

# Strain Elastography of Breast and Prostate Cancer: Similarities and Differences

## Strain-Elastografie des Mamma- und Prostatakarzinoms: Gemeinsamkeiten und Unterschiede

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### Key words

- ◉ breast
- ◉ prostate
- ◉ ultrasound

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### Abstract

Typically both breast and prostate cancer present as tissue with decreased elasticity. Palpation is the oldest technique of tumor detection in both organs and is based on this principle. Thus an operator can grade a palpable mass as suspicious for cancer. Strain elastography as modern ultrasound technique allows the visualization of tissue elasticity in a color coded elastogram and can be understood as technical finger. The following article shows similarities and differences of ultrasound strain elastography in the diagnosis of breast and prostate cancer.

#### Key Points:

- ▶ In prostata cancer elastography, in breast cancer B-mode is the primary sonographic search modality.
- ▶ The diagnostic value of the search modalities change with increasing age.
- ▶ A cut-off value for a strain ratio is hard to obtain in the elastography of the prostata, because there is no stabile reference tissue in the prostata.

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### Zusammenfassung

In der Regel stellen sich sowohl das Mammakarzinom als auch das Prostatakarzinom als Gewebe mit erniedrigter Elastizität dar. Darauf basiert auch die Palpationsmethode, welche beiden Organen als älteste Technik zum Tumornachweis dient und bei der die Untersucher hart ertastete Veränderungen als krebsverdächtig einstufen. Die Strain-Elastografie als moderne Ultraschalltechnik besitzt die

Fähigkeit, die Verteilung der Gewebeelastizität farblich kodiert als Elastogramm am Monitor des Ultraschallgerätes darzustellen und kann somit als technischer Finger verstanden werden. Über Gemeinsamkeiten und Unterschiede der Ultraschall-Strain-Elastografie (USE) des Mammakarzinoms und Prostatakarzinoms wird im Folgenden berichtet.

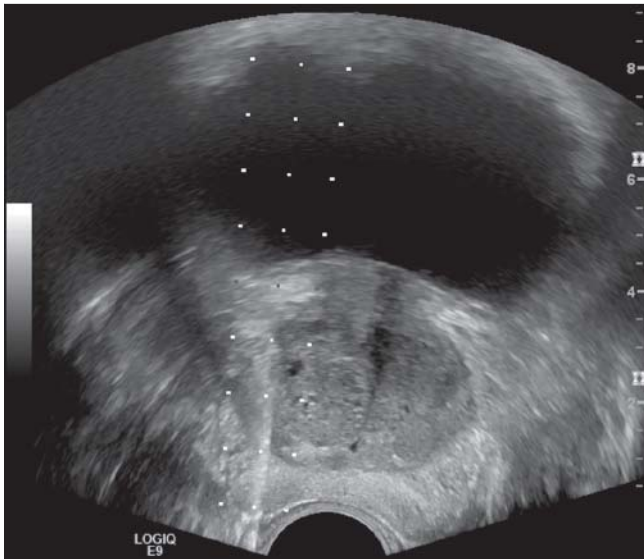
### Introduction

#### Suspicion of a tumor

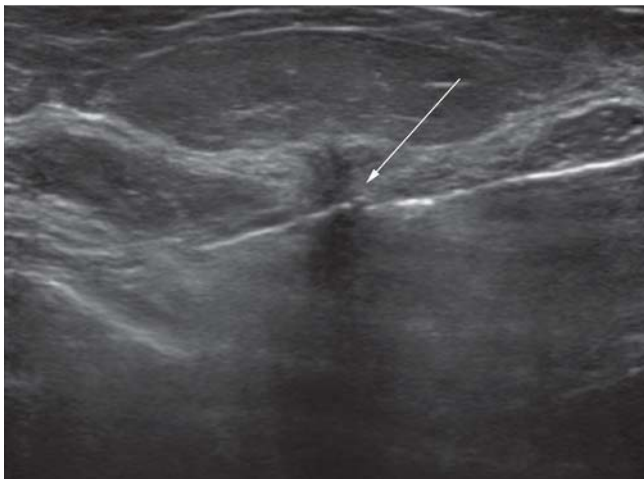
Suspicion of the presence of prostate cancer (PCa) results from a raised PSA level and/or digital-rectal examination (DRE) [1]. Suspicion of the presence of mammary carcinoma results from a positive palpation and/or suspicious imaging [2]. To either confirm or rule out the suspicion of cancer requires a histological examination of punch biopsies of the relevant organs. In this case there is a significant difference.

