Comparison of Real-time Sonoelastography With T2-Weighted Endorectal Magnetic Resonance Imaging for Prostate Cancer Detection

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Objectives—The purpose of this study was to compare the value of real-time sonoelastography with T2-weighted endorectal magnetic resonance imaging (MRI) for prostate cancer detection.

Methods—Thirty-three patients with an elevated prostate-specific antigen level were investigated with real-time sonoelastography and T2-weighted endorectal MRI for prostate cancer diagnosis before systematic prostate biopsy. Real-time sonoelastography was performed to assess prostate tissue elasticity, and hard areas were considered suspicious for prostate cancer. Low–signal intensity nodules on T2-weighted endorectal MRI were considered suspicious for prostate cancer. Imaging findings were assigned to 6 areas of the peripheral zone (sextants), and their cancer detection rates were compared.

Results—Overall, prostate cancer was detected in 13 of 33 patients (39.4%). Both real-time sonoelastography and T2-weighted endorectal MRI detected 11 cancer-positive patients (84.6%). Real-time sonoelastography showed 27 suspicious lesions in 198 sextants, and 15 (55.6%) were cancer positive. T2-weighted endorectal MRI showed 31 suspicious lesions in 198 sextants, and 13 (40.6%) were cancer positive. These findings resulted in sensitivity rates and negative predictive values per patient of 84.6% and 86.7%, respectively, for sonoelastography and 84.6% and 83.3% for MRI. The per-sextant analysis showed sensitivity rates and negative predictive values of 57.7% and 93.6% for sonoelastography and 50.0% and 92.2% for MRI.

Conclusions—Real-time sonoelastography showed comparable results as T2-weighted endorectal MRI for prostate cancer detection.

Key Words—biopsy; magnetic resonance imaging; prostate; prostatic neoplasms; sonoelastography

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Abbreviations

DRE, digital rectal examination; MRI, magnetic resonance imaging; NPV, negative predictive value; PSA, prostate-specific antigen

The diagnosis of prostate cancer is based on histopathologic findings from systematic biopsy. Patients with an elevated prostate-specific antigen (PSA) serum level, suspicious digital rectal examination (DRE) findings, or both are scheduled for this procedure. Current recommendations for systematic biopsy of the prostate suggest 10 to 12 transrectal sonographically guided biopsy cores.[1] The limitations of systematic transrectal sonographically guided biopsy are well known because this approach can miss up to 35% of clinically relevant cancers. Furthermore an elevated serum PSA level is often caused by benign changes of the prostate,

eg, prostatitis or benign prostatic hyperplasia.[2–4] In addition, the increasing use of PSA for prostate cancer screening has led to an increased number of men scheduled for prostate biopsy in the last decades, which is associated with increased diagnosis of indolent prostate cancer, increasing costs, and biopsy-related complications.[5]

New diagnostic imaging techniques for prostate cancer have been investigated to reduce the overall number of prostate biopsy cores as well as the overdiagnosis of indolent prostate cancer. Currently, highly sophisticated sonographic techniques, including 3-dimensional sonography, contrast-enhanced sonography, and elastography, and endorectal magnetic resonance imaging (MRI) are the most investigated methods for prostate cancer imaging. Many study groups prefer endorectal MRI with 1.5- or 3-T scanners for prostate cancer diagnosis. Real-time sonoelastography is a novel technique for assessment of tissue elasticity. Several study groups have already shown the potential of real-time sonoelastography in the detection of prostate cancer.[6–8] Nevertheless, before real-time sonoelastography can be recommended as a new routine tool for prostate cancer detection and screening, a comparison of real-time sonoelastographic findings with endorectal MRI would be desirable. Therefore, in this study, we compared the value of real-time sonoelastography with T2-weighted endorectal MRI for prostate cancer detection and screening.

