they entered the prostate, rather than the intraprostatic branches penetrating into the gland. Once the pulsatile waveforms of a given Doppler spectrum became stable for the consecutive five repeats, the peak-systolic velocity (PSV), end-diastolic velocity (EDV), and the resistive index (RI) of each site were measured and recorded. Since PSV and EDV measurements are angle dependent, the angle was fixed to 56° for all of the studied groups. During the entire ultrasonographic study, care was taken to avoid excess probe pressure on the rectal wall. In addition, each patient was asked to empty his urinary bladder to preclude the compression of the intraprostatic vasculature.

The biopsy strategy was systematically random with 10 biopsy cores. The pathology report contained the detail of each core, including benign or malignancy, Gleason grading and score, and the percentage of malignant area. Patients who had <10 cores due to intolerable pain were viewed as inadequate biopsy. Patients both with inadequate biopsy and benign pathology were excluded from the study.

Statistics

Values are expressed as the mean $\pm$ SD and were analyzed statistically using the Prism GraphPad Prism 5.00 for Windows (GraphPad Software, San Diego, CA) software package. When $p < 0.05$, the result is viewed as having statistical significance.

Results

Basic characteristics

For these three consecutive years, a total of 470 patients received TRUS-guided biopsy at our hospital due to either elevated serum PSA, abnormal DRE, or both. Among them, 330 patients had conventional gray scale TRUS, power Doppler, and DSW measurement by the same senior urologist. Meanwhile, 38 patients with benign biopsy were excluded from the analysis due to inadequate prostate biopsy. In addition, 174 symptomatic BPH patients with normal serum PSA level, DRE, and benign imaging were enrolled for analysis. The basic characteristics of all the analyzed patients (174

FIG. 1. Doppler spectral waveform measurements at neurovascular bundle (NVB) vessels bilaterally. The arteries at the NVB sites were examined at the point just before they entered the prostate, rather than the intraprostatic branches penetrating into the gland. Once the pulsatile waveforms of a given Doppler spectrum become stable for the consecutive five repeats, the peak-systolic velocity (PSV), end-diastolic velocity (EDV), and resistive index (RI) of each site were measured with a fixed angle of 56° .

symptomatic BPH and 292 biopsied) are described in Table 1 according to PSA levels and pathological report. In each PSA subgroup, prostate cancer patients exhibited higher age, lower total prostate volume, TZ volume, and TZ index than did those with benign biopsy (each $p < 0.05$).

Effect of patients' age and prostate volume on DSW parameters

Since some basic characteristics (e.g., prostate volume and age) differ statistically significant between patients with benign and malignant biopsies, we evaluated the correlation between the patients' age, prostate volume, and DSW parameters in patients with symptomatic BPH (imaged benign) and benign biopsy. The results revealed that the patients' age was negatively correlated with EDV of right NVB (Pearson r , -0.247 ; p -value, 0.02) and RI of left NVB (Pearson r , -0.238 ; p -value, 0.03) in symptomatic BPH patients, but not in the patients with benign biopsy. In terms of prostate volume, both TZ index and total prostate volume positivity correlated with bilateral RI and inversely with EDV of right NVB (p values < 0.05) (Supplementary Table S1; Supplementary Data are available online at www.liebertpub.com/end).

Effect of patients' position on DSW parameters

To investigate whether the patient position can influence the values of DSW parameter, the values of PSV, EDV, and RI at bilateral NVB vessels of symptomatic BPH (imaged benign) patients who had neither serum PSA levels > 4.0 ng/mL nor abnormal DRE were routinely measured in the right lateral decubitus position and compared in a paired manner (right *vs* left). The results showed that there were a significant difference of PSV values between right and left NVB vessels (21.0 ± 8.4 mL/second *vs* 18.6 ± 8.1 mL/second, $p = 0.0028$, paired t -test) and a marginally statistical difference of EDV values (4.1 ± 2.6 mL/second *vs* 3.7 ± 2.0 mL/second, $p = 0.0543$, paired t -test). Despite this, there was no difference for the RI values between both sides (0.78 ± 0.13 *vs* 0.78 ± 0.13 , $p = 0.9283$, paired t -test). A subset of 12 patients was simultaneously measured in the left lateral decubitus position. The results

showed that the PSV values of right and left NVB vessels were 15.7 ± 2.7 mL/second and 17.4 ± 4.7 mL/second, respectively ($p = 0.315$, paired t -test). The EDV values of right and left NVB vessels were 3.78 ± 1.38 mL/second and 3.78 ± 1.17 mL/second, respectively ($p = 0.995$, paired t -test). The RI values of right and left NVB vessels were 0.76 ± 0.11 and 0.77 ± 0.10 , respectively ($p = 0.718$, paired t -test). Despite the lack of any statistical significance, the PSV values seem to be influenced in the left lateral decubitus position, rather than EDV and RI. Taken together, the PSV values might be influenced by the patients' position, but RI might not.

