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REVIEW

Transrectal ultrasonography of the prostate

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Introduction

Ultrasonics is a branch of acoustics that deals with the study of sound waves with frequencies above those within the range of hearing of the average person [1]. During World War II, the principles of ultrasonics were used to develop SONAR (SOund Navigation And Ranging). It was mainly as a result of this application that special attention was paid to the further development of this technology. Ultrasonography in urology was first applied to the kidneys and bladder in the 1950s but there was then no general acceptance because the image quality was poor [2]. However, during the last 25 years, a rapid development in ultrasonography has been achieved by the introduction of gray-scale and real-time scanning. Moreover, intracavity scanning, e.g. TRUS, has substantially increased the potential value of ultrasound in urology.

TRUS of the prostate is a rapidly advancing modality with growing acceptance and importance for diagnosis and management of prostatic diseases. Since its clinical application in 1971 by Watanabe [3], TRUS has now developed into a sophisticated technology. Early in the history of TRUS, bistable 3-MHz transverse images provided information only about prostate size and shape [4]. In the late 1970s and early 1980s, gray-scale longitudinal and transverse scanners were introduced [5]. It was not until then that the visualization of the internal architecture of the prostate became possible and two zones were identified; the transition zone and the external zone. In 1985, studies were carried out with 5 MHz probes scanning in both the transverse and longitudinal planes. Recent advances in electronic real-time ultrasonography have significantly improved dynamic imaging. In 1986, 7 MHz probes were introduced and the improvement in resolution allowed the visualization of the infrastructure of the prostate, corresponding to McNeal's concept of zonal anatomy [6].

Ultrasonographic appearance of the prostate

There is no accepted standard for topographical relationships in prostate imaging. The prostate is best considered as a fusion of different glandular regions contained within a discontinuous capsule [7]. McNeal first proposed that there were different zones of the prostate gland; the transition zone, the peripheral zone and the central zone [8]. In young men, the normal inner prostate generally has low echogenicity compared with the outer gland. As the transition zone enlarges, a distinct demarcation between these regions becomes clear. The transition zone produces a hypoechoic image compared with the generally isoechoic peripheral zone. With increasing enlargement, the transition zone can compress the central and peripheral zones. The margin separating the hyperplasia from the peripheral zone is considered to be the surgical capsule. Hyperplasia can allow further visualization of multiple adenomas, or even capsular bulging, but never capsular infiltration [9].

Besides BPE, other prostatic diseases can also be visualized. The use of TRUS to detect prostatic cancer was first described by King *et al.* [4] among others. In early prostatic ultrasonography, using low-frequency probes, it was suggested that prostate cancer was densely echogenic or hyperechoic [4,10]. Through the 1980s, higher frequency probes, combined with gray-scale imaging, markedly improved the imaging of the prostate and the intraprostatic anatomy could be defined reproducibly. It is now generally accepted that prostatic cancer can have echographic variability and is influenced by tumour grade, stage, size and location. Shinohara *et al.* compared the ultrasonographic appearance with histological findings and determined that approximately 60-75% of prostate cancers appear hypoechoic (Fig. 1), whereas 25-40% are isoechoic and 1-2% are hyperechoic [11]. Other criteria that help in the differentiation of prostate cancer include asymmetry in size, particularly in the peripheral zone, capsular distortion and loss of the normal demarcation between the central gland and the peripheral zone [9,12,13] (Fig. 2). The reason for these

