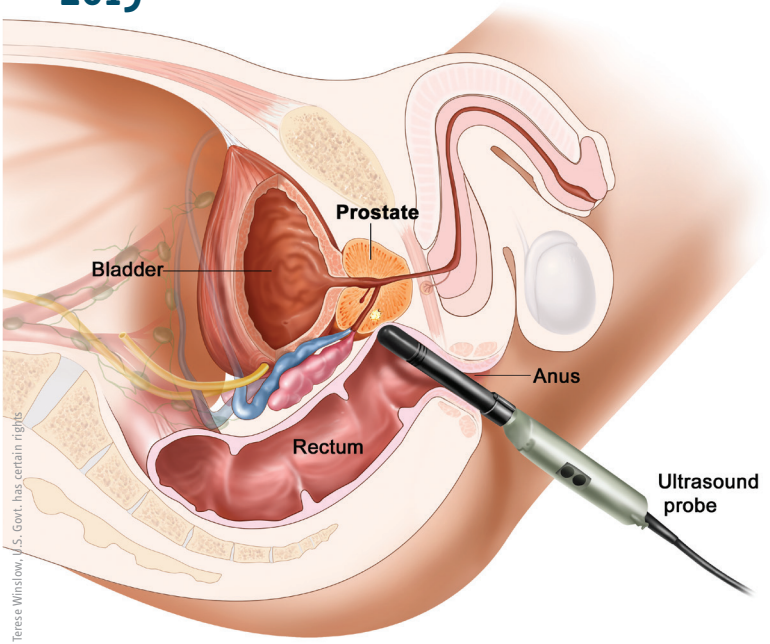
Evidence-based Guidelines for
Best Practice in Urological Health Care

Transrectal Ultrasound Guided Biopsy of the Prostate

2019



European Association of Urology Nurses

Evidence-based Guidelines for
Best Practice in Urological Health Care

Transrectal Ultrasound Guided Biopsy of the Prostate

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Preface

The European Association of Urology Nurses
The European Association of Urology Nurses (EAUN) was established in 2000 to represent the interests of European urological nurses. The EAUN's underlying goal is to foster the highest standards of urological nursing care throughout Europe. With administrative, financial and advisory support from the European Association of Urology (EAU), the EAUN also encourages research and aspires to develop European standards for education and accreditation for urology nurses. Improving standards of urological nursing care has been top of the agenda, with the aim of directly helping our members develop or update their expertise.

This update of our evidence-based guidelines on Transrectal Ultrasound Guided Biopsy of the Prostate (2015) aims to provide a standard and reliable protocol for the procedure, based upon a comprehensive review of the published literature, and includes recommendations clearly stating the level of evidence.

Local policies
We believe that excellent health care goes beyond geographical boundaries. This document is intended to support good clinical practice and should only be used in conjunction with local policies and protocols, and following assessment of the needs of the individual patient.

Distribution
This text is made available to all individual EAUN members electronically.
The full text can be accessed and downloaded from the EAUN website at no cost (www.eaun.uroweb.org).

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1. Introduction

Topic
Transrectal ultrasound (TRUS)-guided prostate biopsy remains the gold standard for diagnosing prostate cancer, by which tissue samples of the prostate are obtained for histological analysis (http://www.erspc.org/prostate-cancer/erspc-background/). Ultrasound-guided biopsy is now sometimes combined with MRI to characterise suspicious lesions in the prostate. An increasing number of nurses now undertake this procedure independently. The role of nursing continues to progress and to cross professional boundaries.

Aim
The aim of these guidelines is to assist in the professional development of nurses carrying out TRUS biopsy, while ensuring patient safety, dignity and comfort, and the delivery of the highest quality patient care. [1] These guidelines provide a benchmark against which the individual can be measured and their competence assessed. It may also inform those practitioners not directly involved in the procedure as they support patients.

Intended users
These guidelines are intended to complement and support clinical practice of new practitioners and those seeking updates on best practice. The intended readership is specialist urology nurses and other health care professionals working in urology or prostate cancer diagnostics. It is acknowledged that there is wide variation in nursing titles: for the purpose of this document, the term specialist nurse is used to mean nurses undertaking this advanced practice role. It is acknowledged that throughout Europe nurses have different levels of involvement with the biopsy procedure.

Inclusions
These guidelines include anatomy and physiology of the prostate, aetiology of prostate cancer, steps to undertake the biopsy procedure, pre-biopsy considerations, post-biopsy complications, and knowledge and understanding required by health care professionals to carry out the procedure.

Limitations
These guidelines are limited to transrectal ultrasound-guided biopsy and do not include ultrasound-guided transperineal biopsy and other imaging technologies (e.g. magnetic resonance imaging; MRI) used for prostate cancer diagnosis, although the working group recognises that these approaches are becoming more widely used.

These guidelines should be used within the context of local policies and existing protocols.

Rationale
In the European Union prostate cancer is currently the most frequently diagnosed cancer among men. [2] This has led to an increased demand for TRUS-guided prostate biopsy for prostate cancer diagnosis.

Workforce
An ongoing workforce problem continues in Europe where the medical profession remains under constant pressure to deliver high-quality clinical services in a timely and cost-effective manner. This requires nurse specialists to perform routine diagnostic services as a solution. To accelerate the prostate cancer patient journey, an increasing number of nurses working within the specialty are now performing prostate biopsies independently. Nurse-led prostate biopsy has highlighted improved access, reduced patient waiting time, and an enhanced patient journey with continuity of care. [3]

Skills and development
The ability to undertake prostate biopsy competently and safely is a developmental process and is only expected of specialist health care professionals, such as specialist nurses, physician assistants, or urologists, who are technically skilled as well as rational decision makers. The practitioner should:

- hold an expert understanding of the prostate cancer patient journey, including the risks, benefits, complications and disadvantages of undertaking prostate biopsy;
- have a comprehensive understanding of the anatomy and physiology of the male urinary system, factors that affect prostate-specific antigen (PSA) measurement, and other conditions of the urinary system and their management;
- have an understanding of the role of TRUS and possible ultrasound findings; and
- be familiar with the possible complications of TRUS and their management, and always ensure that senior staff are available should an emergency situation arise.

Supervision from an expert practitioner is necessary during the training period and auditing the procedure performed by nurses to measure clinical outcomes is important to support future accreditation. [3,4] Ultimately, competence for independent practice should be assessed by the senior urologist.

Specialist-nurse-led prostate biopsy allows professional development, as expansion of the role suggests that nurses in this position should be proficient with history taking and physical examination, alongside performing the procedure itself. [5]

All independent practitioners are responsible for their continuing professional development in relation to prostate cancer and prostate biopsy and must work within their own professional code of conduct.

Non-physician versus physician performance (PICO 4)
The Hori (2013) study and several audits have contributed to the evidence that an adequately trained non-physician provider is able to perform TRUS-guided prostate biopsy as effectively as an experienced urologist after an initial learning curve. To reach a level of competence, at least 50 biopsy procedures are needed. [5–9]

Recommendations	LE	GR
Health care professionals undertaking prostate biopsies should be trained by a competent practitioner	4	A
Health care professionals undertaking prostate biopsies should be trained in physical assessment including digital rectal examination (DRE)	4	C
The training for undertaking prostate biopsies should include well-structured didactics, hands-on training, and monitoring by a supervisor, and must be recorded in an individual portfolio.	4	C
It is recommended that trainees perform at least 50 biopsies with supervision before being signed off as competent	3	B
Direct supervision should be undertaken until the health care professionals are deemed competent to undertake the procedure independently	4	C
Final competence should be assessed and signed by a senior urologist and should be reviewed every 5 years	4	C
Health care professionals are required to remain up to date with the latest advances in the field of which they should be a member of a professional organisation and follow continuing education	4	C

2. Methodology

2.1 Guideline working group

The guidelines working group consisted of a multi-professional group of specialist nurses, and a medical colleague. Information about the authors can be found on page 56.

2.2 Literature search

The scientific basis of the information offered in these guidelines was obtained through a systematic literature search. All group members participated in the critical assessment of the scientific papers identified.
A search of the medical literature was conducted by Yuhong (Cathy) Yuan, Research Associate at McMaster University, Hamilton, Ontario, Canada. The initial search was conducted in July 2016 and repeated in November 2017 in the following databases:

- Cochrane Central Register of Controlled Trials
- Cochrane Database of Systematic Reviews
- Embase
- Epub Ahead of Print
- Ovid Medline(R) Daily and Ovid Medline(R)

Both medical subject headings (MeSH) and free-text terms, as well as variations of root words, were searched. The search was based on the keywords listed below.