DSW parameters in patients with one-side malignancy

According to pathological results from prostate biopsy, there were 143 patients with benign diseases, 56 with one-side malignancy, and 93 with bilateral prostate cancer. Among 56 patients with one-side prostate cancer, the NVB vessels of malignant sides had significantly higher EDV values and lower RI values as compared with the other benign sides (EDV, 7.4 ± 5.5 mL/second *vs* 4.5 ± 2.9 mL/second, $p < 0.0001$; RI, 0.67 ± 0.11 *vs* 0.75 ± 0.13 , $p = 0.001$, paired t -test) (Fig. 2).

DSW parameters according to PSA levels

Overall, the PSV values of right NVB vessels at benign and malignant sides were 21.4 ± 8.1 mL/second and 24.0 ± 11.0 mL/second, respectively ($p = 0.039$), and those of left NVB vessels were 21.5 ± 9.2 mL/second and 24.5 ± 12.0 mL/second, respectively ($p = 0.031$). The EDV values of right NVB vessels at benign and malignant sides were 4.3 ± 2.8 mL/second and 6.9 ± 5.0 mL/second, respectively ($p < 0.0001$), and those of left NVB vessels were 4.2 ± 2.6 mL/second and 6.9 ± 5.1 mL/second, respectively ($p < 0.0001$). The RI values of right NVB vessels at benign and malignant sides were 0.79 ± 0.12 and 0.71 ± 0.12 , respectively ($p < 0.0001$), and those of left NVB vessels were 0.79 ± 0.12 and 0.70 ± 0.14 , respectively ($p < 0.0001$).

The significance of these DSW parameters was further investigated according to the PSA subgroups. The analysis was done only using data obtained from a 10-core biopsy. As for patients with PSA < 10 ng/mL, the EDV value of left NVB

TABLE 1. BASIC CHARACTERISTICS OF PATIENTS RECEIVING PROSTATE BIOPSY ACCORDING TO PSA LEVELS AND PATHOLOGY

Values (Mean $\pm$ SD)	Symptomatic BPH	Patients with prostate biopsy					
		PSA < 10 ng/mL (n = 97)		10 $\leq$ PSA $\leq$ 20 (n = 93)		PSA > 20 (n = 102)	
		Benign	Malignancy	Benign	Malignancy	Benign	Malignancy
Total, n	174	75	22	51	42	17	85
Age (years)	61.6 $\pm$ 11.7	65.6 $\pm$ 9.5	70.5 $\pm$ 7.2	65.2 $\pm$ 8.7	71.3 $\pm$ 7.3	68.5 $\pm$ 8.6	75.2 $\pm$ 6.7
*p			0.03		0.0005		0.0005
PSA (ng/mL)	1.6 $\pm$ 1.0	6.4 $\pm$ 2.2	6.3 $\pm$ 2.0	13.3 $\pm$ 2.3	15.2 $\pm$ 3.2	29.8 $\pm$ 9.1	58.9 $\pm$ 12.89
*p			0.84		0.0013		0.08
Prostate size (mL)	27.3 $\pm$ 14.1	45.1 $\pm$ 17.1	24.7 $\pm$ 18.0	57.5 $\pm$ 19.7	45.4 $\pm$ 23.1	75.3 $\pm$ 35.0	50.7 $\pm$ 24.8
*p			< 0.0001		0.0077		0.0008
TZ size (mL)	8.6 $\pm$ 11.5	26.1 $\pm$ 16.6	10.9 $\pm$ 13.1	37.5 $\pm$ 20.2	24.0 $\pm$ 20.9	56.1 $\pm$ 36.6	29.7 $\pm$ 22.3
*p			0.0002		0.0022		0.0001
TZ index	0.25 $\pm$ 0.19	0.52 $\pm$ 0.22	0.35 $\pm$ 0.20	0.62 $\pm$ 0.19	0.46 $\pm$ 0.21	0.66 $\pm$ 0.22	0.51 $\pm$ 0.23
*p			0.0016		0.0002		0.0145

*p, unpaired t -test, benign versus malignancy.