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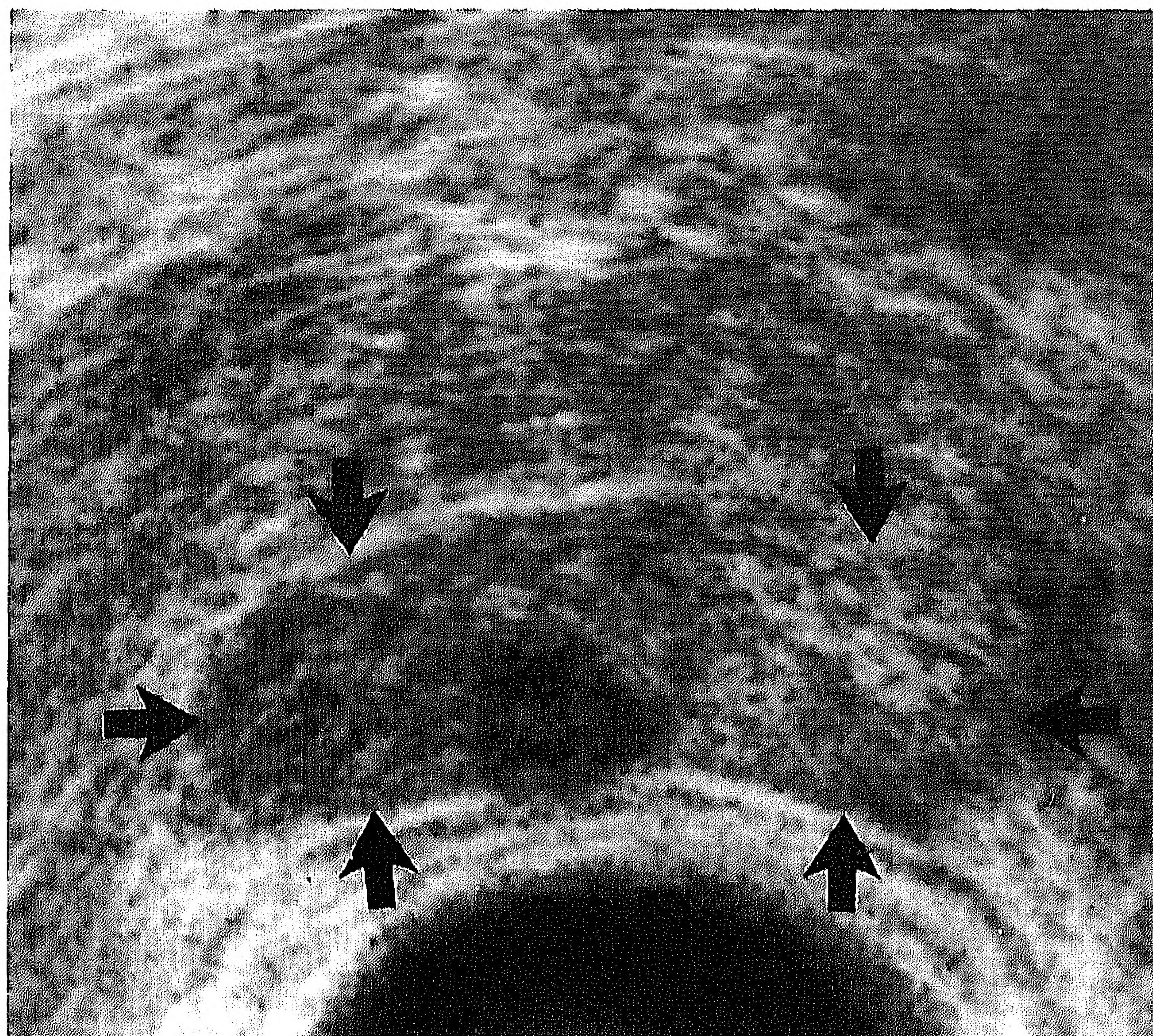


Fig. 1. An hypoechoic lesion in the right prostate lobe (contour indicated by arrows).

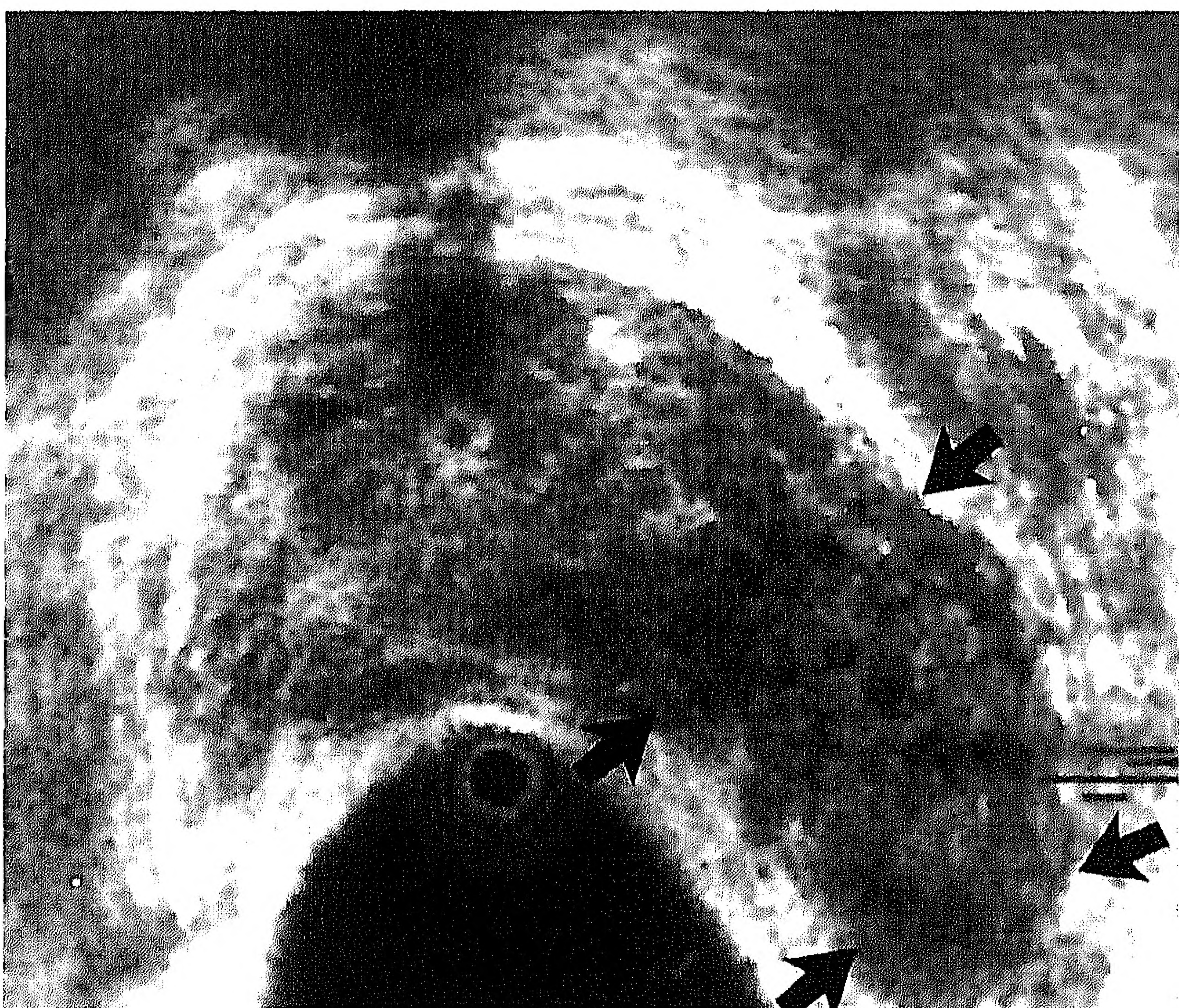


Fig. 2. Prostate cancer with capsular distortion (indicated by arrows).