#### Punch biopsy

Although numerous original studies emphasize that significant prostate cancer can be reliably visualized using various imaging techniques, according to EAU guidelines, randomized biopsy of the prostate using transrectal ultrasound (TRUS) is still currently the gold standard [1, 3, 4]. As a rule, the ultrasound B-mode image is only used to detect the zonal anatomy of the prostate, in order to subsequently obtain 10–12 “blind” tissue samples from the predefined anatomical prostate zones. As the term “randomized” implies, TRUS is not used to visualize the prostate cancer (◉ Fig. 1). In contrast, when there is suspicion of breast cancer, a lesion visible in imaging is biopsied selectively based on the image and not randomly biopsied (◉ Fig. 2).



**Fig. 1** Randomized prostate biopsy with removal of a core from the center right anatomical zone without abnormalities in the B-mode image.



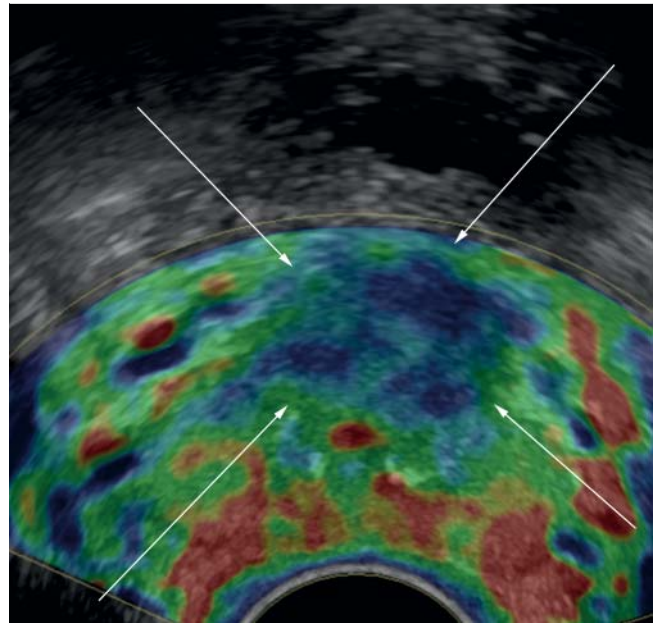
**Fig. 2** Targeted breast biopsy with removal of a core from a suspicious region in the B-mode image (arrow).

### Palpation

Due to the increased cell and vessel density of carcinoma of the breast and prostate, both types of tumors are harder than the normal surrounding tissue [5]. Although palpation of the breast can be performed by a woman herself is recommended as precautionary measure [2], prostate self-examination by men is not performed, due to the less accessible location of the prostate as well as other inhibitions. Furthermore, since only the portions of the prostate accessible by finger lie against the rectal wall, anterior tumors can escape detection in a clinical examination (◉ Fig. 3). Due to both its exposed location as well as its deformability, the female breast is not subject to the same limitations of palpation.

### Ultrasound strain elastography

Originally developed by Ophir et al. and introduced in 1991, USE was rapidly accepted as a means to exhibit elasticity



**Fig. 3** Anterior tumor which escaped digital-rectal examination, yet in strain elastography displays a region with increased tissue stiffness (coded blue, arrow).

distribution in organs through imaging (color coded) [6]. The advantage of this modern technique is that inaccessible and thus impalpable hard – and therefore suspicious – changes can be detected (◉ Fig. 3).