2.3 Limitations of the search

PICO questions describe the four elements of a good clinical question, namely patient/ problem, intervention, comparison, and outcome. For this guideline four PICO questions were defined (see 2.4). and the studies resulting from the search that seemed relevant for each question were evaluated.
The search results were not limited to randomised controlled trials (RCTs), controlled trials, meta-analyses or systematic reviews. In all databases, output was limited to human studies, adults aged >19 years, and English-language publications. The initial search was limited to 1 January 2010 until 23 July 2016, and the repeat search to 23 July 2016 until 28 November 2017.

Conference abstracts, editorial letters and case reports were excluded during the search.

2.4 PICO questions

PICO 1
In TRUS-guided prostate biopsy should the number of biopsy cores to find initial prostate cancer, independent of prostate volume, be between 10 and 12 cores, or more or less?

PICO 2

Is there any evidence that concomitant use of oral anti-coagulants influences the rate of bleeding complications in patients who undergo TRUS-guided prostate biopsy?

Is there any evidence that discontinuation of novel oral anti-coagulants influences the rate of bleeding complication in patients who undergo TRUS-guided prostate biopsy?

PICO 3

Is there any evidence that giving patient information before undergoing TRUS-guided prostate biopsy improves quality of life and patient experience, and reduces physical or psychological side effects?

Is there any evidence that giving information to patients after undergoing TRUS-guided prostate biopsy improves quality of life and patient experience, and reduces physical or psychological side effects?

PICO 4

Is there any evidence of an effect on quality, safety, outcome, follow-up or patient satisfaction of a nurse (specialist, practitioner, oncology) or physician assistant performing TRUS-guided prostate biopsy compared to a urologist or trainee performing TRUS-guided prostate biopsy.

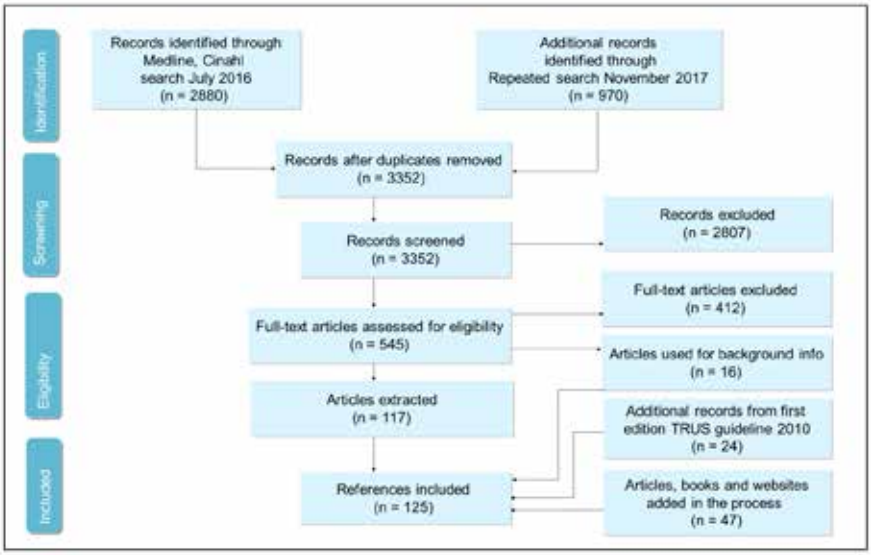
2.5 Search keywords

The reference search included the following keywords:

- TRUS
- ultrasound
- prostate
- biopsy
- not: cancer related terms

2.6 Search results

Flowchart 1. Literature search "TRUS prostate biopsy"



Numbers of records identified in search and update search
PICO 1: prostate biopsy and ultrasound, remove cancer terms; n = 3261 (2393 + 868)
PICO 2 = PICO 1 AND anti-coagulants; or anti-coagulants + urologist; n = 342 (280+ 62) (of them, 36 already captured by PICO 1).
PICO 3 = PICO 1 AND education = 143 (107+36) (all included in PICO 1);
PICO 4 = PICO 1 AND nurse: n = 16 (12+4) (all included in PICO 2);
CINAHL revised: n = 109 (88+21) (same search as for PICO 1 or anti-coagulants + urologist in Ovid)

It was a policy decision to restrict the search in the way described. Adding more keywords would have resulted in missing studies. In the process of working on the guidelines, some new references were found and added to the reference list, if they were relevant to the topic and cited in the text.

Screening and data extraction of the papers
Two panel members screened each abstract and two screened each full-text paper in Covidence. The most relevant studies were extracted. For PICO 2, 3 and 4 there were few relevant studies. For PICO 1 31 papers were extracted, and for Complications 67 papers were extracted. All extractions were performed in an Excel sheet. Systematic reviews were not extracted but reviewed separately during the writing process.

2.7 Exclusion criteria when selecting the abstracts

- transperineal prostate biopsy
- MRI
- saturation
- abstract
- studies written in a language other than English
- duplicates
- guidelines

2.8 Disclosures

All members of the EAUN guidelines working group have provided disclosure statements of all relationships that might be a potential source of conflict of interest. The information has been stored in the EAU(N) database.
The EAUN is a not-for-profit organisation and with the exception of administrative assistance, travel and meeting expenses, no honoraria or other reimbursements have been provided. There was no external financial funding.

2.9 Limitations of document

The EAUN acknowledges and accepts the limitations of this document. Guidelines provide a standardised approach to patient care and management and practitioners must tailor care towards individual patients. The aim of guidelines is to help health care professionals to make informed decisions about their patients. Adherence to guidelines does not guarantee a successful outcome. Ultimately, health care professionals must make their own decisions about care on a case-by-case basis, using their clinical judgement, knowledge and expertise, and after consultation with their patients. Therefore these guidelines provide recommendations without legal implications.

Cost-effectiveness considerations and non-clinical questions are best addressed locally and therefore fall outside the remit of these guidelines. Other stakeholders, including patient representatives, have not been involved in producing this document.

When high-quality publications were lacking, the recommendations were based on expert reports or expert consensus. This is clearly indicated in the document.

2.10 Review process

Prior to publication, blinded review was carried out by 11 reviewers, including nurse specialists, two patients, an oncologist, an oncological pathologist and a urologist. After discussion of all comments received, appropriate revisions were made by the Working Group and the document was approved by the EAUN Board and the EAU Executive Board member responsible for EAUN activities.

2.11 Rating system

The recommendations provided in this document are based on a rating system modified from that produced by the Oxford Centre for Evidence-based Medicine (OCBM) in 2011. [10].

Whenever possible, the Working Group graded treatment recommendations using a three-grade system (grade of recommendation; GR A–C) and inserted levels of evidence (LEs) to help readers assess the validity of the statements made. The aim of this practice is to ensure a clear transparency between the underlying evidence and the recommendations given. This system is further described in Tables 1 and 2.

Some of the literature was not easy to grade. However, if the EAUN Working Group thought that the information would be useful in practice, it was ranked as LE 4 and GR C. Low-level evidence indicated that no higher level evidence was found in the literature when writing the guidelines, but cannot be regarded as an indication of the importance of the topic or recommendation for daily practice.

The literature used in these guidelines included one qualitative study, but no recommendation was made based on this study.

The recommendations in these guidelines are based on a synthesis of evidence from the articles.

The Working Group aims to develop guidelines for evidence-based nursing, as defined by Behrens (2004) [11]: "Integration of the latest, highest level scientific research into the daily nursing practice, with regard to theoretical knowledge, nursing experience, the ideas of the patient and available resources". The Working Group based the text on evidence whenever possible, but if evidence were missing, it was based on best practice.

Four components that influence nursing decisions can be distinguished: personal clinical experience of the nurse, existing resources, patient wishes and ideas, and results of nursing science. [11] This statement implies that, although literature is important, the experience of nurses and patients is also necessary for decision making. Consequently, it is not only the written guidelines that are relevant for nursing practice.