Materials and Methods

Patients

Study data were obtained between January 2005 and July 2007. The 33 patients included in this study were scheduled for prostate biopsy because of an elevated PSA serum level (total PSA, ≥1.25 ng/mL; free PSA, <18%). Patient characteristics are summarized in Table 1. All patients in this study underwent T2-weighted endorectal MRI and real-time sonoelastography before systematic prostate biopsy. Approval was obtained from the local Ethical Review Board (study UN3538). Each participant provided written informed consent before participation.

Table 1. Patient Characteristics (n = 33)

Characteristic	Value
Mean age (range), y	62.6 (43–82)
Mean total PSA (range, median), ng/mL	9.3 (1.9–41.5, 6.4)
Mean free PSA (range, median), %	14.5 (2.2–21.3, 14.7)
Mean prostate volume (range, median), mL	48.1 (15–150, 41)

PSA indicates prostate-specific antigen.

Endorectal MRI

Endorectal MRI was performed on 1.5-T scanners (Symphony Vision and Magnetom Vision; Siemens AG, Erlangen, Germany) using a 4-channel phased array body coil combined with an endorectal coil (MEDRAD, Inc, Warrendale, PA). After DRE, insufflation of the balloon of an endorectal coil was performed with 30 to 50 mL of air. The entire prostate and the seminal vesicles were investigated in axial and sagittal planes using T2-weighted turbo spin echo sequences. T2-weighted endorectal MRI parameters are shown in Table 2.

Real-time Sonoelastography

Real-time sonoelastography was performed using an EUB 8500 ultrasound system (Hitachi Medical Corp, Tokyo, Japan) attached to an end-fire transrectal probe operating at frequencies of 4.0 to 8.0 MHz. Real-time sonoelastographic images were obtained by slight compression and decompression of the prostate, which was manually induced by the investigator using the transrectal probe, based on previous experience.[7] Prostate tissue elasticity was displayed with a color overlay on the gray scale sonogram, which ranged from red (soft) to green (intermediate) and blue (hard), and only the peripheral gland was investigated.

Biopsy Protocol

All patients underwent a systematic 10-core biopsy by an experienced urologist who was blinded to the MRI and sonoelastographic findings. Systematic cores were taken from the peripheral zone of the base (1 time), the mid gland (1 time), and the apex (2 times) of both sides (Figure 1). Additionally, 1 biopsy core was taken from each side of the transition zone. For the purpose of this study, analysis was limited to peripheral zone biopsies.

Table 2. Endorectal Magnetic Resonance Imaging Parameters

Parameter	Symphony Vision[a]	Magnetom Vision[a]
Repetition time, ms	5680/4530	7217/3500
Echo time, ms	122/154	112/119
Slice thickness, mm	3 mm/3 mm	3/3
Field of view, mm	160/160	200/200
Matrix	256 × 256/256 × 256	512 × 512/256 × 256
Acquisition time, min + s	4 + 28/3 + 7	6 + 22/5 + 58

Values are axial/sagittal T2-weighted turbo spin echo sequence parameters.

[a]Siemens AG (Erlangen, Germany).

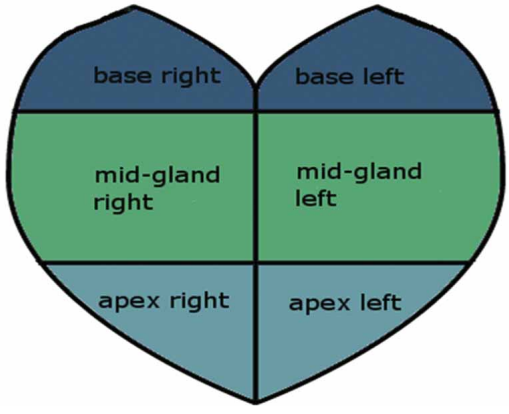
Image Interpretation

Image interpretation was performed by 2 experienced uroradiologists in consensus. Tissue alterations on MRI and sonoelastography were assigned to the sextant regions of the peripheral zone of the prostate (base, mid gland, and apex on the right and left sides). On MR images, low–signal intensity nodules in the normally bright peripheral zone were considered suspicious for prostate cancer (Figure 2A). On sonoelastographic images, hard areas in the peripheral zone colored blue were considered suspicious for prostate cancer, whereas normal prostate tissue was green to red (Figure 2B). The prostate cancer detection rates were compared for the two imaging modalities on the basis of histopathologic findings from systematic biopsy for the peripheral zone only.