differences in the echogenic appearance of prostatic cancer is uncertain but may be related to the index of cellular differentiation, tumour size, intermixing of BPH with cancer, fibrotic changes and other as yet undefined causes [14,15].

Finally, the appearance on TRUS of the prostate in patients with inflammatory prostatic diseases is still under discussion. Echogenic and hypoechoic appearances throughout the gland have been reported [16,17]. The only image that is agreed to be characteristic in inflammation of the prostate is the presence of an anechoic to hyperechoic lesion, with a thin or a thick wall. To reach the correct diagnosis, the ultrasonographic findings should be complementary to the clinical findings.

Considerations concerning TRUS

Several aspects need to be considered when performing TRUS. First, before ultrasonography, the operator should be aware of the history of the patient and the findings of a DRE. Therefore, it is recommended that the examiner should always carry out a DRE and include these findings in the interpretation of the ultrasonogram of the prostate. Moreover, ultrasonography of the prostate is a dynamic process; subtle abnormalities noticed during TRUS are often poorly presented on a photographic print. Therefore, the interpreter of the ultrasonographic findings and the operator of the machine should be the same person. The technique used to perform the investigation is also important. An evaluation using TRUS is performed best using axial, sagittal and oblique coronal axial projections, manipulating the probe within the rectum to ensure that all areas of the gland lie within the optimal focal zone of the transducer. The use of at least two imaging planes allows visualization in three dimensions, thus permitting a more accurate localization of abnormalities and extent of disease. The initial scan is made with some 'stand-off' from the posterior prostate. Placing the prostate within the near field is better without compressing the peripheral zone too much. An additional scanning pass should be made with the probe slightly compressing the prostate, which improves the penetration of ultrasound and the evaluation of the anterior prostate, while possibly enhancing any subtle posterior abnormalities. Compression in the sagittal plane may also be required to measure the height and width of large glands. In the sagittal projection, levering the probe quickly from the far-left to the far-right aspects of the gland may help to confirm any subtle hypoechoic asymmetry or architectural distortion in the lateral peripheral zones seen on axial scanning.

Applications of TRUS

Prostate volume

The estimation of prostate volume may be useful in several ways. A precise estimate of the amount of BPH would help to decide the appropriate therapy and assist in the interpretation of serum PSA levels for the presence of cancer [18]. Also, any decrease in the prostate mass after hormonal manipulation or radiation therapy can be used to indicate therapeutic efficacy [19]. The goal of many researchers is to estimate accurately the volume of the prostate and there have been several studies performed to achieve this [18,22]. Earlier studies used suprapubic ultrasonography to measure prostate size and although some studies reported accurate results with this technique, others felt this method had an inherent problem [20].

However, an accurate estimate of prostate volume only seems possible transrectally. The three most commonly used methods to estimate the size of the prostate are the planimetric method, the use of three dimensions of the prostate and the ellipsoid method. The step-section planimetric method comprises a sequential area summation of multiple sections of the prostate [21]. The method using three dimensions of the prostate comprises measurements of height (H), width (W) and length (L) and the formula to calculate the volume, $H \times W \times L \times \pi/6$ [22]. The ellipsoid-volume calculation is a feature available on some ultrasonography scanners that allows the operator to delineate the prostate contour transversally at the mid-gland and then define a hypothetical axis of rotation for that area with distance markers. The volume is then calculated as $8A/3\pi L$, where A is the area of the outlined ellipse and L the length determined by the distance markers. It is generally accepted that the step-section planimetry method is the most accurate [23,24] but it is tedious, time-consuming and requires sophisticated computer software to execute the planimetry. Therefore, the best method to estimate prostate volume is a variation of the prolate spheroid formula, using the transverse diameter as the major axis and the anteroposterior diameter as the minor axis. This formula is optimal for prostates weighing <80 g; in large glands (>80 g) the spherical volume formula [$\pi/6$ (transverse diameter)³] provides the best estimate of prostate weight [22]. The use of this formula in preference to those using the length of the prostate is supported by the difficulty of accurately measuring the latter. The measurement of cephalocaudal distance is sometimes technically difficult, as the junction between the prostatic apex and distal urethra is frequently poorly visualized. Likewise, the definition between the base of the prostate and the seminal vesicles and the bladder neck is often not clear [22,23]. Finally, the ellipsoid-volume techniques are rapid and available on most ultrasound machines, yet are not as accurate as the previous two methods [25].

To overcome the inaccuracy of measuring prostate volume, an automated method has been investigated in our department [26], based on planimetric volumetry, to overcome the subjectivity of volume measurements using ultrasonography (Fig. 3). Moreover, this method is a useful tool in the objective determination of PSA level in proportion to the prostate volume [27].

