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Ultrasound of prostate cancer: recent advances

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Abstract Prostate cancer is the most common cancer in men. In the future, a significant further increase in the incidence of prostate cancer is expected. Therefore, improvement of prostate cancer diagnosis is a main topic of diagnostic imaging. The systematic prostate biopsy ("ten-core biopsy") is now the "gold standard" of prostate cancer diagnosis but may miss prostate cancer. Contrast-enhanced colour Doppler ultrasound (US) and elastography are evolving methods that may dramatically change the role of US for prostate cancer diagnosis. Contrast-enhanced colour Doppler US allows for investigations of the prostate blood flow and consequently for prostate cancer visualization and therefore for targeted biopsies. Comparisons between systematic and contrast-enhanced targeted biopsies have shown that the targeted approach detects more cancers and cancers with higher Gleason scores with a reduced number of biopsy cores. Furthermore, elastography, a new US technique for the assessment of tissue elasticity has been demonstrated to be useful for the detection of prostate cancer, and may further improve prostate cancer staging. Therefore, contrast-enhanced colour Doppler US and elastography may have the potential to improve prostate cancer detection, grading and staging. However, further clinical trials will be needed to determine the promise of these new US advances.

Keywords Ultrasound · Colour/power Doppler · Contrast agent · Elastography · Prostate cancer

Introduction

Prostate cancer is the most common cancer in men. In the future, a significant further increase in the incidence of prostate cancer is expected. Therefore improvement of prostate cancer detection is a main topic of diagnostic imaging.

In 2006, it was estimated that there were 230,000 new cases and 30,500 deaths due to prostate cancer in the United States [1]. More than 70% of cases are diagnosed in men over age 65. The death rate from prostate cancer has been declining since the early 1990s but, as stated, a further increase in the incidence of prostate cancer is expected in future years. The American Cancer Society guidelines for the early detection of prostate cancer include annual screening by digital rectal examination (DRE) and serum prostate-specific antigen (PSA) levels for men age 50 years or older who have a ten-year life expectancy [2].

PSA is used for early diagnosis of prostate cancer and for monitoring for disease recurrence. Men with a PSA level greater than 2.5 ng/ml have a 20% chance of finding prostate cancer at biopsy, and this increases to 50% if the PSA is greater than 10 ng/ml. As PSA is not a specific test for prostate cancer; other tests have been and are being developed [3].

It is known that the frequency of finding prostate cancer relies on the zonal anatomy of the prostate gland. Cancer is found in the peripheral zone in approximately 80%, in the transition zone in 15% and in the central zone in 5% [4]. Ninety-five percent of prostate cancers are adenocarcino-

mas that develop in the acini of the prostatic ducts. Other histologies are rare and do not have specific imaging features. The Gleason grade is used to quantify the histologic characteristics of prostate tumours.

Because tumours may not be visualized by conventional ultrasound (US), systematic biopsy has been advocated. The sextant approach has been suggested by Hodge and coworkers. It involves three cores from each lobe in a parasagittal plane at the base, midgland, and apex of the prostate and yields approximately a 25% cancer detection rate when the serum PSA levels are between 4 and 20 ng/ml. [5] In men with a persistently elevated serum PSA level and a negative initial biopsy, repeat biopsy demonstrates cancer in 20–23% of cases. More than 20% of men require more than two sets of biopsies for diagnosis. [6] To decrease the rate of repeat biopsies, an increased number of cores have been advocated by some investigators. [7] Further improvements with higher number of cores (up to 45) have been performed; however, a recent study has shown that 24-core saturation prostate biopsy did not appear to offer benefit over a ten-core biopsy as an initial biopsy technique. [8]

Based on the above-mentioned, new imaging techniques are desirable to improve prostate cancer diagnosis. In this article we discuss the value of contrast-enhanced US and elastography.

Contrast-enhanced US

Colour/power Doppler US

Prostate cancer tissue is associated with an increased microvessel density (MVD) due to the proliferation of neovessels. In malignant tissue, the microvessels are small and uniform [9, 10]. Increased MVD is also associated with the progression of prostate cance [11–13]. Conventional colour/power Doppler US imaging can not visualize microvessels, but contrast-enhanced US can. US contrast agents enable improved detection of low-volume blood flow by increasing the signal-to-noise ratio [14–16] and therefore allow a more complete delineation of the neovascular anatomy, by enhancing the signal strength from small vessels. Further US contrast agents are confined to the vascular lumen until they dissolve and they are many times more reflective than blood, thus improving flow detection. The US contrast agent vibrations generate higher harmonics to a much greater degree than surrounding tissues.