SD = standard deviation; BPH = clinical benign prostatic hyperplasia; PSA = prostate-specific antigen; TZ = transitional zone.

FIG. 2. Side-to-side comparisons of PSV, EDV, and RI values in patients with one-side malignancy. Among 56 patients with one-side prostate cancer, the vessels of the malignant sides had significant higher EDV values and lower RI values as compared with the other benign sides (EDV, 7.4 ± 5.5 mL/second vs 4.5 ± 2.9 mL/second, $p < 0.0001$; RI, 0.67 ± 0.11 vs 0.75 ± 0.13 , $p = 0.001$, paired t -test).

vessels was significantly higher at the malignant sides than those at the benign ones (6.8 ± 5.4 mL/second vs 4.2 ± 3.0 mL/second, $p = 0.013$). The RI value of left NVB vessels was significantly higher at the malignant sides than those at the benign ones (0.69 ± 0.11 vs 0.80 ± 0.12 , $p = 0.0006$). Among patients with PSA between 10 and 20 ng/mL, the malignant halves exhibited significantly higher EDV values and lower RI values of bilateral NVB vessels as compared with the benign halves (all p -values < 0.05). The PSV values at the left NVB site were significantly higher in the malignant prostate halves than those in benign prostate ones (25.0 ± 11.1 mL/second vs 20.0 ± 9.1 mL/second, $p = 0.046$). Among patients with PSA more than 20 ng/mL, the EDV values at the right NVB site were significantly higher in the malignant prostate halves than those in benign prostate ones (7.3 ± 5.5 mL/second vs 4.1 ± 2.4 mL/second, $p = 0.017$). The RI values at the right NVB site were significantly higher in the malignant prostate halves than those in benign prostate ones (0.71 ± 0.12 vs 0.79 ± 0.12 , $p = 0.012$) (Table 2).

Diagnostic performance of DSW parameters

Among the 292 biopsied patients, the diagnostic performances of EDV and RI were comparable (area under the curve [AUC], 0.687 and 0.657, respectively), and both of the two were better than PSV (AUC, 0.575). Nevertheless, the diagnostic performances of all the three DSW parameters were less significant compared with the PSA level (AUC, 0.812). Among patients with PSA levels < 20 ng/mL, both of EDV and RI were comparable with PSA in terms of diagnostic performance (AUC, 0.690, 0.692 and 0.684, respectively). There was no significance noted with regard to PSV (Fig. 3). If the cutoff value of EDV is 4.5 mL/second, the sensitivity and specificity of EDV will be 65.5% and 66.7%, respectively. If the cutoff value of RI is 0.71, the sensitivity and specificity of EDV will be 71.5% and 60.3%, respectively.

Discussion

As compared with normal prostate tissue, prostate cancer tends to have increased vascular density for oxygen and nutrition requirement.¹² As displayed by power Doppler ultrasonography, the vascular anatomy of the normal prostate demonstrates a reproducible and symmetric flow pattern.¹⁴ There were several flow patterns categorized as a sign

of prostate cancer, including increased flow within or surrounding a lesion, asymmetric flow in comparison to adjacent tissue or contralateral areas, and mass effect changes (a gap in perfusion around the lesion due to the compression of vessels by the pressure of the tumor mass) on the vessel structures.^{3-5,16,17} The image interpretation of Doppler-related techniques in most studies of prostate cancer detection depends on either the change of Doppler signal in density or distribution on the conventional gray-scale TRUS image. Such interpretation can only provide some qualitative information. In the current cohort, we found that several statistically significant differences are seen in the DSW