Prostate biopsy

The presence of prostate cancer can be established only by tissue sampling and a histological analysis. The main purpose of TRUS-guided biopsies is to obtain tissue for such a histological diagnosis. To identify areas of potential extraprostatic spread and to achieve an accurate

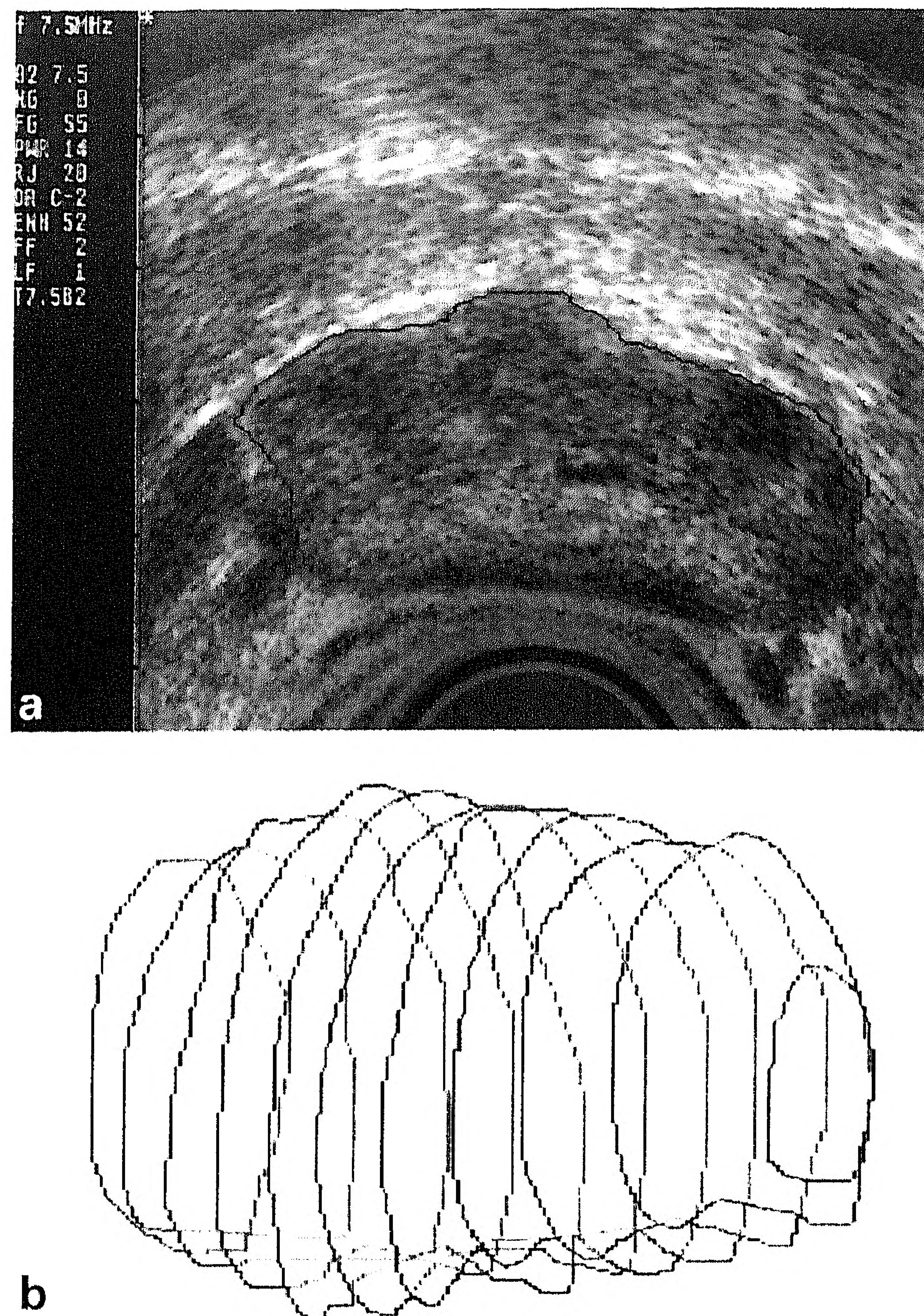


Fig. 3. Planimetric volumetry. An image of, a, a transverse section and, b, a schematic presentation of the planimetric method.

histological grade, several cores should be obtained using strategic TRUS-guided biopsies at known sites of anatomical weakness [28]. Initially, ultrasonographically guided prostate biopsies used a transperineal approach for the biopsy, with TRUS guidance [29]. Although described initially using an axially orientated scanner, greater accuracy and simplicity were achieved using a longitudinally orientated ultrasonogram for guidance. The availability of an automatic biopsy device, using an 18G biopsy needle, facilitated transrectal biopsies. This route has many advantages; it is relatively painless, easily performed, readily accepted by the patients and it is highly accurate for small lesions [30]. Complications with biopsy can include haematuria, bleeding from the rectum, clot retention, septicaemia or urinary tract infection. To reduce these potential complications, patients should be asked if they have had any bleeding dyscrasia, use sodium warfarin, have a prosthetic heart valve or joints or if they have clinical heart murmurs, any of which may indicate that appropriate prophylaxis should be used [31].