Statistical Analysis

Patient characteristics were summarized with frequencies and percentages or with mean, range, median, minimum, and maximum values. Sensitivity rates and negative predictive values (NPVs) were calculated for the two examination methods per patient and per sextant region. A McNemar test was used to compare the proportions of cancer detection for T2-weighted endorectal MRI and real-time sonoelastography in the 198 sextants. All reported *P* values were 2 sided. An α error level of 5% was considered statistically significant for all comparisons. Calculations were performed with SPSS version 16.0 software (SPSS Inc, Chicago, IL).

Figure 1. Zonal anatomy of the prostate (coronal plane). The peripheral zone is divided into 6 regions: base, mid gland, and apex on both sides.



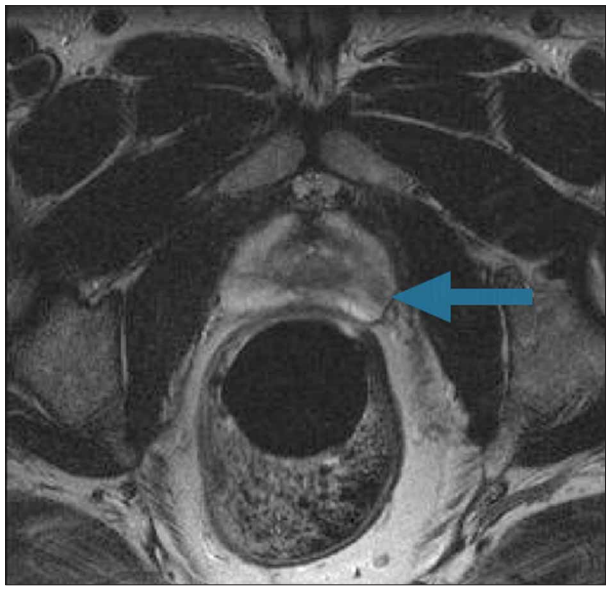
Results

Systematic Biopsy Findings

On systematic biopsy, 13 of the 33 men (39.4%) and 26 of the 198 sextants (13.1%) were cancer positive. The median Gleason score was 6 (range, 5–8). Furthermore, in cancer-negative men, histologic evaluation revealed prostatitis (n = 10), hyperplasia (n = 8), and adenomyomatosis (n = 2).

Figure 2. T2-weighted endorectal magnetic resonance imaging and real-time sonoelastography in a patient with prostate cancer (Gleason score, 7) in the left apex. **A**, Axial magnetic resonance imaging shows nodular-shaped low signal intensity in the left apex (arrow). **B**, Transverse sonoelastography shows a hard blue area (arrow) in the left apex. The sonoelastographic findings correlate with the magnetic resonance imaging findings. No abnormality is shown on gray scale sonography.

A



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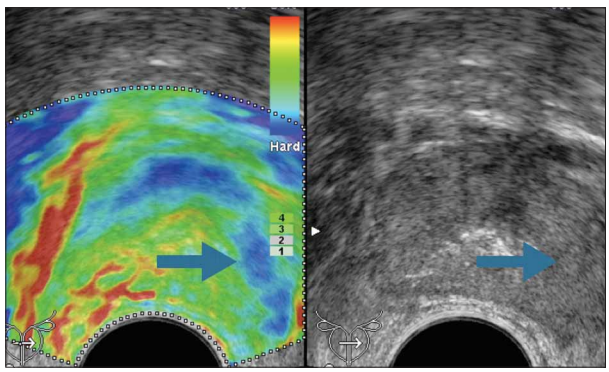


Imaging Findings

On T2-weighted endorectal MRI, findings suspicious for malignancy were shown in 21 of the 33 men (false-positive findings, n = 10) and 32 of 198 sextants (false-positive findings, n = 19). On real-time sonoelastography, findings suspicious for malignancy were shown in 18 of the 33 men (false-positive findings, n = 7) and 27 of the 198 sextants (false-positive findings, n = 12). The average lesion size on MRI was 10.2 mm (range, 5–22 mm), and the size on sonoelastography was 12.6 mm (range, 7–25 mm). The sensitivity rates and NPVs for MRI and real-time sonoelastography are summarized in Table 3.