Table 1. Level of evidence (LE)

Level	Type of evidence
1a	Evidence obtained from meta-analysis of randomised trials
1b	Evidence obtained from at least one randomised trial
2a	Evidence obtained from one well-designed controlled study without randomisation
2b	Evidence obtained from at least one other type of well-designed quasi-experimental study
3	Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports
4	Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

Adapted from the Oxford Centre for Evidence-Based Medicine (OCBM) [10]

Table 2. Grade of recommendation (GR)

Grade	Nature of recommendations
A	Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomised trial
B	Based on well-conducted clinical studies, but without randomised clinical trials
C	Made despite the absence of directly applicable clinical studies of good quality

Adapted from the Oxford Centre for Evidence-Based Medicine (OCBM) [10]

3. Terminology

3.1 Prostate

Accessory male reproductive gland; produces a third of seminal volume including fluids that activate sperm.

3.2 Seminal vesicles

Coiled glands that secrete a significant proportion of fluid that ultimately becomes semen.

3.3 Transrectal ultrasound

An ultrasound technique whereby an ultrasound probe is inserted into the rectum.

3.4 Digital rectal examination

Examination of the anus, lower rectum and prostate with the index finger.

3.5 Prostate-specific antigen

PSA is a glycopeptide that is produced exclusively in the prostate gland and secreted in the ejaculate, where its concentration is 106 times greater than in serum.

3.6 Prostate biopsy

A procedure whereby prostatic tissue is obtained for histological evaluation. Usually guided by TRUS.

3.7 Gleason score

Summation of the most prevalent and the worst Gleason grade, or if only one grade present its doubling, determining the aggressiveness of the prostate cancer.

3.8 ISUP 2014 Grade

Simplified five-grade group system based on the Gleason score that gives more understandable grade stratification. [12]

3.9 Specialist nurse

A nurse working in a specialist area, often at an advanced level with advanced practice qualifications.

4. Prostate anatomy

There is a requirement to be intimately familiar with the gross and glandular anatomy of the prostate as well as its ultrasound appearance (Fig. 2, 3, 4, 5).

4.1 Gross anatomy

In the post-pubescent man the prostate gland has a volume of up to 25 ml, being approximately 3.5 cm long, 4.0 cm wide and 2.5 cm deep from posterior to anterior, which is about the same size as a walnut.

The prostate is an extraperitoneal structure, lying anterior to the rectum and at the bladder neck. The prostate encircles the urethra and it empties its secretions into the urethra. It comprises a number of smaller glands that are surrounded by smooth muscle and connective tissue. During ejaculation the smooth muscle contracts and compresses the glands, forcing secretions into the urethra. Prostatic secretions contain several enzymes including PSA that help to liquefy semen by breaking down coagulation factors plus citrate, which the sperm uses for energy.

Between the gland and the rectum lies Denonvilliers' fascia – an obliterated peritoneal plane or a potential space. The prostate shape conforms to the anatomical limitations of the deep pelvic boundaries, and it looks like an inverted cone or pyramid. On either side are the levator ani and obturator internus muscles. The base of the inverted cone lies against the bladder and the apex on the urogenital diaphragm; a fibrous supporting ring that also contains the urethra. The gland is surrounded by the prostate (pseudo) capsule.

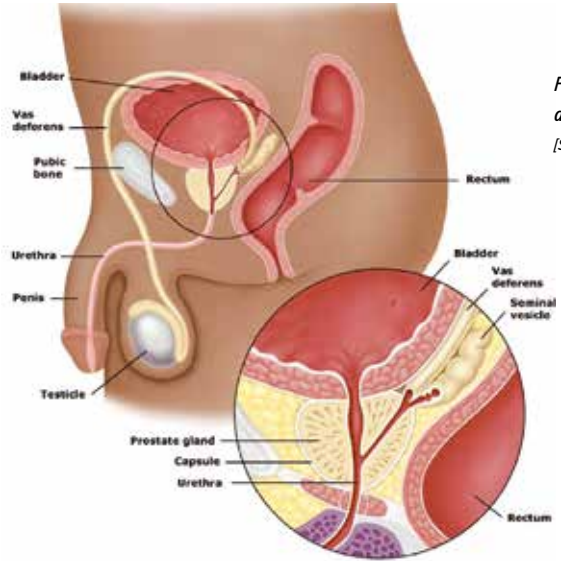


Fig. 2 Gross anatomy – male reproductive and urinary system
[Source: unknown]

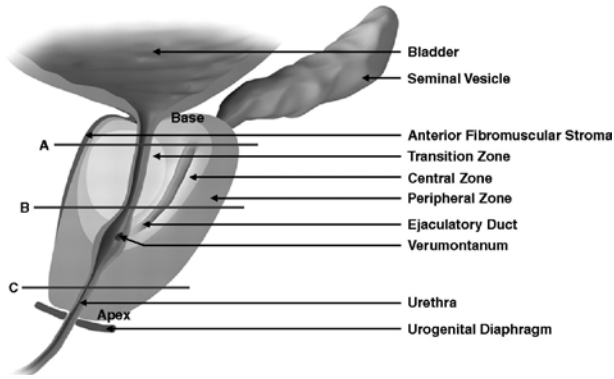


Fig. 3 Gross anatomy – prostate ((sagittal) - A base, B mid, C apex of gland

4.2 Zonal anatomy

Three glandular regions can be identified in the prostate: central, peripheral and transition zones. There is a further non-glandular area called the anterior fibromuscular stroma.

The peripheral zone accounts for 75% of the prostate tissue in young men but the transition zone increases in size with ageing due to benign prostate enlargement (BPE), while the central zone atrophies and the peripheral zone stays static. Thus, for clinical purposes the important regions are the peripheral and transition zones.

It is the peripheral zone in which the majority of prostate cancers occur, whereas BPE arises in the transition zone.

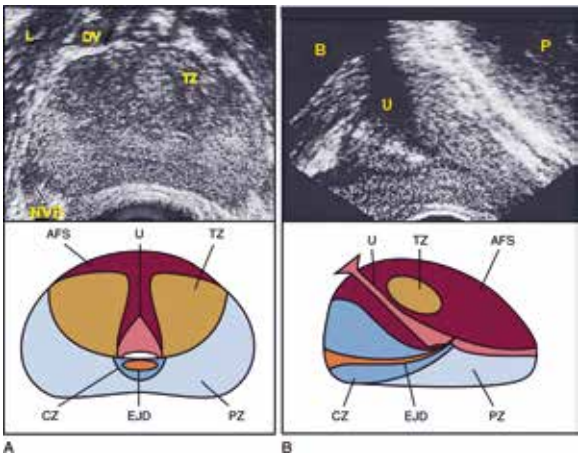


Fig. 4 Normal prostate ultrasound images with zonal anatomy
Normal prostate ultrasound images (top) with diagrams (bottom) at approximately the level of the verumontanum demonstrating zonal anatomy. A, Transverse view. B, Sagittal view. AFS, anterior fibromuscular stroma; CZ, central zone; DV, dorsal vascular complex; EJD, ejaculatory ducts; NVB, neurovascular bundle; L, levator muscles; PZ, peripheral zone; TZ, transition zone; U, urethra.

[Source: Campbell Walsh Urology, permission see page 44.]

Fig. 5 Ultrasound image of transition and peripheral zone

(Courtesy of: S. Hieronymi)

4.3 Vascular anatomy

The prostate has a rich arterial blood supply. The prostate artery is a branch from the inferior vesical artery (Fig. 6), a branch of the internal iliac artery, which divides into capsular and urethral arteries. Branches of the inferior vesical artery supply the seminal vesicles and occasionally the base of the gland. Santorini's venous plexus lies anteriorly and has small perforating vessels into the prostate. The neurovascular bundles lie postero-laterally at 5 and 7 o'clock and contain the branch arteries, veins and nerves that go to the penis and urethral sphincter.

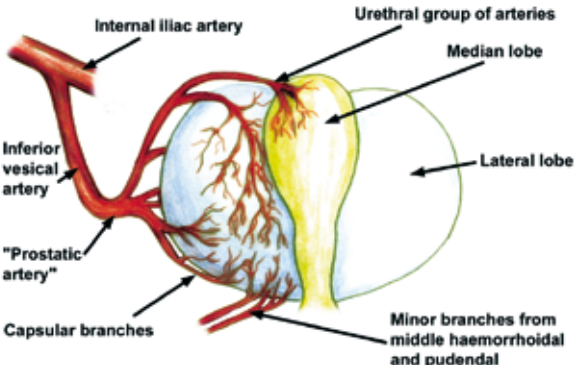


Fig. 6. Prostate arterial supply

(Source: eMedicine.com, permission see page 44)

4.4 Prostatic urethra

The prostatic urethra runs through the prostate from the base of the bladder to the apex of the prostate. It is a midline structure unless there is asymmetric glandular enlargement. There is a triangulated portion at the verumontanum where the ejaculatory ducts drain into the urethra. There is a variable amount of smooth muscle around the urethra and this, with the urogenital margin, accounts for its visibility on ultrasound in the collapsed state.