Which strategy is best to perform prostate biopsies under TRUS guidance? Several approaches have been proposed; either 'random systematic' or directed

ultrasound-guided biopsies. If the lesion is visible then obviously it should be biopsied. If no lesion can be detected and prostate cancer is suspected, then random biopsies should be considered. Hodge *et al.* stated that random systematic ultrasonographically guided biopsies provide valuable additional information about the volume of cancer, if present [32]. Others have supported the utility of this biopsy technique for detecting prostate cancer [33]. Additionally, the extent of tumour in each biopsy core has been used to indicate tumour volume [32]. The disadvantages include the possibility of detecting insignificant small tumours and not knowing how frequently a cancer can be undetected by this technique [34]. Random systematic TRUS-guided transrectal biopsies can detect the 68% of cancers arising in the peripheral zone and the 8% arising in the central zone, but cannot help with the 24% that arise in the transition zone [32]. Terris *et al.* advocated measuring the extent of cancer in patients with only one positive biopsy [35]. The volume of cancer was proportional to the length of cancer in the biopsy core and additional biopsies were taken from patients with a tumour of ≤ 3 mm on one positive biopsy. In view of this elegant technique, cytological aspiration biopsies are of only limited use and not to be recommended.

Prostate cancer

Accurate staging is an important guide to prognosis and forms the basis upon which the initial management of patients with prostatic cancer is decided [36]. A DRE often underestimates the extent of the disease [37], sometimes overestimates [38] and correlates poorly with the volume of cancer [39]. TRUS is the imaging technique most used for the diagnosis and staging of prostatic cancer and it offers some valuable complements to the results of DRE and PSA measurements [42]. McNeal, with his description of the zonal anatomy of the prostate, has identified the likely sites of cancer within the gland and provided further understanding of the way in which prostate tumour spreads [7]. Lee *et al.* have described two potential weaknesses facilitating possible extraprostatic spread [28]. The invaginated extraprostatic space follows the ejaculatory duct and extends to the verumontanum. The beak of the seminal vesicle is the site of entry of the seminal vesicles and vas deferens into the central zone. In both cases, no capsules surround these areas [8]. On TRUS, the possibility of capsular penetration should also be considered when any bulging, thickening, irregularity or asymmetry is present. Although the findings of TRUS are dependent on the operator, it has the capacity to characterize the tumour by volume, location and extent, and therefore provides valuable clinical staging [41]. Scardino *et al.* compared staging

by DRE and TRUS with the surgical findings and found that of 60 tumours extending beyond the prostate, 92% were correctly identified by TRUS compared with only 20% by DRE. Finally, they concluded that the predictive value of TRUS was greater than that of DRE in identifying those tumours that would be localized, and was slightly better at identifying which tumours were extensive [42]. On the other hand, Lorentzen *et al.* investigated whether TRUS could predict the local stage of prostate cancer. They concluded that TRUS was probably superior to DRE as an initial staging tool, but TRUS of low specificity could upgrade the findings on DRE in cases where the prostate cancer was localized [43].

TRUS-aided therapies

Throughout the 20th century, urologists have sought an alternative to radical prostatectomy that would provide the same control of the disease without the associated morbidity. Among other methods, interstitial radiotherapy for prostate cancer has been investigated. Following the first reports by Young and Fronz in 1917, several modifications to the application of interstitial radiotherapy have been described [44–46]. There was increased interest in the implantation of radioactive isotopes in the prostate in 1982, when a technique for placing iodine 'seeds' under ultrasound guidance was developed [47]. It was not until 1989 that another ultrasound-aided therapy for the treatment of the prostate was introduced; transurethral ultrasound-guided laser-induced prostatectomy (TULIP) [48]. Laser treatment has become increasingly attractive for the treatment of bladder outlet obstruction due to BPH; currently almost 20 different treatment devices are available for the application of laser energy to the prostate. TULIP was one of the first laser systems designed to treat BPH; the procedure is carried out exclusively under transurethral ultrasonographic guidance. The advantage of such a treatment is a decreased morbidity, while aiming for the same efficacy as a TURP [49]. Because of the lack of direct visual control associated with the TULIP device and its expense and relative complexity, less expensive and easier laser technologies are being performed [50].

More recently, two applications of ultrasound in the treatment of prostate cancer have been reported; cryosurgery of the prostate and high-intensity focused ultrasound (HIFU). In the early 1960s, cryosurgery of the prostate was first performed for bladder outlet obstruction [51]. However, the use of prostate cryotherapy was limited by significant local complications resulting from inaccurate positioning of the probe and inadequate control of ablation, but ways of reducing the complications emerged with the advent of TRUS. Modern ultrasonography allows the precise placement of the percutaneous cryoprobe and

accurate regulation of the freezing zone, resulting in maximum destruction of the prostate and the minimum ablation of the surrounding tissues [52]. Several promising studies have been reported, with elimination of the local tumour and minimal complications [52,53]. The wavelength of the ultrasound used medically is sufficiently short to be brought to a tight focus at depth within the body. This ability to focus the energy means that good resolution may be obtained in diagnostic ultrasonography and that, if sufficient energy is carried by the ultrasound beam, regions of intense ultrasonic power are created in which therapeutic effects can be obtained. Using HIFU, a region of high energy-density can be produced within the tissue, which is then destroyed with no damage to overlying or intervening tissue. Initial reports of this technology in the treatment of prostate cancer and BPH are very encouraging [54,55].