The pathologic findings associated with our false-positive cases are enumerated in Table 4. For both MRI and sonoelastography, false-positive findings were associated with prostatitis, adenomyomatosis, and benign prostatic hyperplasia (Figure 3).

Detection Rate per Patient

Both real-time sonoelastography and T2-weighted endorectal MRI correctly detected 11 cancer-positive patients (per-patient sensitivity, 84,6%). The NPVs were 86.7% for sonoelastography and 83.3% for MRI (Table 3).

Detection Rate per Sextant

Among 27 suspicious lesions in the peripheral zone shown on real-time sonoelastography, 15 were cancer positive (sensitivity, 57.7%; NPV, 93.6%). Among 31 suspicious lesions in the peripheral zone shown on T2-weighted endorectal MRI, 13 were cancer positive (sensitivity, 50.0%; NPV, 92.2%; Table 3). There were no significant differences in prostate cancer detection rates between the two imaging modalities for the sextants (base, mid gland, and apex of both sides of the prostate; $P > .05$) and all 198 sextant regions ($P = .58$).

Discussion

Prostate cancer is the most common cancer in men in the western world. The American Cancer Society estimated 192,280 new prostate cancer cases and 27,360 deaths from prostate cancer in the United States in 2009.[9] The current standard of care for diagnosis of prostate cancer is based on histopathologic findings from systematic biopsy, during which 10 to 12 cores are taken under sonographic guidance.[1] Transrectal sonography is used in the B-mode to assess prostate anatomy and to guide the biopsy to standardized areas of the prostate, ie, base, mid gland, and apex (Figure 1). However, published literature suggests that systematic biopsy can miss up to 35% of clinically relevant cancers.[3] Saturation biopsy with a minimum of 24 cores has also failed to substantially improve prostate cancer detection.[10] Simon et al[11] reported that there was no significant increase in the cancer detection rate in an extensive saturation biopsy regimen compared with published series using fewer cores, although the morbidity was increased. Therefore, a more intelligent approach to prostate cancer diagnosis is needed.

New methods for prostate cancer imaging, mainly MRI and advanced sonographic techniques, have been proposed with promising preliminary results. Magnetic resonance imaging for detection and local staging of prostate cancer requires the use of an endorectal coil in conjunction with a pelvic phased array coil with a magnetic field strength of at least 1.5 T.[12] However, MRI has several limitations related to limited availability, high cost, and the lack of standardized imaging parameters.[13] Newer sonographic techniques such as color and power Doppler sonography, contrast-enhanced Doppler imaging, contrast-enhanced harmonic imaging, and real-time sonoelastography have been described.[14–16] Contrast-enhanced sonography has been used for visualization of neovascularity within the prostate and in conjunction with targeted prostate biopsy to improve cancer detection compared with systematic biopsy.[17] However, comparisons between endorectal MRI and modern sonographic techniques for prostate cancer detection are lacking.

Table 3. Sensitivity Rates and Negative Predictive Values for the Imaging Methods

Parameter	T2-Weighted Endorectal MRI	Real-time Sonoelastography
Sensitivity per patient, %	84.6 (55–98)	84.6 (55–98)
Sensitivity per area, %	50.0 (30–70)	57.7 (37–77)
NPV per patient, %	83.3 (52–98)	86.7 (60–98)
NPV per area, %	92.2 (87–96)	93.6 (89–97)

Values in parentheses are 95% confidence intervals. MRI indicates magnetic resonance imaging; and NPV, negative predictive value.

