Elastography of the prostate in the detection of prostate cancer

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Introduction

This paper presents initial experience with a new Toshiba elastography imaging system used to detect prostate cancer. Since this is a preliminary evaluation, the elastography imaging procedure was performed in addition to our standard procedure of ten systematic biopsies, plus extra biopsies of suspicious areas where appropriate. The elastography images did not influence the biopsy pattern and the elastography findings were subsequently compared with tumour detection on the biopsy cores (all cores are labelled separately) and with radical prostatectomy specimens where available.

The number of patients studied is not yet sufficient to present hard data, but the following initial impressions of the procedure, illustrative case reports and discussion of the possible role of elastography in the detection of prostate cancer may provide a starting point for further studies.

Background

With patients showing a high serum prostate specific antigen (PSA) level and/or an abnormal digital rectal examination there is a high probability (40–66 %) of clinically significant prostate cancer.

The standard method to detect prostate cancer in these patients is to perform multiple biopsies of the prostate obtained in a set pattern throughout the gland which also allows for histological (Gleason) grading of any cancer detected.

There are, however, certain problems with this procedure:

1) It is invasive and unpleasant. Multiple biopsies – at least 8 or 10 – are necessary. Repeat biopsies for a rising PSA level and a negative initial set of biopsies require more than 10 biopsies.

2) A proportion of cancers will be missed (false negative tests). The number of false negative tests is difficult to determine as there is no gold standard, but based on positivity rates on second or third biopsies the rate may be between 10 and 33 %.

3) Increasing the number of biopsy cores obtained increases positivity rates but also increases the number of "clinically insignificant" tumours found. These are small, low grade tumours that, evidence suggests, are unlikely to progress to clinically significant tumours.

4) The size of a detected tumour can be estimated from biopsy data, i.e. the number of cores involved and the length of tumour in each core. The estimate is often inaccurate because the biopsy core may just detect the edge of a large tumour and a tumour may be multi-focal.

Because of these disadvantages attempts are being made to visualise tumours on the ultrasound image so that biopsies can be targeted to the tumour. Greyscale ultrasound and colour Doppler studies, however, are disappointing. More recently, contrast-enhanced ultrasound and elastography imaging are being studied.

If prostate cancer could be imaged with a method that produces a high negative predictive value then patients with negative imaging would not need biopsies. So far, no imaging method has achieved this objective and even from an unbiased point of view it seems unlikely that elastography imaging can close this gap.

There are, however, some limited, but nevertheless very important goals that may be achieved.

1) Adding elastography-guided biopsies to the standard biopsy regime may increase positivity rates (reduce false negative results).

2) If a tumour is visualised, diagnosis can be supported by targeting the abnormal area with fewer biopsy cores than conventional biopsies.

3) The size of the tumour may be more accurately estimated and it might be possible to distinguish significant from insignificant tumours.

Technique

The elastography system features a split screen with one screen showing a conventional greyscale image, while the other one visualizes movement using colour Doppler. This is so to speak the basic real-time elastography image.

The greyscale image allows positioning within the prostate gland. The gland is then compressed and allowed to relax by applying 3 or 4 simple "flicks" of the transducer at about 1–2 second intervals. This produces the data for the more sophisticated strain imaging.

The colour Doppler "elastography" image enables gain adjustments which optimise the elastography image. Although the colour Doppler elastography image is inherently inferior to the strain images, it is a real-time image which means if any suspicious areas are detected, the image plane to study these can be accurately determined.

Once the data is stored the strain image can be produced. The process takes approximately 10 seconds, and then the image can be viewed.

Depending on the number of planes examined, obtaining the data for the images adds 1 to 2 minutes to the examination.

Although the patient feels the movement of the transducer during the "flicks" that compress the prostate, this is not painful or uncomfortable.