TABLE 2. VALUES OF DOPPLER SPECTRAL MEASUREMENTS AT BILATERAL NEUROVASCULAR BUNDLE VESSELS

	Benign	Malignancy	p values*
PSA, < 10 ng/mL			
N	75	22	
PSV, right NVB	20.8 ± 8.4	21.4 ± 7.9	0.801
PSV, left NVB	22.1 ± 10.2	21.1 ± 12.1	0.732
EDV, right NVB	4.5 ± 3.2	5.1 ± 3.0	0.562
EDV, left NVB	4.2 ± 3.0	6.8 ± 5.4	0.013
RI, right NVB	0.77 ± 0.12	0.73 ± 0.10	0.253
RI, left NVB	0.80 ± 0.12	0.69 ± 0.11	0.0006
PSA, 10–20 ng/mL			
N	51	42	
PSV, right NVB	21.8 ± 7.4	22.6 ± 8.7	0.703
PSV, left NVB	20.0 ± 9.1	25.0 ± 11.1	0.046
EDV, right NVB	4.1 ± 2.4	7.5 ± 4.6	0.002
EDV, left NVB	4.0 ± 2.3	7.7 ± 5.8	0.004
RI, right NVB	0.80 ± 0.12	0.67 ± 0.13	< 0.0001
RI, left NVB	0.78 ± 0.13	0.69 ± 0.14	0.011
PSA, > 20 ng/mL			
N	17	85	
PSV, right NVB	22.0 ± 9.0	25.2 ± 12.1	0.296
PSV, left NVB	20.1 ± 8.1	23.8 ± 12.4	0.255
EDV, right NVB	4.1 ± 2.4	7.3 ± 5.5	0.017
EDV, left NVB	4.6 ± 1.9	6.8 ± 4.9	0.081
RI, right NVB	0.79 ± 0.12	0.71 ± 0.12	0.012
RI, left NVB	0.75 ± 0.11	0.70 ± 0.14	0.207

* p , unpaired t -test.

NVB=neurovascular bundle; PSV=peak systolic velocity; EDV=end-diastolic velocity; RI=resistive index.

FIG. 3. Comparisons of diagnostic performance of PSV, EDV, and RI values with the prostate-specific antigen (PSA) values in all biopsied patients (**A**) or in patients with PSA values <20.0 ng/mL (**B**). Among the 292 biopsied patients, the diagnostic performances of EDV and RI were comparable (area under the curve [AUC], 0.687 and 0.657, respectively), and both were better than PSV (AUC, 0.575). Among patients with PSA levels <20 ng/mL ($n=190$), both EDV and RI were comparable with PSA in terms of diagnostic performance (AUC, 0.690, 0.692, and 0.684, respectively). There was no significance as for PSV (**C**). C.I., confidence interval.

measured data. For example, increased EDV and reduced RI values at NVB vessels were significantly found in the prostate halves with malignancy. Although the measured DSW parameters demonstrate significant overlap, but appear statistically distinct, it is interesting from a scientific perspective. In addition, it implicates a hypotheses that whether a correlation between tumor angiogenesis and the changes of DSW parameters of NVB vessels of prostate cancer exists.

Although there were some technical differences among three Doppler-related perfusion imaging techniques, the accuracy rate reported in prostate cancer detection was similar and had a wide variation (color Doppler, 53%–84%; power Doppler, 40%–83%; contrast-enhancing Doppler, 40%–91%).¹⁸ Therefore, it is thought that Doppler techniques might not be suitable as a tool for early detection of prostate cancer. Indeed, in a cohort of 579 patients with a PSA of more than

3.5 ng/mL, 20 of 39 patients with T1c cancer were basically invisible when using the power of Doppler imaging alone.¹⁹ Eisenberg and colleagues, in a cohort of 620 men receiving radical prostatectomy, reported that 443 (71.5%) patients had a hypervascular lesion seen on preoperative TRUS imaging.²⁰ Such data reflect the limited performance in diagnosing early prostate cancer. Doppler-related techniques have been thought to be used as a tool for optimizing the number of useful biopsy cores and to avoid some unnecessary biopsy cores mainly in advanced diseases.^{19,21} Like other Doppler techniques, DSW parameters at NVB vessels investigated in the present study are not good for prostate cancer detection in patients with PSA levels <10 ng/mL. Nevertheless, we demonstrated that EDV and RI rather than PSV might help in differentially diagnosing prostate cancer in patients with PSA levels between 10 and 20 ng/mL.

Our data also demonstrated that prostate cancer patients had smaller total prostate volumes, TZ volumes, and less TZ indexes than those with benign biopsy. Like prostate volume, patients' age differs statistically significant between patients with benign and malignant biopsies. In exploring whether these two basic characteristics are confounding factors for the significance of DSW parameters, both total prostate volume and TZ index positively correlate with bilateral RI, inversely with EDV of right NVB, but patients' age does not. Taken together, there were complex interactions existing between basic parameters and DSW parameters. Clinically, these significant DSW parameters can be used for establishing a predictive nomogram of prostate cancer detection in combination with several basic characteristics (e.g., patients' age, PSA or % free PSA values, prostate volume, TZ index).