Bree [17] demonstrated the potential use of contrast-enhanced colour Doppler to enhance the diagnostic yield in a group of 17 patients with normal grey-scale transrectal US and elevated PSA values. Correlation of biopsy sites with colour Doppler US abnormalities revealed a sensitivity of 54%, a specificity of 78%, a positive predictive value (PPV) of 61%, and a negative predictive value (NPV) of 72% for the detection of prostate cancer. Three of the cases with a positive contrast-enhanced biopsy site had negative transrectal US random biopsy within the previous year.

Frauscher et al. [18] compared contrast-enhanced colour Doppler US targeted biopsy of the prostate with grey-scale US guided systematic biopsy. Two hundred and thirty male screening volunteers were included and the US contrast agent, Levovist (Schering, Berlin, Germany), was used. Cancer was detected in 69 of the 230 patients (30%), including 56 (24.4%) by contrast-enhanced targeted biopsy and in 52 (22.6%) by systematic biopsy. Cancer was detected by targeted biopsy alone in 17 patients (7.4%) and by systematic biopsy alone in 13 (5.6%). The detection rate for targeted biopsy cores (10.4% or 118 of 1,139 cores) was significantly better than for systematic biopsy cores (5.3% or 123 of 2,300 cores, $P < 0.001$), and contrast enhanced targeted biopsy in a patient with cancer was 2.6-fold more likely to detect prostate cancer than systematic US-guided biopsy. Pelzer et al. [19] thereafter investigated the impact of a combined approach of contrast-enhanced colour Doppler targeted biopsy and systematic biopsy for the prostate cancer detection in 380 men with PSA 4.0–10 ng/ml. Cancer was detected in 143 of 380 patients (37.6%, mean total PSA 6.2 ng/ml). The cancer detection rate for targeted biopsy and for systematic biopsy was 27.4% and 27.6%, respectively. The overall cancer detection rate with the two methods combined was 37.6%. Similarly to the previous study, contrast-enhanced targeted biopsy in a patient with cancer was 3.1-fold more likely to detect cancer than systematic biopsy. They concluded that colour Doppler targeted biopsy allows for the detection of cancers that can not be found on systematic biopsy, with a significantly reduced number of biopsy cores. However, the combined use of colour Doppler targeted and systematic biopsy allows for maximal cancer detection with a detection rate of 37.6% in patients with PSA 4–10 ng/ml.

Roy et al. [20] evaluated the accuracy of contrast-enhanced colour Doppler US to guide biopsy for the detection of prostate cancer. They investigated 85 patients with grey-scale and colour Doppler before and during intravenous injection of US contrast agent made of galactose-based air microbubbles (Levovist, Schering, Berlin, Germany). The diagnostic efficiency with and without contrast medium injection for detecting prostate cancer were compared based on biopsy results. They found cancer in a total of 58 biopsy sites in 54 patients. Contrast-enhanced colour Doppler had higher sensitivity (93%) than unenhanced colour Doppler (54%), while specificity increased only 79% to 87% for enhanced imaging. Roy et al. concluded that contrast enhanced colour Doppler endorectal US increases the detection of prostate cancer, by improving sensitivity, while the difference in specificity was not as pertinent. Obtaining

additional biopsy cores of suspicious enhancing foci significantly improves the detection rate of cancer.

Recently, Mitterberger et al. [21] evaluated systematic prostate biopsy versus contrast-enhanced colour Doppler targeted biopsy for the impact on Gleason score findings. The study included 690 men and the US contrast agent Sonovue (Bracco, Milano, Italy) was applied. Prostate cancer was identified in 221 of 690 subjects (32%) with a mean PSA of 4.6 ng/ml (range: 1.4-35.0 ng/ml). Cancer was detected in 180 of 690 subjects (26%) with contrast-enhanced targeted biopsy, and in 166 of 690 patients (24%) with systematic biopsy. The Gleason score of all 180 cancers detected by contrast-enhanced targeted biopsy was 6 or higher, mean 6.8. The Gleason score of all 166 cancers detected by systematic biopsy ranged from 4 to 8 and the mean Gleason score was 5.4. Since contrast-enhanced biopsy detected significantly higher Gleason scores compared with systematic biopsy, this techniques may allow identification of more aggressive cancers, which is important for defining prognosis and deciding treatment.