Initial impressions

1) The system is easy to use. Data acquisition takes little time. The increased time required for the scan is quite acceptable. The split screen displays a greyscale image which makes it easy to align the elastography scan plane accurately to the plane which needs to be studied. The colour Doppler overlay allows an estimate of appropriate gain settings and indicates how much movement is being produced while flicking the transducer. Obviously abnormal areas are visible in real time on the colour Doppler image.
2) The technique is not uncomfortable or painful.
3) Post-processing and measurement of the images is easy, though best practices are not yet clear. The images appear to be reproducible over a range of different pressures when flicking the transducer and over a range of gain settings. This makes the procedure highly reproducible and relatively operator-independent.
4) The method does demonstrate prostate cancer but initial studies indicate that sensitivity is too low to use elastography as the sole examination technique.
5) Both tumours which were not visible on the

greyscale images and tumours that, as confirmed later, were only visible on the grayscale images were detected.
6) Initial studies indicate that elastography imaging may well have a place in the detection of prostate cancer but further research as to its precise role is required.

Case reports
Case 1 Normal study

A 32-year-old man with haematospermia was referred for transrectal ultrasound imaging of the prostate and seminal vesicles. The results showed no findings. The patient agreed to an elastography study of his prostate. The normal pattern is shown. In the figures the greyscale image and the elastography image are displayed alongside each other (a, b). The colour Doppler image used in real-time to aid acquisition of the elastography image is shown in fig. (c).

The colour scale depicts elasticity. Green is medium elasticity, red is higher elasticity, blue is less elasticity. The darker the blue, the less the elasticity. Tissues that do not react to pressure are black. The colour elastography image is overlaid onto the greyscale image. It is possible to vary the merged image from 100 % greyscale to 100 % elastography. Most of the images shown are 50 % of each.

Fig. 1.1 a and b show the mid-gland in the transverse plane. A continuous band of green (medium elasticity) is seen across the posterior gland. This does not correspond to the peripheral

zone which is much wider in this young man. It may be simply because the tissue nearest the transducer moves more on flicking the transducer than the more distal tissues. The more posterior part of the gland is shown in medium blue with irregular, rather random areas of green. Rotating the transducer, so that the lateral horns are in the midline of the image, results in a green band along the horns. This is often not as clearly continuous as that in the posterior gland (Figs. 1.2, 1.3). The base of the gland (Fig. 1.5) shows a similar pattern as the mid-gland (Fig. 1.4). At the apex the green band is discontinuous or often absent.

Case 2

A 58 year old man with a serum PSA of 30.5. Digital rectal examination showed a firm left gland. Greyscale ultrasound (Fig. 2.1) showed a hypoechoic nodule in the left peripheral zone. Elastography showed a gap in the normal green band (Fig. 2.2) and on a slightly different plane a dark, stiff area (Fig. 2.3) that matched with the hypoechoic nodule. This corresponded to positive biopsies in this area, Gleason grade 7. In cases where greyscale match elastography results biopsies of the abnormal area might be all that is necessary. Fig. 2.4 shows the corresponding velocity gradient image.

Case 3

A 62-year-old man with a serum PSA level of 3.9. Digital rectal examination showed an enlarged prostate with no palpable nodules. Greyscale
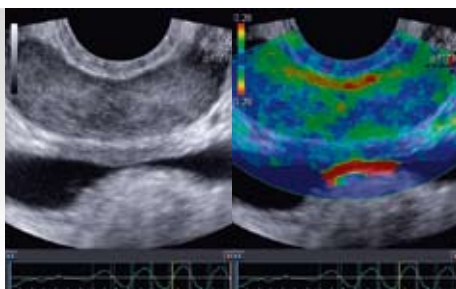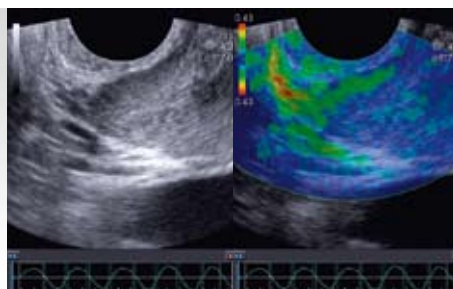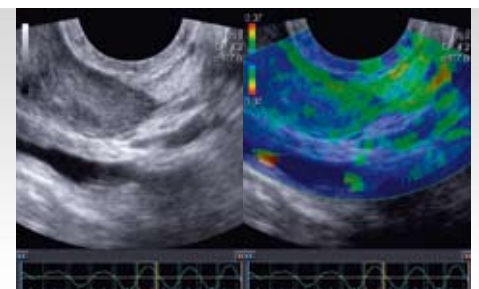