Actually, many factors may influence or interfere with Doppler signals, which make imaging interpretation complicated and difficult. These factors include treatments with α -blockers,²² 5- α reductase inhibitors,²³ ejaculation,²⁴ inflammation, infection, and prostate calculi.²⁵ In the current study, the patient's position may be a confounding factor. The PSV values of right NVB vessels were significantly higher than those of left NVB ones, and EDV was marginally higher when the patients lay in the right lateral decubitus position. This effect is nearly half as big as the mean differences seen between benign and malignant prostate halves. Although the real mechanism is unclear, the gravity effect or heart position may influence the blood flow velocity (such as PSV or EDV) rather than vascular resistance (RI). It also implicated that such a study can be applied into the researches regarding the end organ perfusion (i.e., vascular impotence). Further, to improve the utility of the Doppler signal as a cancer detector or prognostic indicator, it should be taken into consideration how these factors influence it quantitatively.

The European Association of Urology (EAU) 2012 guideline suggested that at least eight cores should be sampled at a prostate volume of 30–40 mL²⁶ and there were still 10% cancers omitted even in the 12-core random biopsy.²⁷ The major limitation in the current study is the sampling error. The use of only a 10-core biopsy to characterize the benign status of each prostate half is not absolutely accurate. Thus, due to incorrect labeling of a number of prostate halves as benign when cancer is present, would cloud any distinction that might exist between DSW parameters associated with malignant versus benign tissue. Such limitation may affect the statistical significance, particularly the determination of cutoff values of DSW parameters, which will restrict their clinical application in detecting prostate cancer. In fact, a much better characterization of benign or malignant status would result from the pathologic assessment of whole gland prostatectomy specimens (in those operated on for cancer) allowing exact determination of the presence/absence of prostate cancer on each side of the prostate and also a quantification of volume of prostate cancer. However, it is not easy to conduct such a perfect study with adequate number of patients in a single institute because the large proportion of patients receiving radical prostatectomy were not at the earlier stage in Taiwan.²

There were still some limitations in this study. First, all the measurements in this study were done by the same urologist, who may not have been blind to the presence of prostate cancer. Second, the measurements of DSW parameters are

time-consuming, which may discourage the clinical application. In this case, a tool for dynamic and automatic Doppler waveform analyses is worth developing.

Conclusions

In this study, the measured DSW parameters of NVB vessels of the prostate lobes categorized as benign and malignant demonstrate significant overlap, but appear statistically distinct (mainly EDV and RI). This has implications for understanding the underlying physiologic process that leads to these differences in NVB flow parameters and generates additional hypotheses, such that the influences of the patients' position and prostate volume on PSV and RI, respectively. These findings might provide some diagnostic information before prostate biopsy.

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Disclosure Statement

No competing financial interests exist.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013;63:11–30.
2. Pu YS, Chiang HS, Lin CC, et al. Changing trends of prostate cancer in Asia. *Aging Male* 2004;7:120–132.
3. Kuligowska E, Barish MA, Fenlon HM, et al. Predictors of prostate carcinoma: Accuracy of gray-scale and color doppler US and serum markers. *Radiology* 2001;220:757–764.
4. Halpern EJ, Frauscher F, Strup SE, et al. Prostate: High-frequency doppler US imaging for cancer detection. *Radiology* 2002;225:71–77.
5. Roy C, Buy X, Lang H, et al. Contrast enhanced color doppler endorectal sonography of prostate: Efficiency for detecting peripheral zone tumors and role for biopsy procedure. *J Urol* 2003;170:69–72.
6. Toi A, Neill MG, Lockwood GA, et al. The continuing importance of transrectal ultrasound identification of prostatic lesions. *J Urol* 2007;177:516–520.
7. Loch T, Eppelmann U, Lehmann J, et al. Transrectal ultrasound guided biopsy of the prostate: Random sextant versus biopsies of sono-morphologically suspicious lesions. *World J Urol* 2004;22:357–360.
8. Kapoor A, Mahajan G, Sidhu BS. Real-time elastography in the detection of prostate cancer in patients with raised PSA level. *Ultrasound Med Biol* 2011;37:1374–1381.
9. Hoeks CM, Barentsz JO, Hambrock T, et al. Prostate cancer: Multiparametric MR imaging for detection, localization, and staging. *Radiology* 2011;261:46–66.
10. Watanabe H. History and applications of transrectal sonography of the prostate. *Urol Clin North Am* 1989;16:617–622.
11. Mitterberger MJ, Aigner F, Horninger W, et al. Comparative efficiency of contrast-enhanced colour doppler ultrasound targeted versus systematic biopsy for prostate cancer detection. *Eur Radiol* 2010;20:2791–2796.