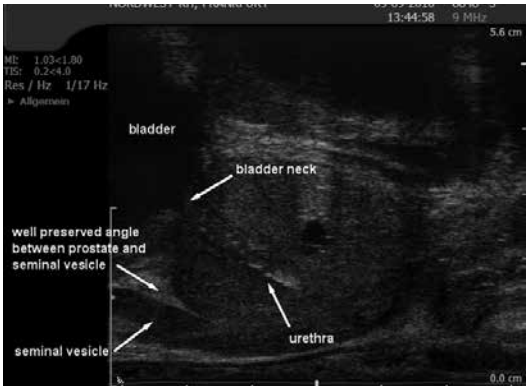


Fig. 7. Ultrasound of the gross anatomy of the prostate demonstrated on TRUS
(Courtesy: S. Hieronymi)

4.5 Seminal vesicles and ejaculatory ducts

The seminal vesicles are paired sac-like structures of variable size and shape and lie just posterior and superior to the base of the prostate. A minor degree of asymmetry is common. The paired ejaculatory ducts formed by the union of the vas deferens and the seminal vesicles run through the prostate in the central zone. They communicate with the prostatic urethra at the verumontanum. [13–15] See Fig. 7, section 4.4.

4.6 Prostate cancer, grading and staging

The incidence of prostate cancer varies considerably internationally with the lowest incidence in Southeast Asia and highest in Australia/New Zealand and Northern Europe. The age-standardised incidence rates range from around 5.0 per 100,000 in Asia to 86.4 per 100,000 in Australia/New Zealand. [16] In any one population the incidence is higher in men of Afro-Caribbean heritage than Caucasians. [17] Across the world mortality rate varies from about 3.3 to 10.2 per 100,000. [16] Worldwide, prostate cancer is among the most common cancers, with an estimated 1,276,106 new cases and 358,983 deaths in 2018. [18] The incidence of prostate cancer has increased significantly over the past two decades; almost exponentially in some areas. [19–21] This increased incidence is explained by the introduction of the PSA blood test [22,23] and an ever-ageing population.

Autopsy studies have shown that the prevalence of prostate cancer increases sharply with age, and foci of prostate cancer can be detected in up to 70–80% of 80-year-old men who have died of other causes. [24–26] In contrast to the rate of clinical or biopsy-detectable prostate cancer, there was no significant international difference in the incidence of prostate cancer in autopsy studies. [24,25] International variation in the incidence of prostate cancer, and the fact that incidence increases in the first and second generations of migrants from low- to high-risk areas, indicate that the manifestation of clinically significant prostate cancer depends on exogenous factors. [27–29]

Grading

The original prostate cancer grading system was developed in 1966–1974 by Donald Gleason. [30,31]. Since then, several consensus meetings have helped to improve and update the histological interpretation of prostate cancer. [32,33] The latest World Health Organization classification was released in 2016. [33]

The Gleason grading system is based on the architectural pattern of the tumour, and the grade is defined as the sum of the two most common grade patterns (Gleason score; GS). [30,31,34] The primary predominant and secondary (second most prevalent) architectural patterns are assigned a number from 1 (most differentiated) to 5 (least differentiated). It is now recognised that, in most circumstances, Gleason grade (GG) should only be given from 3 to 5. GG 1 is ultimately a benign feature, and was mistaken for tumour tissue before the era of immunohistochemistry. GG 2 should not be given to prostate biopsy specimens. [32] Therefore, if only GG 3 is seen on the biopsy, the tumour has to be reported as 6 (3+3). In case of mixed features of GG 3 and 4, the predominant amount will be placed first as either (3+4) or (4+3). However, as the presence of even a small focus of GG 5 pattern tumour may be prognostic, in the case of a tumour with a large amount of GG 3 and a significant amount of GG 4 but only 5% GG 5, the cancer should be reported as (3+5). Each biopsy is to be reported separately and it appears that the highest GS is what drives prognosis even if this is only found in a single biopsy.

Consequently, this has resulted in an odd situation in which biopsy GS ranges from 6 to 10. This has been resolved with the introduction of the Gleason Grade Groups (GGGs). These grade groups are numbered from 1 to 5 with GS 6 (3+3) as the lowest and least aggressive group (GGG 1). This is especially important for GS 7 (3+4) and 7 (4+3). These two settings have a different outcome, and the new GGG system allows one to make a clear distinction between GGG 2 [7 (3+4)] and GGG 3 [7 (4+3)] [12,35,36]. The new system is also known as ISUP Grade Groups after the consensus conference in 2014 where they were agreed.

Table 3. ISUP Grade Groups

Gleason score	ISUP Grade group
6 (3+3)	1
7 (3+4)	2
7 (4+3)	3
8 (4+4); 8 (3+5); 8 (5+3)	4
9 (4+5); 9 (5+4); 10 (5+5)	5

Staging

Table 4. Tumour Node Metastasis (TNM) classification of PCa [52]

T 1

T1 Clinically inapparent tumour not palpable or visible by imaging

T1a Tumour incidental histological finding in 5% or less of tissue resected

T1b Tumour incidental histological finding in more than 5% of tissue resected

T1c Tumour identified by needle biopsy (e.g. because of elevated prostate-specific antigen (PSA)

T2

T2 Tumour confined within the prostate[1]

T2a Tumour involves one half of one lobe or less

T2b Tumour involves more than half of one lobe, but not both lobes

T2c Tumour involves both lobes

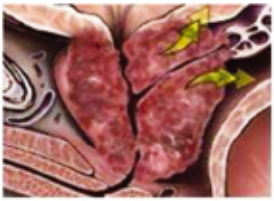
T3

T3 Tumour extends through the prostatic capsule[2]

T3a Extracapsular extension (unilateral or bilateral) including microscopic bladder neck involvement.

T3b Tumour invades seminal vesicle(s)

T4



T4 Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall

T Primary tumour
TX Primary tumour cannot be assessed
T0 No evidence of primary tumour

N Regional lymph nodes[3]
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis

M Distant metastasis[4]
M0 No distant metastasis
M1 Distant metastasis
M1a Non-regional lymph node(s)
M1b Bone(s)
M1c Other site(s)

[1] *Tumour found in one or both lobes by needle biopsy, but not palpable or visible by imaging, is classified as T1c.*
[2] *Invasion into the prostatic apex, or into (but not beyond) the prostate capsule, is not classified as T3, but as T2.*
[3] *Metastasis no larger than 0.2 cm can be designated N1 mi.*
[4] *When more than one site of metastasis is present, the most advanced category should be used.*

Adapted from Sobin (2009). [37]

5. Patient assessment and preparation

5.1 Indications

The need for an initial prostate biopsy is based on PSA level, familial risk, and suspicious DRE or imaging. Age, potential comorbidity, and therapeutic consequences should also be considered and discussed beforehand. A single limited PSA elevation alone should not prompt immediate biopsy. PSA level should be verified after a few weeks using the same assay under standardised conditions (i.e., no ejaculation, manipulations, and urinary tract infections) in the same laboratory. [38,39]

Despite this, for men with PSA 4–10 ng/ml, the chance of finding cancer is ~25% but many of these tumours are insignificant. Risk stratification is a potential tool for reducing unnecessary biopsies. [40] Risk calculators may be useful in helping to determine (on an individual basis) what the potential risk of cancer may be. Several tools developed from cohort studies are available from:

- the Prostate Cancer Prevention Trial Risk Calculator Version 2.0 (PCPTRC 2.0) http://myprostatecancerrisk.com/;
- the European Randomized Study of Screening for Prostate Cancer: http://www.prostatecancer-riskcalculator.com/seven-prostate-cancer-risk-calculators

An updated version was presented in 2017, including prediction of low and high risk, based on the International Society of Urological Pathology (ISUP) grading system and presence of cribriform growth in histology. [41]

Prior imaging with MRI for detecting prostate cancer remains controversial but evidence from the PROMIS and PRECISION studies [42,43] has suggested that upfront multi-parametric MRI (mpMRI) with targeted biopsy of abnormal lesions is significantly better for detecting clinically important prostate cancer compared to TRUS biopsies, and reduces the number of insignificant cancers detected.