Fig. 1.1 a   Fig. 1.1 b

Fig. 1.2 a   Fig. 1.2 b
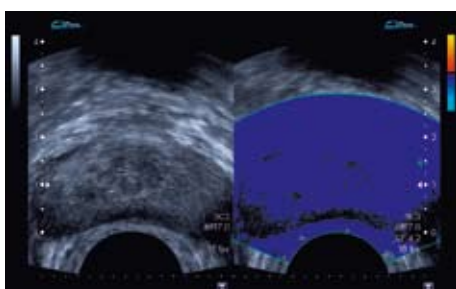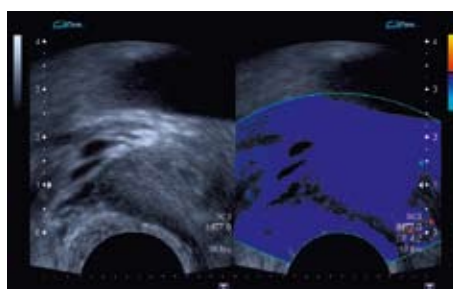

Fig. 1.3 a   Fig. 1.3 b
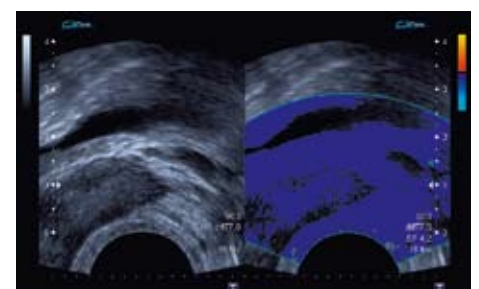

Fig. 1.1 c

Fig. 1.2 c

Fig. 1.3 c

ultrasound (Figs. 3.1 a, 3.2 a) showed no obvious focal nodules. Elastography showed loss of elasticity in the left peripheral zone laterally in the mid-gland (Fig. 3.1 a) but not in the base (Fig.3.2 b). Biopsies revealed a Gleason 6 tumour in the area of decreased elastography. Figs. 3.1 c and 3.1 d show elasticity measurements of the abnormal area and the corresponding area on the normal side. The different graphs are obvious.

Case 4
A 58-year-old man with a serum PSA level of 9.6. Digital rectal examination was computable with a T2A tumour on the right. Greyscale ultrasound (Fig. 4.1 a) showed a large hypoechoic area on the right extending into the transitional zone. Elastography imaging (Fig. 4.1 b) showed a matching area of decreased elasticity, shown as an area of darker blue. As the tumour was fairly anterior, the green posterior band is unaffected.

Case 5
A 65-year-old man with increased serum PSA. Digital rectal examination showed a hard gland compatible with a T2A tumour. Greyscale imaging (Figs. 5.1 a, 5.2 a) showed an inhomogeneous gland but no focal nodules. Elastography (Figs. 5.1 b, 5.2 b) showed decreased elasticity throughout the gland with loss of most of the peripheral green band and areas of deep blue in the deeper parts of the gland. Biopsies showed extensive tumour with Gleason 9 tumour in all 10 cores taken.

Two clinical workflows including elastography
The "easy" way to study the prostate with elastography imaging is to perform a transrectal scan of the prostate using greyscale ultrasound imaging together with Doppler studies if this is the standard practice of the department. In addition, elastography images of the prostate are acquired. After the examination the images are reviewed and measurements are obtained as appropriate. The prostate biopsies are obtained at a later date and are planned according to the elastography results. This has the advantage of allowing ample time to analyse the images. The examination, however, becomes a two-stage procedure which might be justified with patients with a rising serum PSA level and negative previous biopsies. With patients undergoing their first transrectal ultrasound and biopsy examination such a two-stage procedure is more difficult to justify. If future studies were to show that this two-stage approach provides a significant advantage, either higher positivity rate or the need for less biopsies, it would be acceptable.

An alternative approach is to analyse the elastography images immediately while the transducer remains in the patient and then to perform the biopsies with an appropriately modified pattern during the same procedure. This allows less time to analyse the images and multiple measurements are not possible. It is, however, possible to review the images in less than 10 minutes which means

that together with the time needed to collect the data for the images the total time of the examination increases from about 15 to 30 minutes. During the analysis of the images the transducer could be removed from the rectum or could remain in place (insertion of the transducer is often the most painful part of the procedure).