Since flow abnormalities, resulting from prostatitis, may result in false positive findings on contrast-enhanced Doppler US, Mitterberger et al. [22] studied the effect of pre-medication of dutasteride, a dual 5-alpha-reductase inhibitor, on prostatic blood flow prior prostate biopsy and the impact on prostate cancer detection. Thirty-six patients (age range, 52–74 years) with elevated PSA were treated with dutasteride 14 days prior prostate biopsy. Contrast-enhanced colour Doppler US was performed before, 7 and 14 days after dutasteride treatment. A reduction of blood flow was observed already after 7 days, whereas maximum flow reduction was observed after 14 days. Twelve patients (33%) of our cohort were found to have suspicious blood flow and prostate cancer, and six cancers (17%) were detected solely by contrast-enhanced targeted biopsy. Therefore, pre-medication of dutasteride seems to reduce prostatic blood flow in benign prostatic tissue and therefore improves prostate cancer detection by using contrast-enhanced Doppler US.

Contrast-enhanced colour Doppler has also been assessed in three-dimensional (3D) US imaging. Bogers et al. [23] evaluated contrast-enhanced 3D transrectal Doppler US before and after intravenous administration of 2.5 g Levovist (Schering, Berlin, Germany). Subsequently, random and/or directed transrectal US-guided biopsies were performed. Prostate cancer was detected in 13 of 18 patients. Vascular anatomy was judged abnormal in unenhanced images in six cases, of which five proved malignant. Enhanced images were considered suspicious for malignancy in 12 cases, including one benign and 11 malignant biopsy results. Sensitivity of enhanced images was 85% (specificity 80%), compared with 38% for unenhanced images (specificity 80%) and 77% for conventional grey-scale transrectal US (specificity 60%). Among six patients who showed no grey-scale abnormalities, vascular patterns were judged abnormal in four cases,

of which three were malignant. Based on these findings, they concluded that contrast-enhanced 3D power Doppler angiography is feasible in patients with suspicion of prostate cancer who are scheduled for prostate biopsies. Another analysis by the same group suggested that 3D contrast-enhanced power Doppler US is a better diagnostic tool than the DRE, PSA level, grey-scale US or power Doppler US alone. The most suitable diagnostic predictor for prostate cancer was a combination of 3D contrast-enhanced power Doppler US and PSA level [24].

Sedelaar et al. [25] demonstrated the correlation between MVD and 3D contrast-enhanced power Doppler imaging. In all patients, the enhanced side of the prostate was correlated with a higher MVD count. Concerning the MVD and the colour pixel density, Strohmeyer et al. [26] found similar results using contrast-enhanced colour Doppler US using the US contrast agent Levovist (Schering, Berlin, Germany).

Grey-scale harmonic US

Modern contrast-specific imaging techniques, such as grey-scale harmonic US, use the nonlinear behaviour of the microbubbles to increase sensitivity and specificity to detect signals reflected by microbubbles and allow for US perfusion imaging. Grey-scale harmonic US (i.e. phase inversion, pulse inversion techniques) offers compared with colour/power Doppler US a greater temporal and spatial resolution, and allows for excellent microbubble detection. Therefore with the use of this technique the visualisation of prostate cancer may be further improved.

Halpern et al. [27] used grey-scale and wide-band harmonic US to compare areas of contrast material enhancement in the prostate at US with whole-mount radical prostatectomy specimens to determine if the use of contrast material improves the detection rate of prostate cancer. US was performed in 12 subjects with prostate cancer prior to radical prostatectomy. Each gland was evaluated with grey-scale harmonic US at baseline and again during intravenous infusion of a microbubble contrast agent. Areas of contrast enhancement were identified prospectively in the transverse plane at the base, midgland, and apex of the prostate. The US findings were compared with whole-mount prostatectomy specimens. 31 foci of cancer were present at pathologic evaluation, with multiple foci of cancer in 11 of the 12 glands. Contrast-enhanced imaging demonstrated an additional five cancer foci in the outer gland ($P=0.025$). Seven additional sites of focal contrast enhancement were identified. Five of these sites corresponded to foci of hyperplasia. Two sites were false-positive with no pathologic abnormality. Therefore contrast-enhanced US of the prostate can improve sensitivity for the detection of cancers in the outer gland, but it can also demonstrate focal enhancement in areas of benign hyperplasia. (Fig. 1)
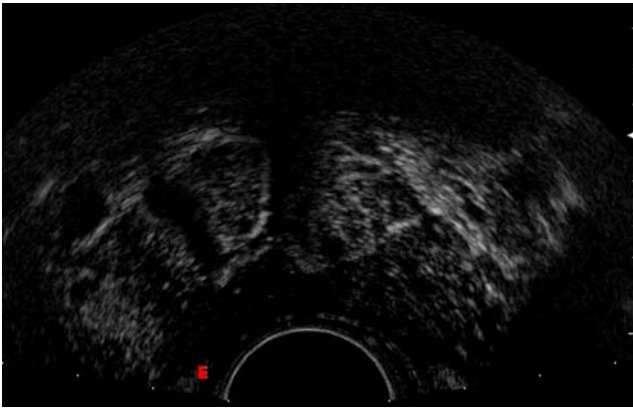
Fig. 1 Transverse contrast-enhanced grey-scale US image of the prostate. The hyperechoic cancer on the right side and mid gland is visible by enhancement and ascertained by biopsy