Prostate biopsy can be performed by either the transrectal or transperineal approach. Xue et al. (2017) have shown that cancer detection rates are comparable between the two approaches, when performed without prior MRI. [44]

The indications for repeat biopsy are:

- rising and/or persistently elevated PSA;
- atypical small acinar proliferation (i.e., atypical glands suspicious for cancer), 31–40% risk [45];
- extensive (multiple biopsy sites, i.e., ≥3) high-grade prostatic intraepithelial neoplasia, 30%. [46]; and
- active surveillance.

5.2 Patient information pre-biopsy (PICO 3)

Giving information to patients who are undergoing TRUS biopsy is crucial as it can lower anxiety before and after the procedure. [47] Patients who feel inadequately informed experience more adverse effects than those that are well prepared. [48]

A patient information leaflet (PIL) should be given to inform every patient before TRUS biopsy. Although there are wide variations in the content of the information in different centres/ hospitals [49], it is agreed that PILs can play a key role in improving patients' experience and manage their expectations about:

- significance or rationale of the procedure;
- procedure explanation: number of cores, analgesia, staff who will carry out the procedure;
- potential adverse effects;
- possible complications and duration;
- how to manage complications; and
- hospital contact numbers. [48]

Unfortunately, however, most of the PILs about TRUS biopsy poorly adhere to the guidelines and are difficult for patients to understand. [50] A PIL without any explanation from the health care giver is insufficient. [51]

Increasingly, an important source of information for patients is the Internet, but there is a wide variance in quality of information on the Web about TRUS biopsies. The health care giver should be aware of that and can be a trusted guide for patients to find reliable medical websites for more information. [50,52]

Health care providers should also be aware that written information on prostate cancer (both on websites and in leaflets) often requires a higher level of understanding than that of the average adult and therefore may present a barrier. [50]

Recommendations	LE	GR
Prior to TRUS biopsy health care providers must provide men with an up-to-date, evidence-based and easy-to-understand PIL and must ensure that the information is well understood	3	C
Prior to undergoing TRUS biopsy and in addition to the written information, patients should be able to talk with a specialist nurse or clinician	3	C

5.3 Pre-investigations and prophylaxis

Patient selection
Appropriate patient selection is important when considering prostate biopsy. Pre-existing comorbidity, medication and infection risk should be assessed both in the context of carrying out the biopsy and considering whether the patient is fit to undergo any treatment if cancer were to be diagnosed. Patients should be questioned to elicit any high-risk behaviour.

Prophylactic antibiotics
Oral or intravenous antibiotics are recommended. Quinolones are the drugs of choice, with ciprofloxacin being superior to ofloxacin. [53]
Antimicrobial prophylaxis should be used on the basis of patients' existing risk factors. In patients with one or more of these risk factors, practitioners should consider utilisation of targeted prophylaxis or augmented antimicrobial therapy. [54–56]
When deciding on the choice of antibiotic, dosage and timing, individual risk factors and local policies and pathways should be taken into account including regional and local antibiotic resistance patterns. Increased quinolone resistance is associated with a rise in severe post-biopsy infection. [57,58]

Assessment of the urinary tract
Pre-biopsy assessment of urinary symptoms is important to exclude risk of urinary retention and current/active urinary infection. [59]

Perineal swabs and antimicrobial resistance
The evidence for perineal swabbing prior to prostate biopsy is weak and conflicting. [60–62]
The evidence supporting pre-biopsy swabbing appears to depend on the patient group. All of the reviewed publications support rectal swabs in high-risk patient groups, that is: patients at high risk of infection; patients with recurrent or recent urinary tract infection treated with antibiotics (in the last 6 months); patients recently treated with antibiotics; and patients who have recently travelled through Asia. [63]

Urinary flow
The risk of urinary retention after biopsy is considered low in most documented series. Overall, the risk is 0.2–0.8%. [64,65] However, stratifying the potential risk of retention before biopsy is a sensible approach through the use of the International Prostate Symptom Score, flow-rate and post-void residual measurement. Patients at highest risk should be treated with an α-blocker and/or laxatives if there is evidence of chronic constipation. [66,67]

Urinary infection
The evidence for collection of mid-stream specimen urine culture over urinalysis is strong and is documented in the 2016 EAU Guidelines on Urological Infections. [68]

Where evidence of bacteriuria is confirmed prior to urological procedure, exacerbation by prostate biopsy can lead to life-threatening sepsis if untreated. [55,69] Patients with symptomatic urinary infections should be deferred until treated.

If a confirmed infection results in elevated PSA level, the biopsy should be deferred and the (urinary) infection treated, and repeat PSA test may be recommended on discussion with the medical team.

Recent antibiotic use

Recent antibiotic use prior to biopsy has also been shown in several studies to increase the rate of infectious complications, mainly due to drug-resistant bacteria. [70] This was most acutely demonstrated in the quinolone-resistant group. [71] The increased infection risk of patients with prior antibiotic use is relevant for a period of 6 months prior to biopsy. [56]

Recent travel

Several studies have alluded to the increased risk of infection due to recent travel, which is significantly higher in people that have travelled to Southeast Asia and India. [63]

Recent hospitalisation

Hospitalisation within the month preceding biopsy is another known risk factor. [54] Kamdar et al. (2008) further found that 75% of patients who developed post-biopsy bacteraemia were either health care employees or had a relative working in health care and living within their household. [72]

Diabetes

Some studies have demonstrated associations between patient comorbidity and infection risk after prostate biopsy. Diabetes in particular confers an increased risk of febrile and infectious complications. [54,73] Practitioners may want to consider delaying prostate biopsy until glycaemic control is adequate; however, there have been no published studies on this measure.

MRI

Correlation with radical prostatectomy shows that mpMRI, associated with T2-weighted imaging with at least one functional imaging technique (diffusion weighting, dynamic contrast enhancement, or H1-spectroscopy), has good sensitivity for the detection and localisation of prostate cancer with GS >7. [74]

As a result, mpMRI is increasingly performed prior to biopsy, with incorporation of additional targeted biopsy of suspicious lesions. Such biopsies can be obtained through cognitive guidance, US/MR fusion software, or direct in-bore guidance. Current literature does not show clear superiority of one technique over the others. [75]

It has been shown that MRI-targeted biopsies improve detection of clinically significant prostate cancer in the repeat biopsy setting. [76]

However, single-centre RCTs performed in biopsy-naïve men provided contradictory findings as to whether the addition of MRI-targeted biopsies to systemic biopsies improved the detection of either prostate cancer or clinically significant prostate cancer. [77–79]

The recent multicentre RCT PRECISION study [42] showed that MRI before biopsy and targeted biopsy was superior to standard biopsy alone. The question remains: is the combination of MRI-targeted biopsy plus systemic biopsy better than targeted biopsy alone.

Rectal preparation

Since the bacteria responsible for prostate-biopsy-related infection primarily originates in the rectum, various rectal agents have been evaluated for their ability to reduce bacterial load and risk of infection.

Enemas: pre-biopsy enema has demonstrated limited benefit in reducing post-biopsy infection rate [80], with one study suggesting that enemas cause local rectal mucosal irritation and a subsequent increased risk of bacterial inoculation. [81]

Rectal cleansing: povidone–iodine solution (a widely available and cost-effective agent) has been studied as a potential rectal cleansing agent. Review of the literature is contradictory with most studies non-blinded or retrospective; however, there is some suggestion that high-risk patients may benefit. [61,82,83]

Methicillin-resistant *Staphylococcus aureus* (MRSA)

Testing for MRSA is not routinely recommended before prostate biopsy, unless a patient is at high risk. Positive MRSA infection does not affect the decision to carry out a biopsy; however, it may affect the use of antibiotics before or after the biopsy. Please refer to any local infection control guidelines.

Anti-aggregants and anti-coagulants (PICO 2)

Anti-coagulant and anti-aggregant drugs eliminate or reduce the risk of blood clots, using different mechanisms. However, both increase the risk of bleeding.

Common anti-coagulants include: heparin, warfarin (Coumadin), rivaroxaban (Xarelto), dabigatran (Pradaxa), apixaban (Eliquis), edoxaban (Savaysa), enoxaparin (Lovenox) and fondaparinux (Arixtra).

Common anti-aggregant drugs include: aspirin, clopidogrel (Plavix), ticagrelor (Brilinta), prasugrel (Effient), dipyridamole, dipyridamole/aspirin (Aggrenox), ticlodipine (Ticlid), eptifibatide (Integrilin).