Future developments

Apart from the therapy of prostatic diseases, TRUS may be applied in the diagnosis of prostate-related abnormali-

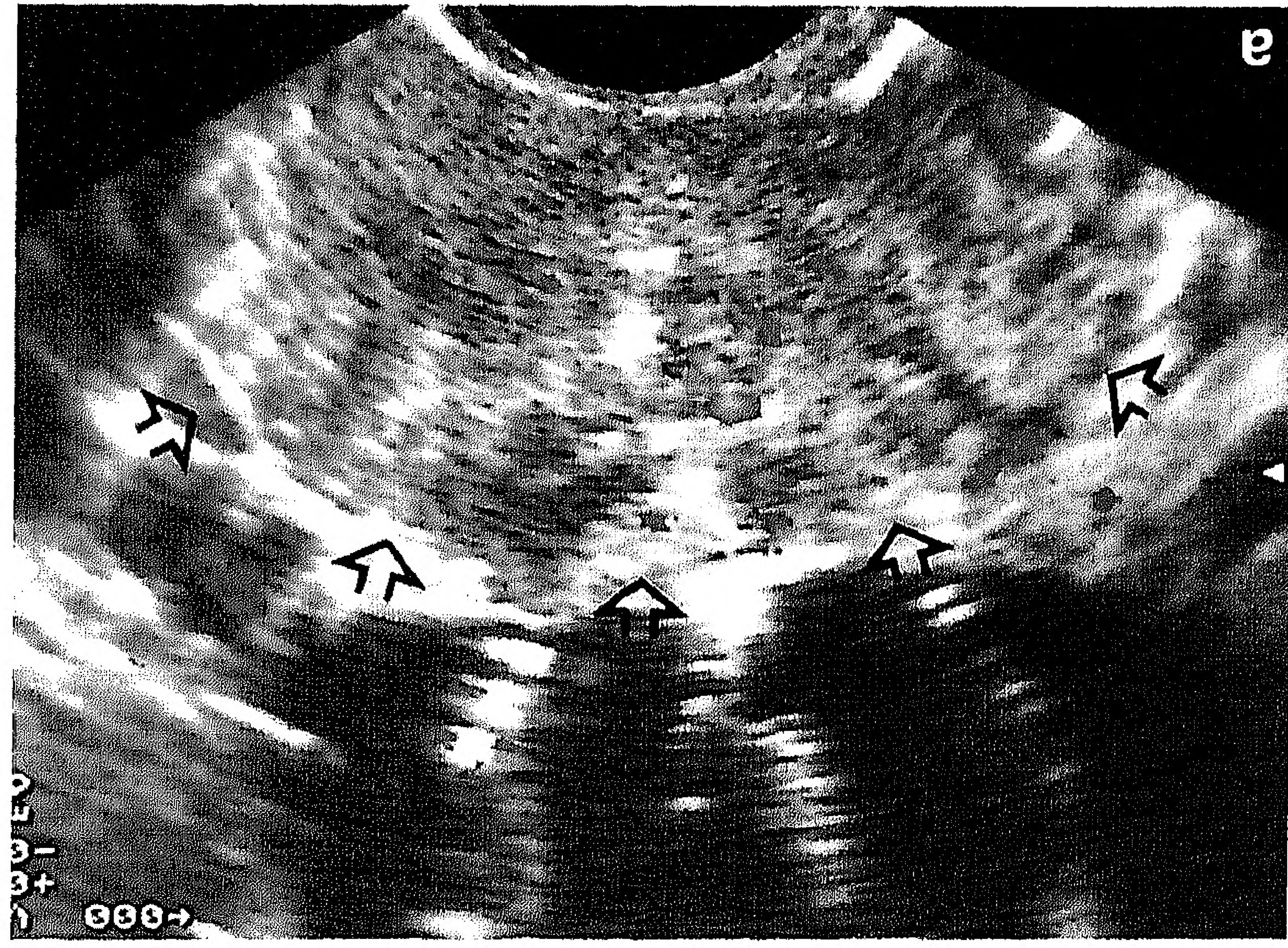


Fig. 4. Colour Doppler ultrasonography in a patient. a, before therapy and, b, 1 h after therapy.

ties. Ultrasonography is an alternative to radiographic cystometry; the ultrasonographic image can be displayed on a monitor and recorded concomitantly with pressures, flow, and EMG [56,57]. The advantages of ultrasound-aided urodynamic investigations were clarified in a study by Bidair *et al.* [58], but there were also disadvantages, predominantly the longer period of training required [58]. Another diagnostic application of ultrasound is colour Doppler ultrasonography (CDU). The advent of endorectal ultrasonography of the prostate brought hope that an earlier and more accurate diagnosis would be possible for prostatic diseases. CDU has, in other organs and anatomical areas, added to the diagnostic capability of gray-scale ultrasonography for both the detection and distinction of different disease processes. Early and very preliminary results with CDU of the prostate have suggested only a limited improvement over conventional gray-scale ultrasonography in differentiating cancer from (benign) processes [59]. However, there is encouragement for those who possess the knowledge and capability to perform CDU of the prostate gland to do so [60]. Besides using this technique in the detection of prostatic abnormalities, it can also be used to study the vasculature of the prostate and the outcome of heat treatments in patients with BPH [61] (Figs 4 and 5); more studies are required to determine the value of the latter.