Halpern et al. evaluated grey-scale harmonic US for directed biopsy for prostate cancer detection. [28] The study group consisted of 40 patients, which were evaluated with harmonic grey-scale US. Sextant biopsy sites were scored prospectively on a six-point scale for suggestion of malignancy at baseline during contrast infusion and after bolus administration. Cancer was identified in 30 biopsy sites in 16 of the patients (40%). A suspicious site identified during contrast-enhanced US was 3.5-times more likely to have positive biopsy findings at than an adjacent site that was not suggestive of malignancy ($P<0.025$). When a suspicious site was evaluated with an additional biopsy core, the site was five times more likely to have a biopsy with positive findings than a standard sextant site ($P<0.01$). They noted no difference in diagnostic accuracy between continuous infusion of and bolus administration of the contrast agent. Though contrast-enhanced grey-scale harmonic US improves the sonographic detection of malignant foci in the prostate, and allows for targeted biopsy.

To further improve the survival of microbubbles in the blood flow, harmonic grey -scale US can be performed with an intermittent imaging mode. [29, 30] Intermittent imaging uses a reduced frame rate to lower the energy deposition into tissue, improve the survival time of microbubbles, and increase the parenchymal enhancement provided by US contrast agents. Intermittent harmonic imaging (IHI) was used to assess prostate cancer detection with contrast-enhanced US. A total of 301 subjects referred for prostate biopsy were evaluated with contrast-enhanced US using continuous harmonic imaging (CHI) and intermittent harmonic imaging (IHI) with interscan delay times of 0.2, 0.5, 1.0, 2.0 s, as well as continuous colour and power Doppler. Targeted biopsy were obtained from sites of greatest enhancement, followed by sextant biopsy. In 104 of 301 subjects (35%) cancer was found. Cancer was found in 15.5% (175 of 1133) of targeted cores and 10.4% (188 of 1806) of sextant cores ($P<0.01$). Among subjects

with cancer, targeted cores were twice as likely to be positive [odds ratio (OR)=2.0, $P<0.001$]. IHI demonstrated a statistically significant benefit over baseline imaging ($P<0.05$). Therefore contrast-enhanced US with IHI provided a significant improvement in discrimination between benign and malignant biopsy sites, and may therefore improve prostate cancer detection.

Recently, more sensitive contrast-enhanced US techniques came available, such as cadence contrast-pulse sequence (CPS) US technique (Siemens Medical Solutions, Mountain View, Calif.). This novel US technique processes the reflections of a series of US pulses, which results in an optimized contrast-to-tissue ratio and a microbubble contrast-only image can be constructed. The detailed technical specifications of the technique are described by Phillips et al. [31]

CPS technique has been shown to be useful for intraoperative detection of liver tumours and follow-up after radiofrequency ablation therapy of hepatocellular carcinomas. [32, 33]