The possible role of elastography imaging
Sensitivity and specificity of elastography imaging need to be assessed further, both alone and when combined with the current standard technique of ultrasound-guided systematic biopsies. Therefore it is currently not possible to determine the role of elastography. Current experience, however, indicates certain possible conclusions.

Firstly, it is important to state what elastography will probably not achieve:
It seems unlikely that elastography imaging alone will replace the need for ultrasound-guided systematic biopsies. It is unlikely that the negative predictive value will prove sufficient to eliminate the need for biopsies in patients with a normal examination.

In cases where a lesion is detected, elastography will not eliminate the need for biopsy. It is unlikely that specificity will be sufficiently high to make an absolute diagnosis. Biopsy will still be needed to confirm the diagnosis and for Gleason grading.
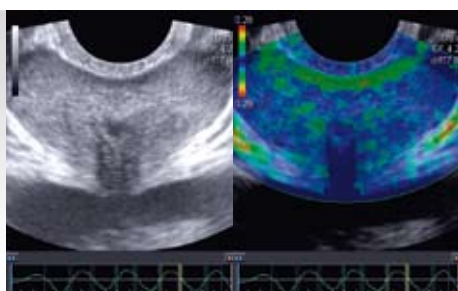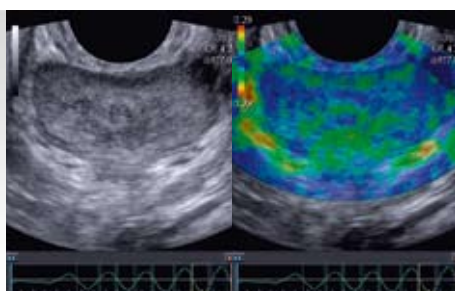

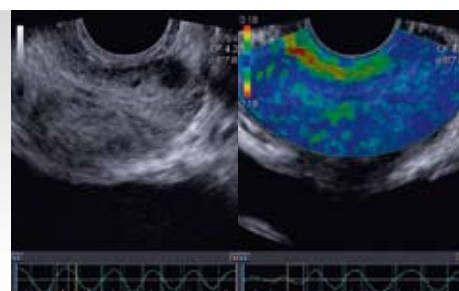Fig. 1.4 a   Fig. 1.4 b

Fig. 1.5 a   Fig. 1.5 b

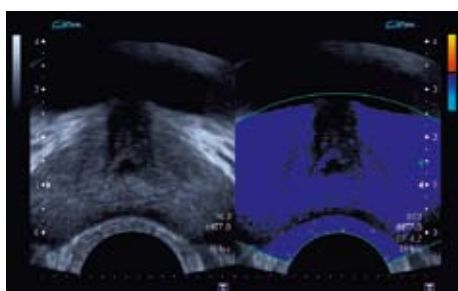Fig. 2.1   Fig. 2.2

Fig. 1.4 c

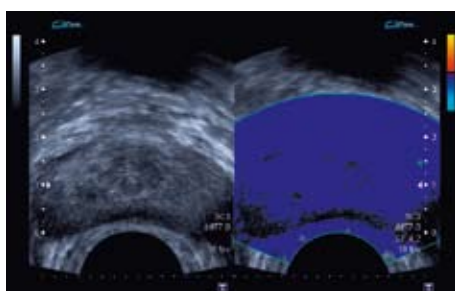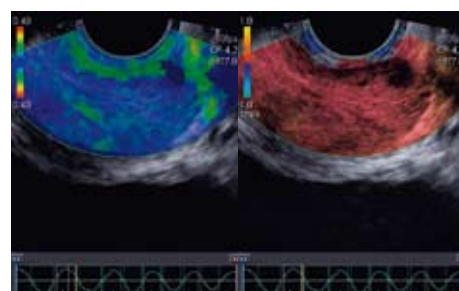
Fig. 1.5 c

Fig. 2.3   Fig. 2.4

Nevertheless, elastography might be used in several different ways:

1) There is a group of patients who have rising serum PSA levels and who have had two or more negative sets of biopsies. In these cases it is likely that a tumour has been missed, possibly because it is in an unusual position such as the anterior part of the gland. Current practice therefore is to perform "saturation" biopsies: about 20 biopsies are obtained including the anterior gland. This usually requires sedation or general anaesthetic. An alternative approach may be to look for the tumour using elastography. If found, it could be biopsied with far fewer cores under local anaesthesia.