The systematic review of the papers defining safe anti-coagulation and anti-platelet levels in TRUS biopsy is incomplete and does not reflect recent changes in prescribing patterns. However the following tables detail both risk groups and current evidence in relation to urological surgery (TRUS biopsy where available).

Risk groups

Anti-coagulants

Determining a patient's thrombotic risk (i.e. of stroke or venous thromboembolism; VTE) if anti-coagulants are stopped is not straightforward and local guidelines should be used where available.

Risk categories of patients using anti-coagulants

This simple chart (Table 5) outlines risk categories as defined by the UK Pharmacy Association (2016). However local guidelines should be followed in regards to the requirements and dose of bridging therapies, for example, low-molecular weight heparin.

Table 5. Thrombotic risk categories of patients using anti-coagulants

Lower thrombotic risk	Higher thrombotic risk
Atrial fibrillation (AF) Patients with non-valvular AF and with no additional risk factors	Atrial fibrillation (AF) Patients with AF and at least one risk factor – prior embolism, transient ischaemic attack (TIA)/stroke, rheumatic heart disease, left ventricular dysfunction (ejection fraction <30%), hypertension, diabetes, age >75 years, or intra-cardiac thrombus
Venous thromboembolism (VTE) Patients receiving anti-coagulants >3 months from scheduled biopsy	Venous thromboembolism (VTE) Any deep vein thrombosis (DVT)/pulmonary embolism (PE) <3 months prior to biopsy Recurrent unprovoked DVT/PE Life-threatening PE or past thrombolytic treatment
Prosthetic heart valves Patients with low-risk heart valves, i.e. aortic biovalves in good condition (Always discuss with cardiologist first)	Prosthetic heart valves Older generation mechanical valves and all mitral valves Patients who are in AF with heart valves (Always check with cardiologist first)

[84]

Anti-aggregants
Patients on anti-aggregant therapy for secondary stroke prevention, especially after a recent stroke should continue with aspirin. Withdrawal of anti-aggregants should be avoided within 12 months of patients undergoing drug-eluting or bare-metal stent placement. If biopsy is required, a cardiology opinion should be sought for bridging therapy guidance, and where there are local guidelines, these should be preferentially followed.

Guidance on use of anti-coagulant, anti-platelet and anti-thrombotic agents pre-biopsy
The following tables give guidance on the common anti-coagulant, anti-platelet and anti-thrombotic agents with respect to when/if they should be stopped pre-biopsy.

Anti-coagulants
Patients in the high-risk group, may require a bridging treatment to their anti-coagulant therapy. Please discuss this with the patient's prescriber or follow local hospital guidelines.

Table 6. Which anti-coagulants should be stopped pre-biopsy and when

Drug	Stop medication Yes/No	When to stop?	Ref.	LE
Warfarin (Coumadin)	Yes	5–7 days	[85]	1a
Heparin	Yes	3–5 h	[85]	1a
Rivaroxaban (Xarelto)	Yes	48 hours	[85]	1a
Dabigatran (Pradaxa)	Yes	48 hours	[85]	1a
Apixaban (Eliquis)	Yes	48 hours	[85]	1a
Edoxaban (Savaysa)	Yes	48 hours	[85]	1a
Enoxaparin (Lovenox)	Yes	6 hours	[85]	1a
Fondaparinux (Arixtra)	Yes	48 hours	[85]	1a

Anti-aggregants (anti-platelets)
Patients who have had recent or recurrent TIA/stroke should be considered high risk; therefore, advice on stopping medication should be sought from the patient's prescriber.

Table 7. Which anti-aggregants should be stopped pre-biopsy and when

Drug	Stop medication Yes/No	When to stop?	Ref.	LE
Aspirin	No	N/A	[86–88]	1b
Clopidogrel (Plavix)	Yes	7 days	[85,87]	1a
Prasugrel (Effient)	Do not stop this medication without consulting a prescriber	7 days	[89]	1a
Dipyridamole/ aspirin (Aggrenox®)	Yes	3 days	[85]	1a
Ticlopidine (Ticlid)	Yes	7 days	[90]	1a
Eptifibatide (Integrilin)	Yes	2–4 h	[91]	According to pharmacology
Ticagrelor (Brilinta)	Do not stop this medication without consulting a prescriber	3 days	[91]	According to pharmacology
Rivaroxaban or Apixaban	Yes	2 days	[85]	1a

5.4 DRE at pre-biopsy examination (diagnosis)

DRE pre-biopsy is recommended for several reasons. DRE allows the practitioner to assess the patient's tolerance of rectal examination and the ultrasound probe.
Pre-prostate biopsy studies have also demonstrated that:
- in ~18% of cases, prostate cancer is detected by suspicious DRE alone, irrespective of PSA level. [92]
- abnormal DRE is associated with an increased risk of higher GS and is an indication for biopsy. [93]

6. Transrectal ultrasound and biopsy procedure

It is important that the environment is suitably prepared and all the required equipment is available and checked to be in working order before the procedure is commenced. All team members must be aware of their roles and emergency procedures, including the location of the emergency equipment trolley. All staff must have the ability to contact a senior clinician should the need arise.

In order to avoid a mix-up of prostate biopsy samples, it is preferable to:
- Prepare the labels with bar code in advance. These labels should contain name, date of birth and hospital number of the patient who will undergo the prostate biopsies.
- Before the procedure, ask the patient to state their complete name (first and last name) and date of birth to verify the label is correct
- Stick the labels on the histology cassettes.
- When all biopsies are performed, take the labelled histology cassettes with the biopsies tissue to the pathology department immediately.
- As soon as the cassettes arrive at the pathology department, they have to be scanned and saved in the patient record on the computer.

6.1 Room preparation

A spacious clinical room at a comfortable temperature is required, and should be suitably furnished with flooring and equipment that can be decontaminated if there are any spillages of body fluids. The standard equipment required includes:

- examination couch
- curtains/privacy screen
- ultrasound machine
- ultrasound probe
- sharps bin
- linen skip
- clinical waste bin

The following items should be prepared ready in advance:
- procedure checklist
- consent form (signed and dated by patient and clinician performing biopsy)

Ultrasound preparation
- latex-free condom/sheath
- lubricating jelly

Personal protective equipment
- apron
- gloves

Digital rectal examination
- lubricating jelly

Local anaesthesia administration
- local anaesthetic (according to local policy, see recommendations in 6.6.1)
- appropriate size syringe
- dilution needle
- long spinal needle

Biopsy performing equipment
- single use biopsy device
- needle guide
- specimen pots (labelled accordingly with local policies to identify cores)
- pathology requisition form

Post-biopsy
- wipes/gauze
- antibiotics (according to local policy)

See Figure 8.

Fig. 8 Example of equipment needed for TRUS prostate biopsy

(Courtesy G. De Lauw)

Emergency equipment should be easily accessible in the rare event of a major complication. This should include:

- oxygen
- suction
- cardiac arrest trolley
- defibrillator
- emergency drugs
- anaphylaxis kit
- monitoring equipment
- intravenous fluids
- intubation equipment

6.2 Patient informed consent

Patients should be aware of the potential complications. Before undertaking the procedure the health care professional must seek permission from the patient. This can be either implied or written consent according to local policy. However, for the consent to be valid patients must be competent to make the decision for the investigation to be undertaken. They must have sufficient information to make that decision and not act under duress.

Patients have a fundamental legal and ethical right to determine what happens to their own bodies. Seeking consent is a matter of common courtesy between health care professional and patient. It is not a legal requirement to seek written consent in all countries but it is recognised as good practice, particularly if the procedure comes with significant risks or side effects or the procedure involves regional anaesthesia or sedation.

Informed consent should include [94]

- what the examination involves
- what is its purpose
- what are the risks
- whether the risk is major or minor
- what happens if the examination is not undertaken

However you should familiarise yourself with your local or national consent policy, if there is no policy you might want to consider the implications of your practice as a nurse. [95]

Patients should be made aware of the risk of a false-negative test result and the potential need for repeat biopsy.
The health care professional responsible for carrying out the procedure is ultimately responsible for patient consent for the examination. [60, 61, 62]

Recommendation	LE	GR
• Ensure that the patient understands the potential complications of the procedure, including any risk factors specific to them	4	A

6.3 Transrectal ultrasound

The prostate gland can be visualised with a transrectal probe allowing close-contact scanning. [13] Ultrasound is essential for examining the echotexture and size of the gland and to aid precision biopsy. It is more accurate than DRE in measuring prostate size. [96]

Fig. 9. Ultrasound machine
(Courtesy: BK Ultrasound)

6.3.1 Probe choice and preparation

The ultrasound probe is a dedicated use probe and can vary in frequency between 6 and 9 MHz; the most frequently used being 7.5 MHz. The probe allows visualisation of the prostate in both the transverse and sagittal planes. Probes are end-firing, biplane or both, and there are several designs marketed by different manufacturers. In practice, the design of the probe is not important as full glandular scrutiny is achieved with either design; however, if true anatomical views are required then a biplane probe is essential. [13] The probe is covered preferably with a latex-free condom or probe cover and is decontaminated according to the manufacturer's recommendations before and after each patient.