We have used CPS imaging for detection of prostate cancer in a small series of 20 patients referred for prostate biopsy for CPS targeted biopsies. CPS technique was used to assess the intraprostatic vasculature during microbubble administration. Transrectal US was performed using a 8C4 probe with a transmitting frequency varying between 4 and 5.0 MHz. To reduce micobubble destruction a low mechanical index (0.14) was used. The US contrast agent SonoVue, was administered by bolus injection, to a maximum dose of 4.8 ml. The blood flow of the peripheral zone was evaluated, and areas of faster and higher contrast enhancement were defined as suspicious for malignancy. Up to five targeted biopsies were performed from suspicious areas, and subsequently another investigator performed ten systematic biopsies in a standard spatial distribution. CPS imaging found suspicious areas on contrast enhancement in 11 of 20 cases (55%) and targeted biopsy revealed cancer in eight of the 11 cases (73%). Systematic biopsy found cancer in five of 20 subjects (25%). In the nine subjects without any abnormal findings on CPS, systematic biopsy was negative for cancer. Based on these preliminary CPS imaging seems to improve prostate cancer detection. Furthermore this technique may have the potential to reduce the number of men scheduled to biopsy. (Fig. 2)

Even these preliminary results are promising, technical improvements of microbubble imaging techniques are necessary. We found in 3 of 11 cases an abnormal contrast enhancement, however no cancer on biopsy. This might rely on the fact that the contrast enhancement was assessed subjectively. Quantification of contrast enhanced US information is generally based upon a classification or subjective estimation by the examiner. [34] Both these approaches are highly user dependent. A system for objective evaluation was presented by Cosgrove et al. [35], who introduced a method of colour pixel and vessel

Fig. 2 Dual transverse view of prostate imaged by cadence contrast-pulse sequence (CPS) US technique (Siemens Medical Solutions, Mountain View, Calif.). Rapid enhancement of the left side was suspicious for malignancy. Prostate cancer was approved by biopsy
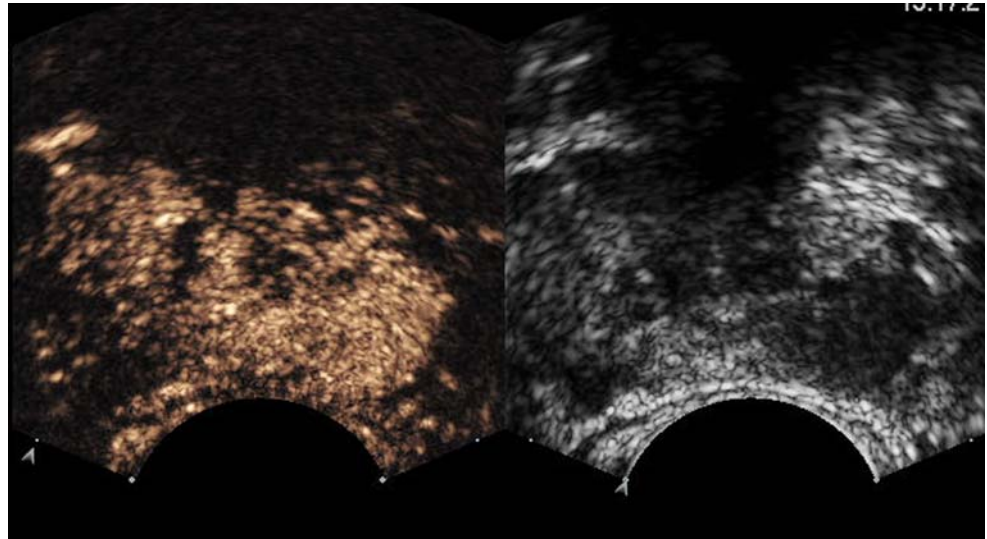
counting. However, this method is cumbersome and does not distinguish pixels with different flow velocity. Although the detection of prostate cancer with contrast-enhanced Doppler US may be improved relative to baseline US, uncertainty remains in the interpretation of contrast-enhanced Doppler US images. In a study, 16% (59/360) of contrast-enhanced transrectal US images were rated as indeterminate with respect to vascular enhancement. [29] Therefore objective assessment of contrast agent kinetics may markedly improve the value of these contrast-specific imaging techniques.

Recently, we have used a prototype software from Bracco Research, Switzerland, which allows for objective assessment of contrast enhancement (echo power), in a few cases with prostate cancer. Contrast enhancement as a function of time was measured in two regions-of-interest drawn in the prostate. The mean transit time obtained from the time-intensity curve measured in normal prostate tissue (*yellow curve*) was 1 min 41 s, while the corresponding value measured in the suspect area was 14 s. In the latter case, a very fast wash-in was followed by a rapid wash-out of the microbubble contrast agent, which is typical for malignant lesions. Huber et al. [36] used a computer-assisted assessment of microbubble transit time in breast lesions. They reported that after microbubble injection, breast carcinomas and benign lesions behave differently in degree, onset, and duration of US enhancement. Thus, time intensity curves may also be useful as another objective measure to differentiate benign from malignant prostatic tissue (Fig. 3).