### Technology

#### Technology

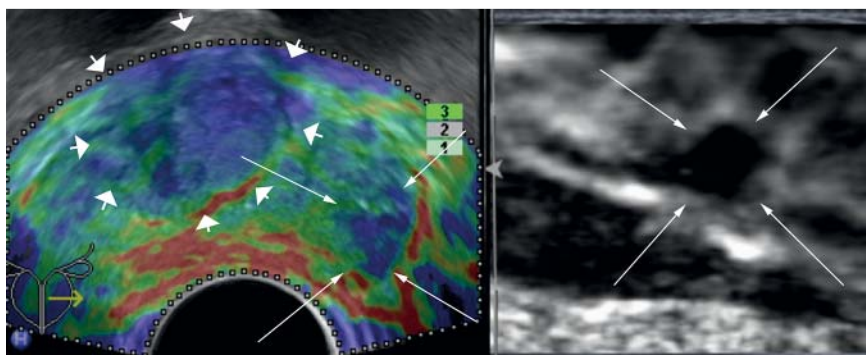
USE generates images with an image reconstruction rate greater than 30/sec during which the organ is compressed and released using an ultrasound probe. Pressure on the organ as well as the expected image quality can be read on an indicator on the ultrasound image screen. After compression, hard tissue recovers at a different speed compared to soft tissue, resulting in runtime differences of echo pairs, which, using a mathematical algorithm, can be measured and then displayed color-coded as an elastogram [7]. The color selection to represent the distribution of tissue elasticity can be arbitrarily defined; for this article, hard regions of the breast are shown in grayscale (black=hard, soft=white), for the prostate, a color scale is used (blue=hard, soft=red) (◉ Fig. 4).

### Transducers

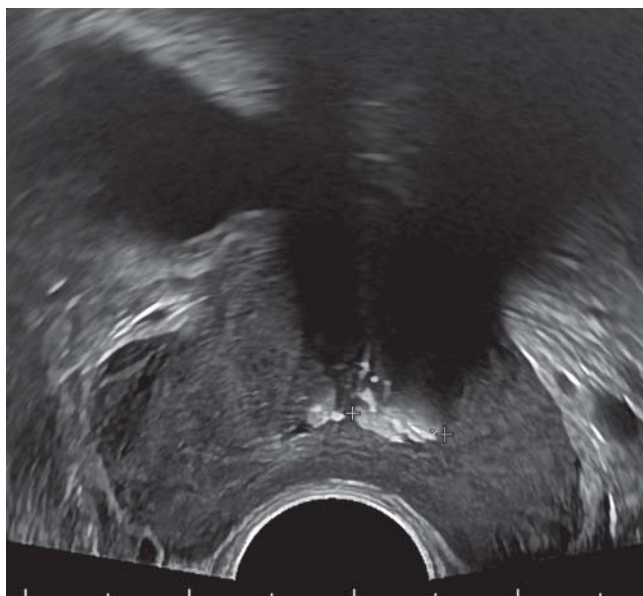
A linear probe is used to examine the breast to determine mammary carcinoma. To determine prostate cancer, the prostate is examined using a transrectal probe; most working groups use an end-fire probe, since a biplanar probe has limitations with respect to this biopsy [8].

### Macrocalcification

If macrocalcifications are present dorsally in the prostate, it is not possible to examine the anterior prostate sections due to sound cancellation and limited alternative access possibilities of the transrectal probe [3] (◉ Fig. 5). The female breast



**Fig. 4** Prostate cancer displayed as hard in the elastogram (left, coded blue, long arrow). The short arrows indicate the hardened inner gland and thus not assessable in the elastogram, likewise coded blue; breast cancer shown as hard in the elastogram (right, coded black, long arrows).



**Fig. 5** Macrocalcification of the prostate with noise cancellation and non-assessable anterior sections.

offers a different situation, since macrocalcification-related sound cancellation can be avoided by changing the position of the organ or the linear probe.

### Organ size

Examination of anterior sections of larger prostate organs is limited by the lack of ductility due to anatomical conditions as well as the limited penetration depth of the USE [9]. For the prostate there is an additional problem: the inner gland generally has more connective tissue, is generally hypertrophic in the elderly and thus harder to assess due to the greater basic hardness [10]. Although the female breast is made up of an individually highly variable combination of glands, connective and fatty tissue, it appears more homogeneously in imaging, and the USE limitation of penetration depth can be compensated for using organ compression, in contrast to the prostate.