Recently, our group reported the use of automated image analysis in the interpretation of TRUS images of the prostate [62]. To overcome problems in detecting prostate carcinoma caused by the poor hypoechoogenicity of some carcinomas during TRUS, we examined other tools and techniques for image analysis are being used regularly, e.g. to interpret satellite photographs, and similar techniques have been applied to medical

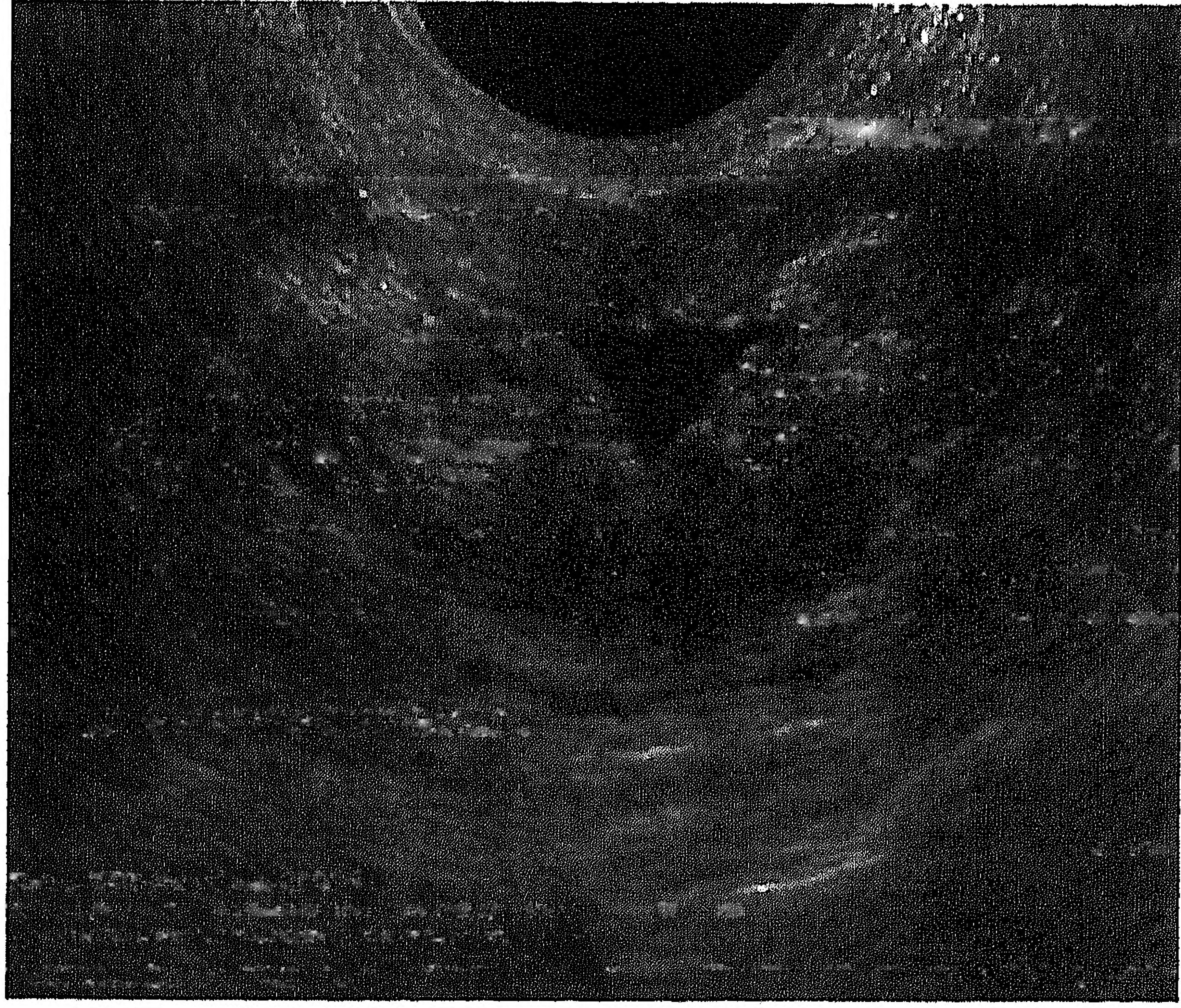


Fig. 5. Formation of a cavity seen in a transverse ultrasonogram 3 months after therapy.