Elastography

It is known that cancer tissue shows an increase in both vessel and cell density. While the increased vascularization can be visualized with contrast-enhanced US, as stated above, the increase of cell density in tumours leads to a change of tissue elasticity. Krouskop et al. [37] described that there is a significant difference in stiffness between normal and neoplastic prostate and breast tissue. For detection of changes in tissue elasticity, Ophir et al. [38] developed in 1991 an imaging technique based on static deformation and called it "strain imaging". This imaging modality is capable of visualising displacements between US image pairs of tissue under "compression". Elastography is based on the fact that the backscattered US signal changes its local characteristic pattern only to a comparably small extent if the insonified tissue is slightly compressed and decompressed (i.e. approximately up to 2%) during the examination. A high internal correlation is maintained within local regions of interest. However, time or space differences between local regions of interest under different compression ratios change with differences in compressibility of the insonified tissue. Time differences between two local regions of interest within two subsequent images recorded under different compression ratios can be calculated for each pixel of the images. Time differences are not absolute but relative values since the compressibility of local tissue regions always depends on the surrounding tissue and the applied compression force.

In order to reduce the time-consuming calculations, Pesavento et al. [39] developed a fast cross-correlation technique, which enables a real-time elastographical imaging. With on-going technical advances, SE was integrated in modern high-end US units. Real-time SE has already shown its promising value in the detection and differentiation of masses in the breast and thyroid gland [40, 41]. Cochlin et al. [42] introduced real-time elastography for the detection of prostate cancer in biopsy specimens. In their study, elastography had a sensitivity of 51% and a specificity of 83% for the detection of prostate cancer in individual patients and a sensitivity of 31% and a specificity of 82% for the detection of individually

biopsied areas of the prostate. Sperandeo et al. [43] in 2003 reported the usefulness of elasticity imaging to differentiate malignant from benign lesions. In their study, they used tissue elasticity to detect cancer based on tissue deformation of grey-scale images under manual compression of the prostate with a transrectal probe.

In a recent pilot study, patients with clinically localised prostate cancer, who underwent radical prostatectomy, were examined prospectively [44]. Prior to surgery these patients were examined with conventional grey-scale US as well as with real-time elastography. Areas suspicious for prostate cancer were depicted. After surgery, the histological specimens were compared with the transverse US images and with elastography findings. Thirty-two foci of prostate cancer were present at pathological evaluation, with multiple foci of cancer in 13 of the 15 glands. Real-time elastography detected 28 of 32 cancer foci (sensitivity: 88%). Four sites were false positive with no pathological abnormality. The by-patient analysis demonstrated that real-time elastography detected at least one cancer focus in

each of the 15 patients. Therefore, we concluded that real-time elastography of the prostate is a sensitive new imaging modality for the detection of prostate cancer. In 78.3% of cases, elastography findings correlated with histological findings.

Konig et al. [45] evaluated elastography for biopsy guidance for prostate cancer detection. After imaging with conventional grey-scale US in conjunction with real-time elastography, 404 men underwent systematic sextant biopsy. Prostate cancer was found in 151 of 404 cases (37.4%). In 127 of 151 cases (84.1%), prostate cancer was detected using real-time elastography as an additional diagnostic feature. They concluded that it is possible to detect prostate cancer with a high degree of sensitivity using real-time elastography in conjunction with conventional diagnostic methods for guided prostate biopsies.