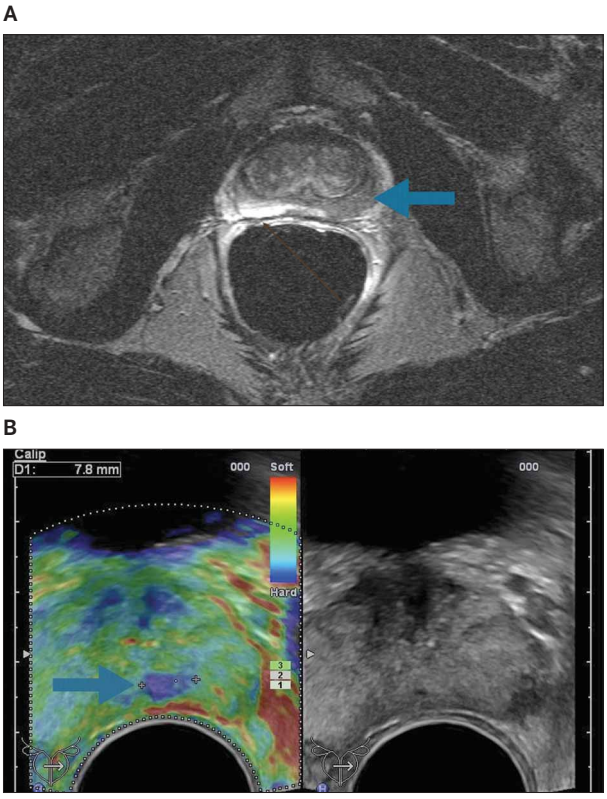
Table 4. False-Positive Imaging Findings

Finding	T2-Weighted Endorectal MRI	Real-time Sonoelastography
Prostatitis	12	4
Hyperplasia	1	3
Adenomyomatosis	6	5
Total	19	12

MRI indicates magnetic resonance imaging.

The increased cellular density in tumors results in a change of tissue elasticity. Detection of peripheral prostate cancer by DRE is based on this change in elasticity. Unfortunately, changes in elasticity that are deep within the prostate may not be palpable on DRE. Therefore, imaging techniques for assessment of tissue stiffness—elastography—have been developed. Krouskop et al[18] used static elastography and described a significant difference in stiffness between normal and neoplastic prostate and breast tissue. New developments have allowed for real-time elastographic imaging. Hard areas that are suspicious for malignancy can be colored (ie, blue). Ongoing technical advances in real-time sonoelastography have enabled the implementation of this method in regular ultrasound units, and the potential of real-time sonoelastography in the detection of prostate cancer has been described in several studies.[6–8] Preliminary studies suggest that elasticity imaging has the potential to target biopsy cores for more consistent diagnosis of cancer and to determine the tumor extent.[19] However, to assess the value of real-time sonoelastography as a new tool for prostate cancer diagnosis, comparison with other well-established imaging modalities such as endorectal MRI is necessary.

Figure 3. T2-weighted endorectal magnetic resonance imaging and real-time sonoelastography in a patient with prostatitis. **A**, Axial magnetic resonance imaging shows a low-signal area in the left mid gland (arrow). **B**, Transverse sonoelastography shows a hard blue area (arrow) in the left mid gland, which is not readily apparent on the corresponding gray scale sonogram.



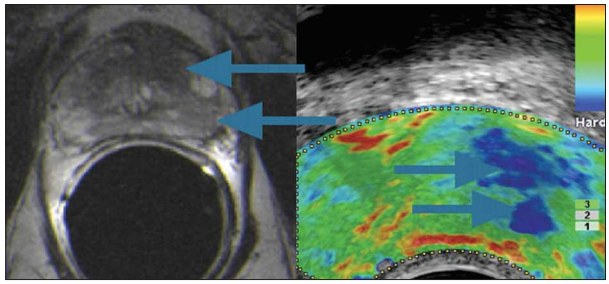
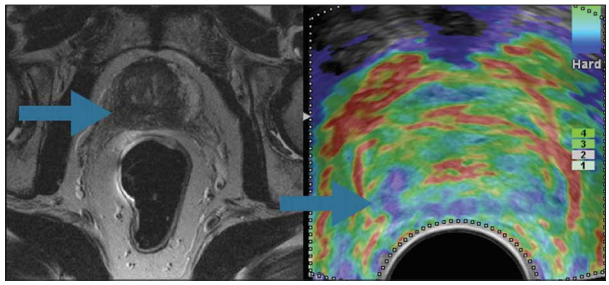