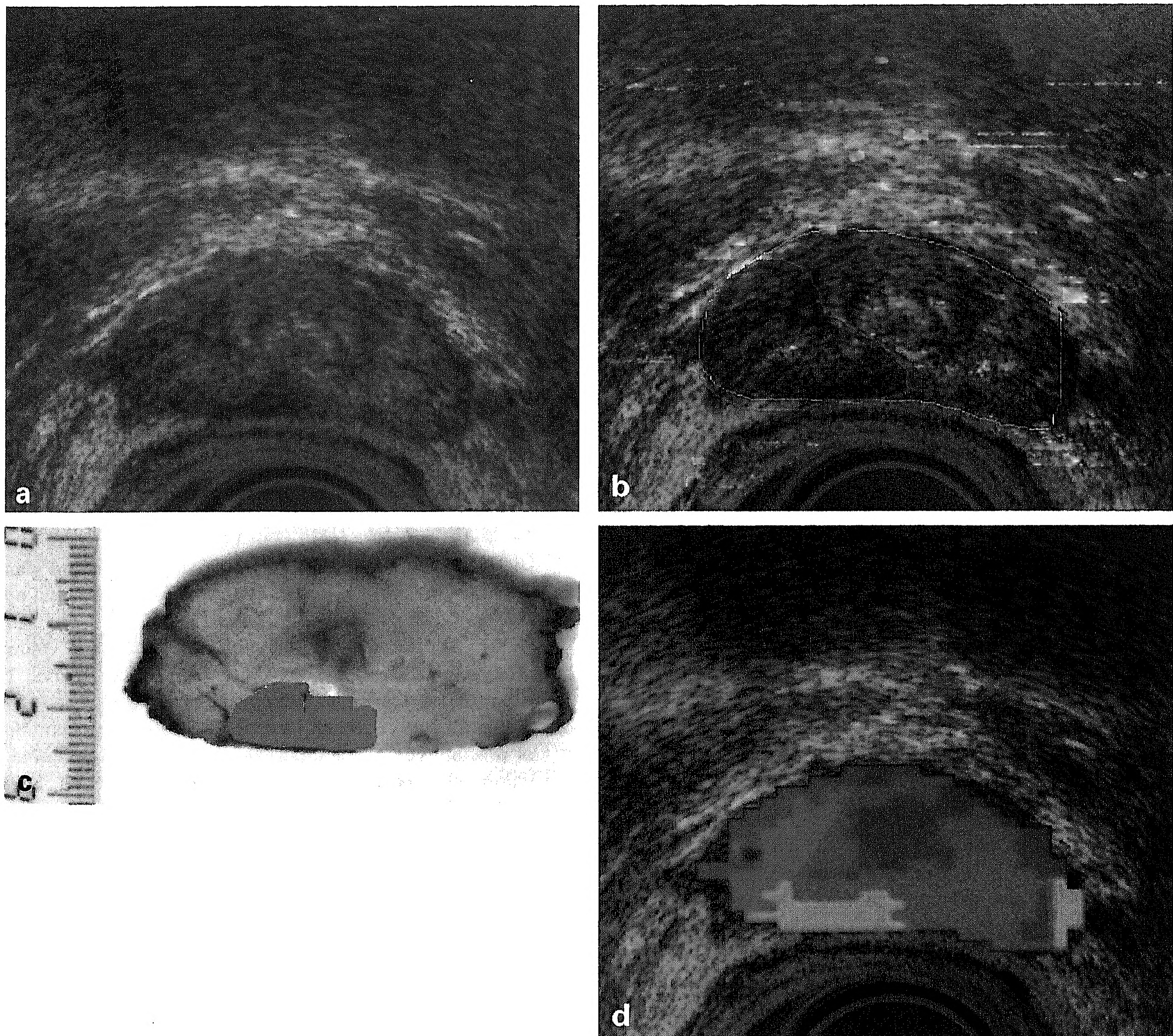


Fig. 6. Visualization of prostate cancer in a right prostate lobe. a, The plain ultrasonogram. b, Delineation by the examiner of the prostate boundary (white) and a prostate tumour (red). c, The corresponding histological section with demarcation of a tumour (red). d, The result of image analysis where suspicious areas are presented (orange).

imaging; early results from these studies are very promising. Therefore, a similar concept was applied to TRUS; we think that automated image analysis can help in the diagnosis of prostate carcinoma. In patients with non-palpable lesions or with poorly visualized tumours, visualization after image analysis is superior to the standard current diagnostic techniques (Fig 6).

Discussion

Prostatic diseases have become a major topic in urological diagnosis and treatment. The incidence of BPH is increasing concomitantly with the ageing population and, with the introduction of many alternative therapies,

the demand for treatment is almost limitless. Moreover, the prostate has become the main site of cancer in men, with prostate cancer now the second leading cause of death from cancer in men in the United States [63]. To diagnose accurately the different prostatic diseases, physicians have searched for adequate tools and techniques. The use of TRUS has increased rapidly since its introduction; over the past few years, there has been much interest and enthusiasm directed toward defining both the value and the limitations of TRUS. Whereas the role of TRUS in the screening and early detection of prostate cancer remains controversial, other applications, e.g. the assessment of prostatic size and volume, staging of prostate cancer, monitoring the response to therapy and

the guidance of prostate biopsy, have received a wider acceptance. Also, the development of an efficient and non-invasive treatment for the many patients with localized cancer of the prostate using HIFU or cryosurgery constitutes a considerable step forward. The existence of a reliable gauge for the development of the cancer and the possibility of repeated controlled biopsies facilitate the monitoring of the efficacy of the treatment. Because of the major impact of prostate cancer on national healthcare and the lack of accurate diagnostic techniques, we think that a significant improvement of the techniques for the detection of prostate cancer, such as computer analysis, will be of major clinical importance. Further studies are underway to decide the exact role of such an image analysis system. Finally, besides the current applications of ultrasound in the diagnosis and treatment of prostate diseases, further developments, e.g. temperature measurements using ultrasound techniques [64], will broaden the scope of the applications of ultrasound.

We conclude that, although there are limitations and restrictions for each of the various applications, thus far TRUS is unmatched as an imaging modality because it is versatile, easy to apply and cost-effective.

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