Pallwein et al. [46] performed a prospective study to determine whether a limited biopsy approach with elastography-targeted biopsy of the prostate would detect cancer as well as grey scale US-guided systematic biopsy
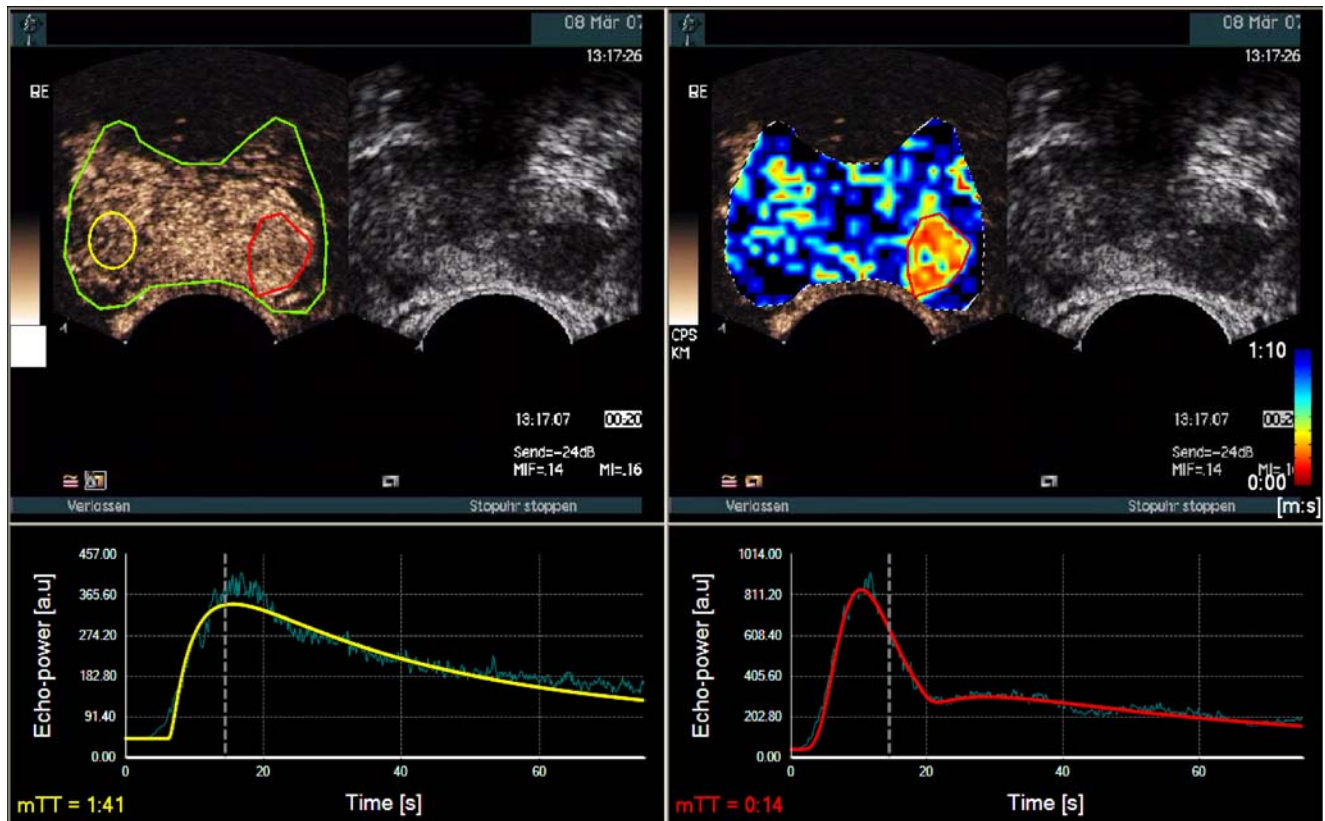

Fig. 3 Time-intensity curves were obtained with a Siemens Sequoia US machine in CPS mode, after a single bolus injection of SonoVue (4.8 ml) contrast agent. Contrast enhancement (Echo Power) as a function of time was measured in two regions-of-interest (ROIs) drawn in the prostate. The first ROI (*red*) was drawn in a suspicious area; a second one (*yellow*) was drawn in an area representing normal prostate tissue. The mean transit time (mTT) obtained from the time-intensity curve measured in normal prostate tissue (*yellow curve*) was 1 min 41 s, while the corresponding value measured in the suspect area was 14 s. In the latter case, a very fast wash-in was followed by a rapid wash-out of the contrast agent, which is typical for a malignant lesion. On the right-hand side of the figure, a parametric image of mTT shows in hot colours (*red* and *yellow*) the suspicious area, i.e. the area corresponding to the tumour, where mTT is substantially shorter compared with the rest of the prostate. (Courtesy of Bracco Research, Switzerland)