6.3.2 Patient positioning

The patient is positioned in the left lateral position ensuring that the knees are bent up towards the chest, or in the lithotomy position. The left lateral position is preferred; particularly with the end-firing probe because imaging of the apex is easier and more comfortable. [13]

6.3.3 Performing a DRE

Immediately before the rectal probe is inserted, DRE should be performed. Particular attention should be paid to the anal tone because a tight sphincter may render the procedure particularly painful. A circumferential examination of the rectum should be

performed, followed by examination of the prostate, which includes size, symmetry on both sides, presence of nodules or induration, tenderness and pain in the prostate. Careful attention should also be paid to exclude the presence of anal pathology such as fissures, haemorrhoids and rectal tumours. If a fissure is present it is unlikely that the patient will tolerate introduction of the probe. If a haemorrhoid is present then care must be taken to avoid puncturing it, otherwise there will be profuse bleeding. If a rectal tumour is felt, the procedure should be abandoned and in all circumstances consideration should be given to colorectal referral.

6.4 Ultrasonic appearance

The sonographic appearance is a combination of the gross and zonal anatomy. The peripheral zone has a homogeneous texture (same level of echoes) throughout and is more echogenic (brighter) than the rest of the gland. The rest of the gland has a heterogeneous texture (different levels of echoes) and poor echo. [13] It is not possible to differentiate between the central and transition zones on TRUS. [13] When scanning the gland the seminal vesicles can be seen from the base in the transverse view and near the lateral in the sagittal view.

The sonographic appearance of the prostate is not specific but there are three ultrasonic findings that may be described as isoechoic (same echogenicity as surrounding tissue), hyperechoic (brighter) or hypoechoic (darker). (Figs. 10 and 11)

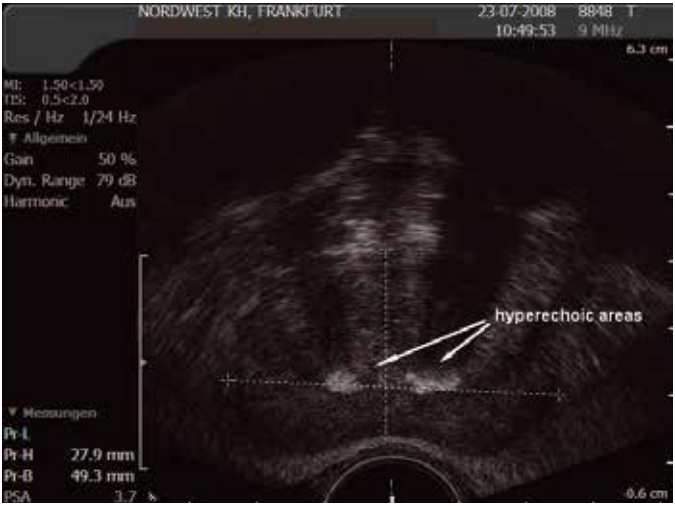


Fig. 10. Hyperechoic areas

(Courtesy: S. Hieronymi)

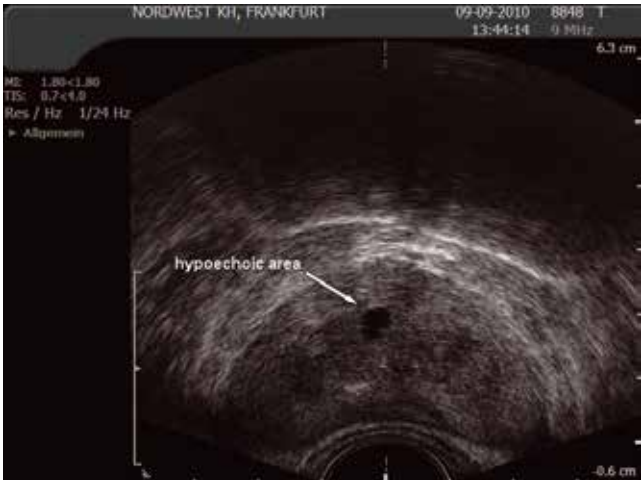


Fig. 11. Hyperechoic areas

(Courtesy: S. Hieronymi)

Ultrasonic findings:

- isoechoic area could be normal tissue or tumour
- hypoechoic area could be cyst, abscess or tumour
- hyperechoic area could be calcification or tumour

Although these findings are interesting, they should not have any impact on the biopsy procedure or cause additional complications.

6.5 Prostate measurement

It is routine to measure the prostate volume (in g/ml)), which may be important in offering treatment options. The prostate is measured in three planes:

In the transverse view: anterior to posterior (width) (1) and height (2); and in the longitudinal plane from the bladder neck to the apex (length) (3). This can be calculated using the formula:

Ω/6 × height × width × length (in cm) (Ω/6 may be substituted by 0.51)

Most ultrasound machines will automatically calculate the volume.

Fig. 12. Prostate measurement – transverse view

(Courtesy: S. Hieronymi)

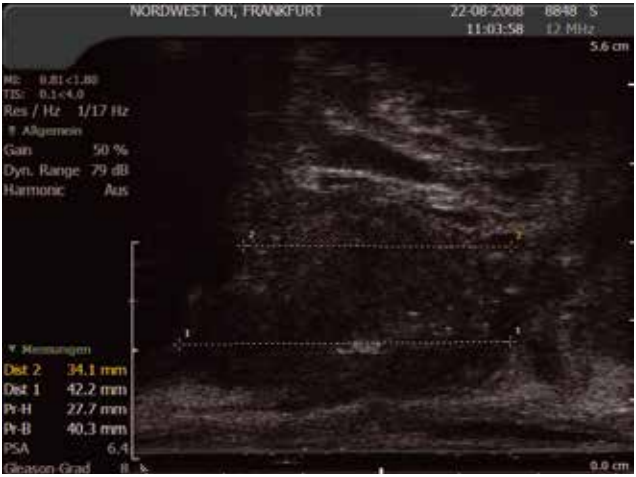


Fig. 13. Prostate measurement – sagittal view

(Courtesy: S. Hieronymi)

6.6 Prostate biopsy

6.6.1 Local anaesthesia

Ultrasound-guided administration of periprostatic nerve block (PPNB) with lidocaine is currently the most reported anaesthetic technique. It is effective in pain control and its effect is immediate, so there is no need to wait to begin the procedure after administering the anaesthetic [97] (LE 1b). To perform PPNB the anaesthetic should be preferentially infiltrated

into the junction between the prostate and the seminal vesicles bilaterally [97,98] (LE 1b and 2a, respectively).
The use of intrarectal local anaesthetics alone shows less efficacy in pain control. However, combining the use of intrarectal local anaesthetics with PPNB is a safe technique that provides less sensation of pain during the procedure. [99] (LE 1b)
Intrarectal local anaesthesia can be performed with lidocaine gel or with a mixture of 2.5% lidocaine and 2.5% prilocaine. The administration should take place up to 30 min to 1 h before the biopsy [99,100] (LE 1b).

6.6.2 Number and location of prostate cores (PICO 1)

Conventional sextant biopsies were introduced by Hodges et al. in 1989. [101] Later, several studies have shown that this scheme is insufficient for detection of prostate cancer (under-sampling). [102–106] The number of prostate cores to detect prostate cancer has been controversial but concerning initial prostate biopsies, the cancer detection rate is sufficient at 10–12 cores [103,104,107–114]. Additional cores should be obtained from suspect areas by DRE/TRUS. [59] In order to increase the cancer detection rate in a large prostate, additional cores could be obtained, although the results of studies are not consistent concerning the cut-off in prostate volume and the optimal number of prostate biopsies. [102,111,113,115]
Randomised studies have shown that a personalised biopsy core scheme according to age, PSA and prostate volume [116] does not increase the cancer detection rate compared to 8–10-core schemes. [109,117] Saturation prostate biopsies are not recommended in initial setting. [108,114,118] An increase in the number of cores does not affect the capacity of biopsy tumour volume to predict final tumour volume after prostatectomy. [119]
At repeat biopsies, an extended core scheme (>12) could be performed in order to detect prostate cancer [110,120], including transition zone biopsies. [110,115]
Random prostate biopsies are still standard for detecting prostate cancer but evidence is accumulating for MRI target biopsies in addition to random biopsies. [38,59]

Location of 12-core scheme biopsies: apex, middle and base of the right lateral (RL), right medial (RM), left medial (LM) and left lateral (LL) parasagittal planes of the prostate.