### Tumor volume

Due to the tilt angle of the end-fire probe, the tumor diameter is correctly determined in all 3 spatial directions only in apical prostate sections, whereas it is underestimated based on height diameter [3] (• Fig. 6). The linear transducer head does not have this problem, since it can flexibly probe the

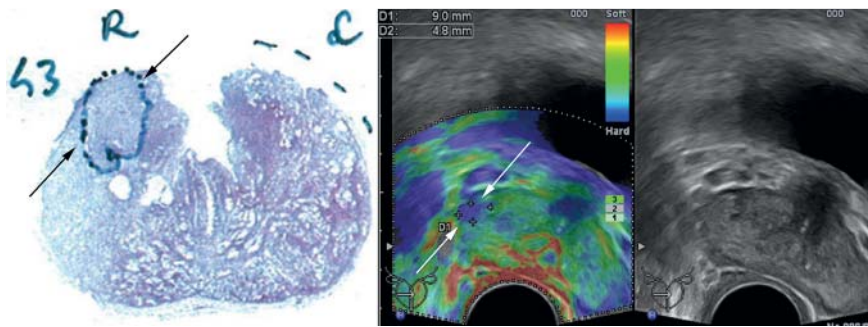
target lesion. It has also been reported that USE can more accurately detect the true size of the mammary carcinoma better than B-mode image ultrasound, since USE also discloses the local invasion, which is not always visible in the B-mode scan [11] (• Fig. 7).

### B-mode image and elastogram

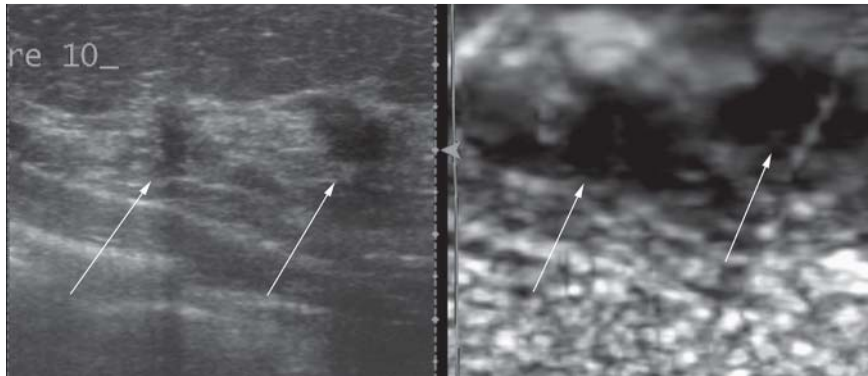
Due to the loss of glandular architecture, an unambiguous image of prostate and breast cancer shows a loss of reflexivity and therefore the B-mode image indicates a hypoechoic tumor area [12–14]. Although some breast cancers can be iso- or hyperechoic, the B-mode image indicates a higher predictive value and high sensitivity to detection of breast cancer. This contrasts with prostate cancer, since non-hypoechoic carcinomas are frequently encountered [15, 16]. This ultimately results in the B-mode image being used as a search modality for breast cancer, and USE used only for additional evaluation/risk assessment [17]. For prostate cancer, USE is superior to the B-mode image with respect to detection, and the B-mode image itself is only included in elastography scoring [18, 19]. The B-mode image itself plays a role in measuring prostate volume and, as mentioned earlier, is used in the identification of anatomical zones for the randomized biopsy [12].

### Strain ratio

The strain ratio (SR) was introduced since USE is an examiner-dependent freehand technique, and additionally because benign changes such as inflammation or fibrosis with hardening can affect the USE [20, 21]. This is a semi-quantitative measurement procedure with which relative elasticity values of lesions are generated. To do this, absolute strain values of elastographically suspicious areas are compared in relation to elastographically unremarkable areas. The ratio value thus calculated shows the degree of hardening compared to the unremarkable tissue. Determining cut-off values was an attempt to obtain values that could distinguish between benign and malignant lesions. The fat-to-lesion ratio (FLR) was established in which the strain of the fat tissue (= reference tissue) of the breast is compared to the strain of the lesion. European studies determined cut-off values of 2.27–2.455, depending on the technical equipment used, to differentiate between benign and malignant focal lesions [20, 21]. FLR appears to be a highly-significant



**Fig. 6** In the large area section, prostate cancer shows a larger diameter (left, black arrows) in the corresponding elastogram (right, white arrows).