2) If elastography imaging is added to grayscale imaging before biopsies are performed and a definite tumour is detected, then limited biopsies of the tumour may be all that is necessary. If no tumour is detected, systematic biopsies will still be necessary. Thus elastography could reduce the number of biopsies in a certain group of patients.

3) If elastography imaging is added to grayscale imaging before biopsies are performed and all patients have ultrasound-guided systematic biopsies by the current standard technique, plus targeted biopsies of elastography-detected lesions, this might increase positivity rates.

4) Elastography possibly assesses the size of tumours and the likelihood of extraprostatic spread. Since greyscale ultrasound is not suited for this task, MRI is often used but is not the ideal solution either. In addition, more aggressive tumours may have a different elastography pattern than less aggressive tumours – very valuable information when assessing treatment options. Both these possibilities need to be tested.

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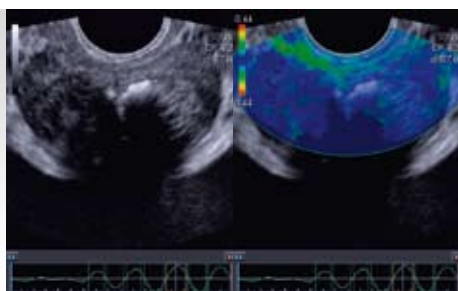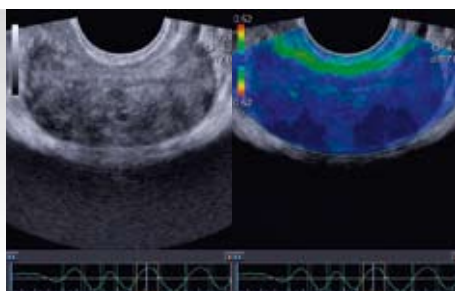
Fig. 3.1a   Fig. 3.1b
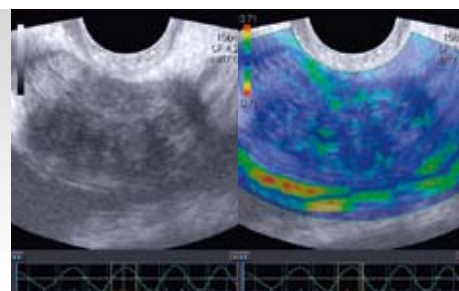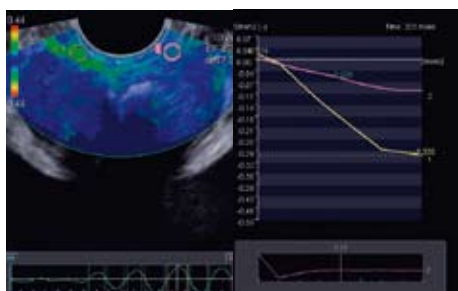

Fig. 3.2a   Fig. 3.2b
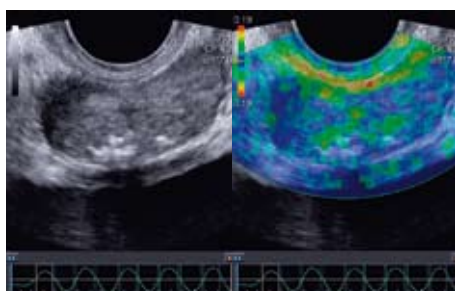

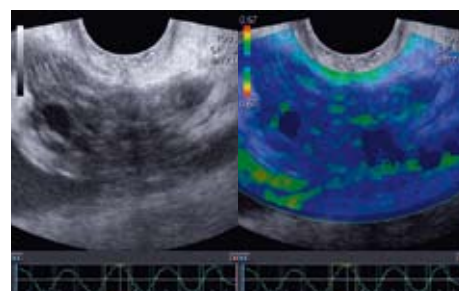Fig. 5.1a   Fig. 5.1b

Fig. 3.1c   Fig. 3.1d

Fig. 4.1a   Fig. 4.1b

Fig. 5.2a   Fig. 5.2b

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