Figure 4. T2-weighted endorectal magnetic resonance imaging and real-time sonoelastography in a patient with prostate cancer (Gleason score, 7) in the left apex. Axial magnetic resonance imaging shows an area of low signal intensity in the left apex, and sonoelastography shows a hard area in the same location (arrows).

T2-weighted endorectal MRI reveals structural and morphologic information that can be correlated directly with real-time sonoelastographic images (Figures 2, 4, and 5). Additional MRI sequences such as dynamic contrast-enhanced MRI, diffusion-weighted imaging, and MRI spectroscopy may improve prostate cancer detection.[20] However, the use of multiple MRI techniques is time-consuming, expensive, and of limited availability.[13] Furthermore, investigations on 3-T MRI may enhance prostate cancer detection even without the use of an endorectal coil, but unfortunately, the availability of 3-T units for prostate studies worldwide still limited.[21]

We therefore chose to compare real-time sonoelastography with T2-weighted endorectal MRI. To the best of our knowledge, only 1 study compared real-time sonoe-

Figure 5. T2-weighted endorectal magnetic resonance imaging and real-time sonoelastography in a patient with prostate cancer (Gleason score, 6) in the right mid gland. Axial magnetic resonance imaging shows an area of low signal intensity in the right mid gland, and sonoelastography shows a hard area in the same location (arrows).



lastography with endorectal MRI. Sumura et al[8] reported cancer detection rates of 74.1% for real-time sonoelastography and 42.1% for T2-weighted endorectal MRI. However the data were obtained in patients with relatively high PSA levels (mean PSA, 10.5 ng/mL).

Our data in 33 patients showed good sensitivity and a high NPV for both real-time sonoelastography and T2-weighted endorectal MRI (Table 3). Cheikh et al[22] reported similar results for T2-weighted endorectal MRI. We found no significant differences in prostate cancer detection rates between sonoelastography and MRI, whether the analysis was performed by level within the prostate ($P > .05$) or by individual sextant regions ($P = .58$). With continued improvement in real-time sonoelastographic technology we look forward to a future in which the number of prostate biopsy cores is limited by real-time sonoelastography. Furthermore, real-time sonoelastography as a cost-effective tool may have the capability to be integrated in nomograms to enhance or exclude the suspicion of prostate cancer in patients with elevated serum PSA levels. One of the advantages of real-time sonoelastography in particular is that it also can be done by urologists and therefore may be implemented in daily routines.

Our study had several limitations: (1) Systematic biopsy served as the reference standard technique, even though it may miss a substantial percentage of prostate cancers. Furthermore, a cancer-positive sextant on systematic biopsy may or may not arise in the area of abnormality seen on sonoelastography or MRI. (2) Our study population was relatively small. (3) We had no data on interobserver and intraobserver variability. (4) Our analysis was confined to the peripheral zone. (5) Sonoelastography was performed using the strain imaging approach, which requires manual application of an external compressive force on the prostate. Further studies will be required to assess newer real-time sonoelastographic techniques along with multiparametric MRI and contrast-enhanced sonography.

In conclusion and with respect to the diagnosis of prostate cancer, real-time sonoelastography and T2-weighted endorectal MRI have similar sensitivity rates and NPVs. On the basis of the relatively high NPVs of these techniques, they may be useful to obviate the need for prostate biopsy in the future.