**Fig. 7** Two breast cancers displayed smaller in the B-mode image (left, arrow) than in the corresponding elastogram (right, arrows).

additive tool for properly classifying a lesion as BIRADS 3 or 4. For the prostate there is to-date only one published study that investigated the value of strain ratio of prostate lesions [22]. Zhang et al. reported that the strain ratio could provide supplementary information regarding prostate lesions in order to better differentiate between benign and malignant lesions. In their study, a cut-off value of 17.44 was determined when the strain of the lesion is compared to the strain of the contralateral side of the prostate used as a reference. Our own unpublished results suggest that there is no stable reference tissue available for the prostate, since the contralateral side can also be infiltrated by infection or tumor. Furthermore, establishing a cut-off of the absolute strain of the lesion seems to be more productive since a reference tissue is not required in this case.

### Physiology-Histology

#### Age

With increasing age, the breast becomes noticeably softer due to a lipomatous involution of the mammary gland parenchyma [23]. An additional consequence is a loss of breast reflex which is generally reflected in general hypoechoicity in the B-mode image. Under these circumstances it becomes increasingly difficult to find hypoechoic breast cancer in the B-mode image due to the lack of contrast in the hypoechoic background. Unlike examinations of the prostate, USE plays an increasingly significant role in detecting breast cancer with advancing patient age (◉ Fig. 8). In contrast to the breast, with increasing age the prostate undergoes hypertrophy, primarily of the inner gland, resulting in a reduction of elasticity and subsequent hardening; this leads to a limitation of the elastographic detectability of

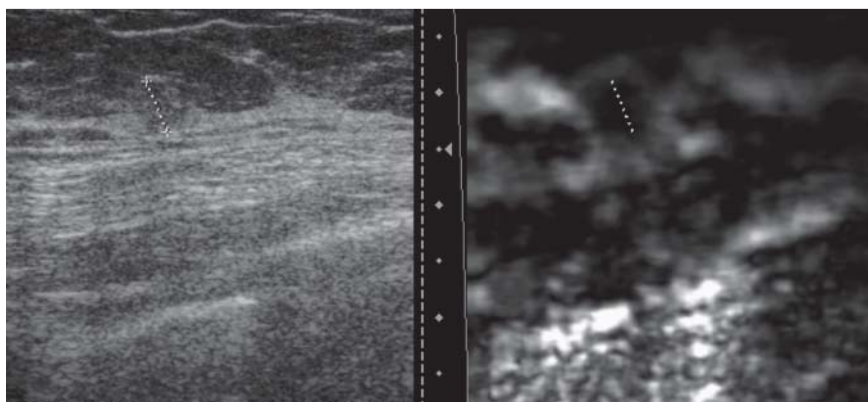
prostate cancer of these organ sections (◉ Fig. 9). Chronic inflammatory processes of the prostate developed later in life additionally aggravate this problem [10]. Consequently the B-mode image plays an increasingly important role in the detection of prostate cancer.

#### False-positive changes

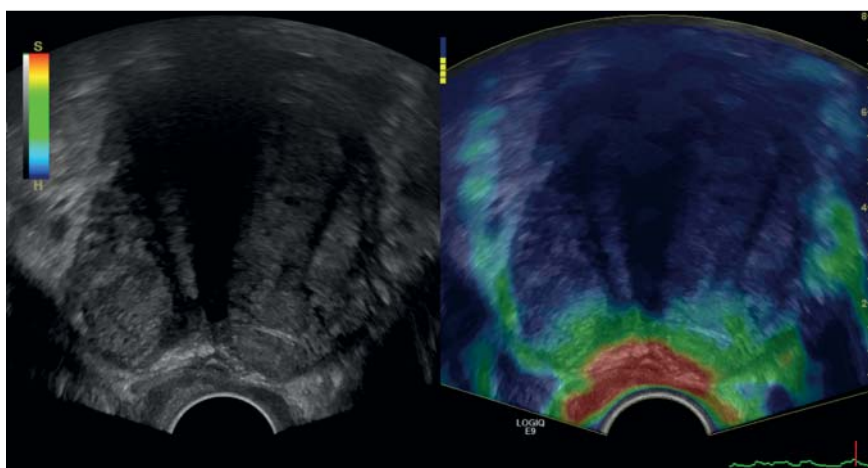
Benign changes of the prostate such as inflammation, fibrosis, atrophy or adenomyomatosis can involve increased tissue rigidity and can therefore be difficult to differentiate elastographically from prostate cancer. This is certainly a reason for the occasionally low positive predictive value of only up to 39%, as we reported in a study of men with PSA serum values  $< 4$  ng/ML [24]. For most mammary lesions, benign tumors are harder than normal glandular tissues, but softer than malignant lesions [25]. False-positive changes can be observed in hyaline fibroadenomas and fatty tissue necrosis, since these can involve tissue hardening [5, 26, 27]. Additionally, USE has difficulty differentiating between postoperative scarring and tumor recurrence, since in both cases there is reduced tissue elasticity. In this instance contrast-enhanced MRI is superior to USE [17, 28].