12. Bigler SA, Deering RE, Brawer MK. Comparison of microscopic vascularity in benign and malignant prostate tissue. *Hum Pathol* 1993;24:220–226.
13. Lan SK, Tsai YS, Lin YH, et al. Diagnostic performance of a random versus lesion-directed biopsy of the prostate from transrectal ultrasound: Results of a 5-year consecutive clinical study in 1 institution in South Taiwan. *J Ultrasound Med* 2007;26:11–17.
14. Leventis AK, Shariat SF, Utsunomiya T, et al. Characteristics of normal prostate vascular anatomy as displayed by power doppler. *Prostate* 2001;46:281–288.
15. Neumaier CE, Martinoli C, Derchi LE, et al. Normal prostate gland: Examination with color doppler US. *Radiology* 1995;196:453–457.
16. Sauvain JL, Palascak P, Bourscheid D, et al. Value of power doppler and 3D vascular sonography as a method for diagnosis and staging of prostate cancer. *Eur Urol* 2003;44:21–30; discussion 30–31.
17. Rifkin MD, Alexander AA, Helinek TG, et al. Color doppler as an adjunct to prostate ultrasound. *Scand J Urol Nephrol Suppl* 1991;137:85–89.
18. Heijmink SW, van Moerkerk H, Kiemeny LA, et al. A comparison of the diagnostic performance of systematic versus ultrasound-guided biopsies of prostate cancer. *Eur Radiol* 2006;16:927–1938.
19. Sauvain JL, Palascak P, Nader N, et al. Power doppler imaging and prostate cancer: Optional or necessary technique? *J Radiol* 2006;87:1063–1072.
20. Eisenberg ML, Cowan JE, Carroll PR, et al. The adjunctive use of power doppler imaging in the preoperative assessment of prostate cancer. *BJU Int* 2010;105:1237–1241.
21. Remzi M, Dobrovits M, Reissigl A, et al. Can power doppler enhanced transrectal ultrasound guided biopsy improve prostate cancer detection on first and repeat prostate biopsy? *Eur Urol* 2004;46:451–456.
22. Pinggera GM, Mitterberger M, Pallwein L, et al. Alpha-blockers improve chronic ischaemia of the lower urinary tract in patients with lower urinary tract symptoms. *BJU Int* 2008;101:319–324.
23. Mitterberger M, Pinggera G, Horninger W, et al. Dutasteride prior to contrast-enhanced colour doppler ultrasound prostate biopsy increases prostate cancer detection. *Eur Urol* 2008;53:112–117.
24. Keener TS, Winter TC, Berger R, et al. Prostate vascular flow: The effect of ejaculation as revealed on transrectal power doppler sonography. *Am J Roentgenol* 2000;175:1169–1172.
25. Takahashi S, Yamada Y, Homma Y, et al. Power doppler ultrasonography-directed prostate biopsy in men with elevated serum PSA levels: An evaluation of the clinical utility and limitations. *Urology* 2002;60:248–252.
26. Heidenreich A, Bellmunt J, Bolla M, et al. EAU guidelines on prostate cancer. Part 1: Screening, diagnosis, and treatment of clinically localised disease. *Eur Urol* 2011;59:61–71.
27. Presti JC, Jr., Chang JJ, Bhargava V, et al. The optimal systematic prostate biopsy scheme should include 8 rather than 6 biopsies: Results of a prospective clinical trial. *J Urol* 2000;163:163–166; discussion 166–167.

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Abbreviations Used

AUC = area under the curve

BPH = benign prostatic hyperplasia

DRE = digital rectal examination

DSW = Doppler spectral waveform

EDV = end-diastolic velocity

NVB = neurovascular bundle

PSA = Prostate-specific antigen

PSV = peak-systolic velocity

RI = resistive index

TRUS = transrectal ultrasound of the prostate

TZ = transitional zone