with a larger number of biopsy cores. Two hundred and thirty male screening volunteers, with a total prostate specific antigen of 1.25 ng/ml or greater and free-to-total prostate specific antigen less than 18%, were examined. In each subject, five SE-targeted biopsies into suspicious regions in the peripheral zone during elastographic examination versus ten systematic prostate biopsies were carried out. The final cancer detection rate of the two techniques was compared. Cancer was detected in 81 of the 230 patients (35%), including 68 (30%) by elastography targeted biopsy and in 58 (25%) by systematic biopsy. Cancer was detected by targeted biopsy alone in 23 patients (10%) and by systematic biopsy alone in 13 patients (6%). The overall cancer detection rate by patient was not significantly different for elastography-targeted and systematic biopsy ($P=0.134$). The detection rate for elastography-targeted biopsy cores (12.7% or 135 of 1,109 cores) was significantly better than for systematic biopsy cores (5.6% or 130 of 2,300 cores, $P<0.001$). SE-targeted biopsy in a patient with cancer was 2.9-fold more likely to detect prostate cancer than systematic US guided biopsy. In comparison with the study of Konig et al. [45], an increase in sensitivity and specificity including the outer prostate gland only was found. They concluded that although an increase in cancer detection was achieved by combining targeted and systematic techniques in this screening population, elastography-targeted biopsy alone is a reasonable approach for decreasing the number of biopsy cores.

In a further study, the value of elastography for prostate cancer detection was compared with systematic biopsy findings in 492 patients, who were scheduled for systematic prostate biopsy [47]. Elastography of the prostate (Hitachi EUB 8500, Hitachi Medical, Tokyo, Japan) was performed prior biopsy, to assess tissue elasticity, and areas with increased stiffness were considered as suspicious for cancer. Cancer was detected in 321/2,952 (11%) outer gland areas (74 in the basis, 106 in the mid-gland, 141 in the apex). On elastography 533/2,952 (18.1%) suspicious areas were detected and 258 of these areas (48.4%) showed cancer. Elastography findings showed a good correlation with the systematic biopsy results. The best sensitivity and specificity was found in the apex region. Most false-positive cancer findings (275/533 areas; 51.6%) were associated with chronic inflammation and atrophy especially at the basal prostate areas. In conclusion, these new computer-assisted techniques allow exact assessment of the tissue elasticity and therefore for a good differentiation between benignity and malignity (Fig. 4).

Conclusion

The recent advances in US for the detection, grading and staging of prostate cancer are promising. New technical developments allow for improved detection of smaller, low flow vessels and better detection of areas of flow asymmetry. Mandatory quantification of enhancement will make an objective grading system available. In summary, contrast-enhanced US and elastography seem to offer novel and great potential in prostate cancer diagnosis.

Fig. 4 Dual image. Elastographic image of prostate (*on the left*); the elastogram shows a clearly visible stiffer area (*blue colour*) with suspicion of a prostate cancer on the left side of the prostate. Corresponding transverse grey-scale US image of prostate with no clear evidence for prostate cancer (*on the right*)
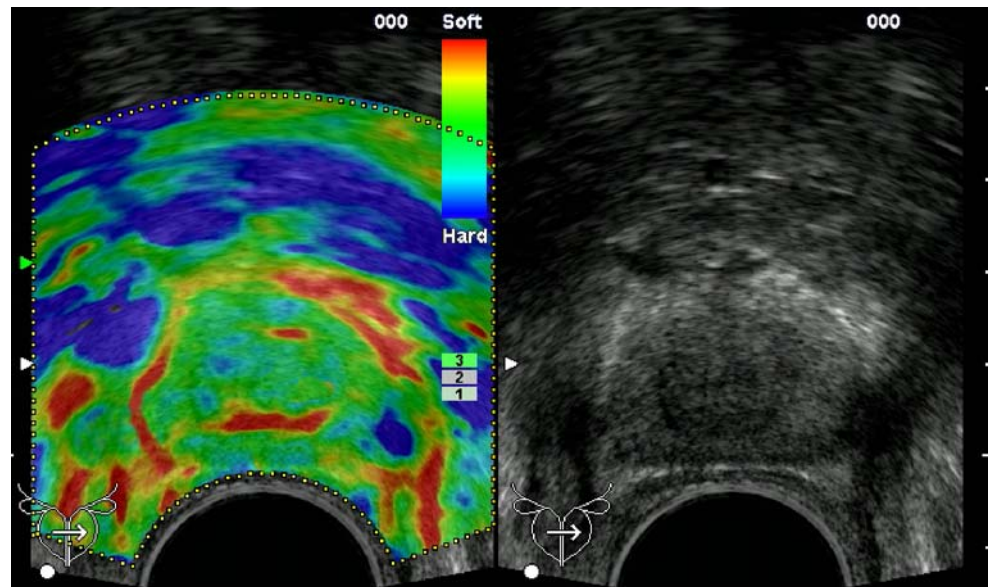
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