#### False-negative changes

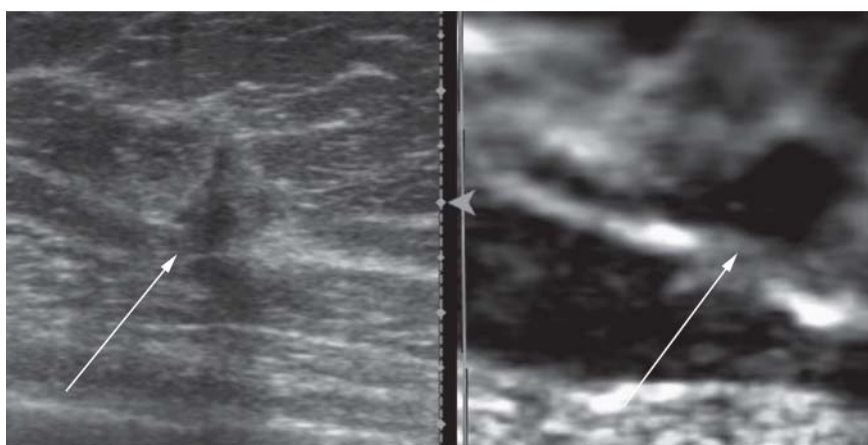
If the prostate cancer tumor is made up of glands with dilated lumina containing substantial mucus or contains sparse architecture, then such tumors can avoid detection by both DRU as well as USE, due to increased tissue elasticity [29, 30]. This type of histological tumor composition is generally found in prostate cancer with primary Gleason pattern 3 (G6 (3+3) or G7 (3+4)). Above G7 (4+3), USE sensitivity for prostate cancer detection is very high, since this cancer type is very compact as a rule (dense architecture) [30]. Since prostate cancer  $\leq$  G7 (3+4) is considered insignificant, and



**Fig. 8** Involved breast with poor B-mode image contrast, but with unambiguous hardened lesion in the related elastogram.



**Fig. 9** Hypertrophied prostate of an elderly man with completely hardened inner gland.



**Fig. 10** Breast cancer <5 mm in B-mode image (left, arrow), typically smaller than in the elastography (right, arrow).

significant if greater than G7 (4+3), USE particularly appears to be a possible technology to reduce the much-criticized over-diagnosis and over-treatment of this cancer [31]. Since USE represents an additive to B-mode sonography, false-negative changes play a reduced role in the detection of breast cancer. Most false-negative changes are found, for example, in phyllodes tumors with a soft center, mucoid breast carcinomas and carcinomas with large central necrosis [5, 17, 26, 27]. In a B-mode image, both entities are shown as suspicious.

### Tumor size

USE appears to play a significant role in the management of breast lesions <5 mm visible in the B-mode image, but not visible in mammography. Verification of reduced elasticity of these lesions can result in a biopsy instead of only monitoring [25, 26] (► Fig. 10). In contrast, there is a finding of a suspicious tumor of the prostate if a hardened area >5 mm can be reproduced on two different planes [32]. For example, sensitivity of 9.7% could be shown for prostate cancer with maximum diameters of 0–5mm; 27% for prostate cancer with maximum diameters of 6–10mm; 70.6% for

prostate cancer with maximum diameters of 11–20mm; and 100% for prostate cancer with maximum diameters of >20 mm [30].

## Summary

In contrast to diagnosis of the prostate, the B-mode ultrasound image is the leading search method in diagnosing the breast, and USE is a useful additive examination technology. Due to age-related changes in both the breast and prostate, the use of these technologies appears to shift with the increasing age of the patient, however. Although there are published multicenter studies regarding the value of USE in the diagnosis of breast cancer, it would be desirable that the same were available for prostate cancer in order to achieve a higher evidence level for this technology.

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