References

1. Scattoni V, Zlotta A, Montironi R, Schulman C, Rigatti P, Montorsi F. Extended and saturation prostatic biopsy in the diagnosis and characterisation of prostate cancer: a critical analysis of the literature. *Eur Urol* 2007; 52:1309–1322.
2. Scardino PT, Weaver R, Hudson MA. Early detection of prostate cancer. *Hum Pathol* 1992; 23:211–222.
3. Norberg M, Egevad L, Holmberg L, Sparén P, Norlén BJ, Busch C. The sextant protocol for ultrasound-guided core biopsies of the prostate underestimates the presence of cancer. *Urology* 1997; 50:562–566.
4. Gómez Veiga F, Ponce Reixa J, Barbagelata López A, Fernández Rosado E, Gonzaĺez Martiń M. Current role of PSA and other markers in the diagnosis of prostate cancer [in Spanish]. *Arch Esp Urol* 2006; 59:1069–1082.
5. 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; 70:1136–1140.
6. 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; 54:1354–1362.
7. Pallwein L, Mitterberger M, Pinggera G, et al. Sonoelastography of the prostate: comparison with systematic biopsy findings in 492 patients. *Eur J Radiol* 2007; 65:304–310.
8. Sumura M, Shigeno K, Hyuga T, Yoneda T, Shiina H, Igawa M. 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; 14:811–816.
9. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. *CA Cancer J Clin* 2009; 59:225–249.
10. Ahyai SA, Isbarn H, Karakiewicz PI, et al. The presence of prostate cancer on saturation biopsy can be accurately predicted. *BJU Int* 2010; 105:636–641.
11. Simon J, Kuefer R, Bartsch G Jr, Volkmer BG, Hautmann RE, Gottfried HW. Intensifying the saturation biopsy technique for detecting prostate cancer after previous negative biopsies: a step in the wrong direction. *BJU Int* 2008; 102:459–562.
12. Mueller-Lisse UG, Miller K. Imaging modalities for primary diagnosis and staging of prostate cancer [in German]. *Urologe A* 2010; 49:190–198.
13. Aigner F, Pallwein L, Pelzer A, et al. Value of magnetic resonance imaging in prostate cancer diagnosis. *World J Urol* 2007; 25:351–359.
14. Loch T. Urologic imaging for localized prostate cancer in 2007. *World J Urol* 2007; 25:121–129.
15. Engelbrecht MR, Jager GJ, Laheij RJ, Verbeek AL, van Lier HJ, Barentsz JO. Local staging of prostate cancer using magnetic resonance imaging: a meta-analysis. *Eur Radiol* 2002; 12:2294–2302.
16. van Moorselaar RJ, Voest EE. Angiogenesis in prostate cancer: its role in disease progression and possible therapeutic approaches. *Mol Cell Endocrinol* 2002; 197:239–250.
17. Frauscher F, Klauser A, Halpern EJ, Horninger W, Bartsch G. Detection of prostate cancer with a microbubble ultrasound contrast agent. *Lancet* 2001; 357:1849–1850.
18. Krouskop TA, Wheeler TM, Kallel F, Garra BS, Hall T. Elastic moduli of breast and prostate tissues under compression. *Ultrason Imaging* 1998; 20:260–274.

19. Pallwein L, Mitterberger M, Struve P et al. Comparison of sonoelastography guided biopsy with systematic biopsy: impact on prostate cancer detection. *Eur Radiol* 2007; 17:2278–2285.
20. Choi YJ, Kim JK, Kim N, Kim KW, Choi EK, Cho KS. Functional MR imaging of prostate cancer. *Radiographics* 2007; 27:63–77.
21. Park BK, Kim B, Kim CK, Lee HM, Kwon GY. Comparison of phased-array 3.0-T and endorectal 1.5-T magnetic resonance imaging in the evaluation of local staging accuracy for prostate cancer. *J Comput Assist Tomogr* 2007; 31:534–538.
22. Cheikh AB, Girouin N, Colombel M, et al. Evaluation of T2-weighted and dynamic contrast-enhanced MRI in localizing prostate cancer before repeat biopsy. *Eur Radiol* 2009; 19:770–778.