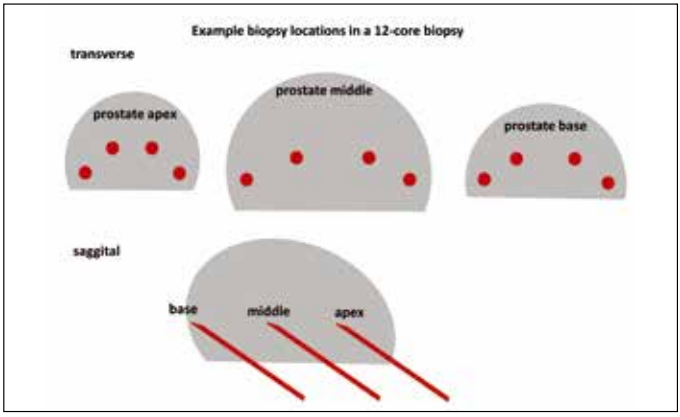


Fig. 14. Example biopsy locations in a 12-core biopsy
(Courtesy: S. Hieronymi)

6.7 Acute complications and their management

Although prostate biopsy can be achieved in an outpatient setting, most men experience at least one minor complication following the procedure.

Table 8. Complications and their frequencies [121,122]

Minor	%	Serious	%
Visible haematuria	66.3	Urosepsis	0.5
Haematospermia	38.8	Rectal bleeding requiring intervention	0.3
Rectal bleeding	28.4	Acute urinary retention	0.3
Vasovagal symptoms	7.7	Transfusion	0.05
Genitourinary tract infection	6.1	Fournier's gangrene	0.05
Prostatitis	1.0	Myocardial infarction	0.05
Epididymitis	0.7		

Haematuria is the most frequently seen complication following TRUS-guided biopsy. It normally persists for between 3 and 5 days but is self-limiting. The formation of clots and the development of retention can occur and it is wise to ensure that men have successfully voided before leaving the department.

Minor rectal bleeding is common and usually resolves over the first 48 h. Rectal bleeding requiring intervention is rare. In the majority of cases, inserting a Foley catheter into the rectum, inflating the balloon with up to 50 mL, and using traction to compress the bleeding points is sufficient to achieve haemostatic control. At least this allows one to control the bleeding while summoning assistance. Rarely, colonoscopy or endoscopic sclerotherapy may be required.

Vasovagal symptoms such as sweating, nausea, paleness, dizziness, and hypotension are commonly seen. They are more common in the presence of anxiety or hypoglycaemia. However, these symptoms resolve if the patient is left lying flat or in slight Trendelenburg position. Rarely, intravenous fluids may be required.

Although the data are not always clear, it is likely that TRUS-guided prostate biopsy causes worsening of sexual function at least over the short term (3 months). This appears to be more pronounced for men over the age of 60 years and for those subsequently found to have prostate cancer. [123]

6.8 Patient information on discharge

Patients with a urethral catheter, or those with diabetes, should be closely monitored for signs of sepsis. Patients should be advised on rest, fluid intake, frequency of urination, prophylactic antibiotics and follow-up.

There is no definitive data to confirm that antibiotics for long courses (3 days) are superior to short-course treatments (1 day), or that multiple-dose is superior to single-dose treatment. [124]

Recommendation	LE	GR
• Ensure that the patients understand what they must do in case of complications after TRUS biopsy and whom to contact	4	A

7. Glossary and abbreviations

Glossary

- Sagittal — Longitudinal (vertical) plane that divides the body or its parts into right and left portions.
- Transverse — A horizontal plane running from left to right separating the body or its parts into inferior or superior parts.
- Transperineal — Through, across or beyond the perineum
- Fusion biopsy — Biopsy with the use of a detailed 3D ultrasound/ MRI view. MRI images, made beforehand, are fused to the ultrasound image during the biopsy, guiding the biopsy taker to the suspicious areas.

Abbreviations

- BPE — benign prostate enlargement
- DRE — digital rectal examination
- EAU — European Association of Urology
- EAUN — European Association of Urology Nurses
- GG — Gleason grade
- GS — Gleason score
- ISUP — International Society of Urological Pathology
- mpMRI — multi-parametric magnetic resonance imaging
- MRI — magnetic resonance imaging
- MRSA — methicillin-resistant Staphylococcus aureus
- PICO question — question that describes the four elements of a good clinical question, namely patient/problem, intervention, comparison, outcome
- PIL — patient information leaflet
- PPNB — periprostatic nerve block
- PRECISION — Prospective Randomized Evaluation of Celecoxib Integrated Safety vs. Ibuprofen or Naproxen
- PSA — prostate-specific antigen
- RCT — randomised controlled trial
- TIA — Transient ischemic attack
- TRUS — transrectal ultrasound
- US/MR — ultrasound/magnetic resonance

8. Other resources

Appendix A.

Transrectal ultrasound guided biopsy of the prostate - Procedure
A complete Transrectal ultrasound and prostate biopsy procedure can be found on the EAUN website adapted from Skills for Health PB2 2008 Performance criteria [125]

The PDF of this document can be found at: www.eaun.uroweb.org/guidelines/

Appendix B.

Transrectal ultrasound guided biopsy of the prostate - Training document
A separate Transrectal ultrasound-guided biopsy of the prostate – Training document can be found on the EAUN website.

The PDF of this document can be found at: www.eaun.uroweb.org/guidelines/

Appendix C.

Anti-coagulant and anti-aggregant use pre prostate biopsy - Guide
A guide on which anti-coagulants and which anti-aggregants should be stopped pre-biopsy and when, can be found on the EAUN website.

The PDF of this document can be found at: www.eaun.uroweb.org/guidelines/

9. Figure reference list

10. References

1. Rodgers BL. Developing nursing knowledge: Philosophical traditions and influences. Philadelphia, USA: Lippincott Williams & Wilkins; 2005.
2. Crocetti E. Epidemiology of prostate cancer in Europe [Internet]. EU Sci Hub 2015 [cited 2018 Jun 1]. http://publications.jrc.ec.europa.eu/repository/handle/JRC101382.
3. Turner B, Aslet P. Nurse Practitioner-Led Prostate Biopsy in the United Kingdom. Urol Nurs 2011;31:351–353 3p. https://library.suna.org/suna/articles/181/view.
4. Benchikh El Fegoun A, El Atat R, Choudat L, et al. The learning curve of transrectal ultrasound-guided prostate biopsies: Implications for training programs. Urology 2013;81:12–5. https://www.ncbi.nlm.nih.gov/pubmed/23273070.
5. Turner B, Pati. J. Nurse practitioner led prostate biopsy: an audit to determine effectiveness and safety for patients. Int J Urol Nurs 2010;4:87–92. https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1749-771X.2010.01099.x.
6. Hori S, Fuge O, Trabucchi K, et al. Can a trained non-physician provider perform transrectal ultrasound-guided prostatic biopsies as effectively as an experienced urologist? BJU Int 2013;111:739–44. https://www.ncbi.nlm.nih.gov/pubmed/22726849.
7. Jones S, Purnendu M, Christian S. Outcome analysis of ultrasound-guided prostate biopsy procedure: a retrospective audit comparing associate consultant and nurse specialist in urology to determine the effectiveness and safety of a nurse-led prostate biopsy clinic. Int J Urol Nurs 2015;9:14–21. https://onlinelibrary.wiley.com/doi/pdf/10.1111/ijun.12033.
8. Henderson A, Andrich DE, Pietrasik ME, et al. Outcome analysis and patient satisfaction following octant transrectal ultrasound-guided prostate biopsy: a prospective study comparing consultant urologist, specialist registrar and nurse practitioner in urology. Prostate Cancer Prostatic Dis 2004;7:122–5. http://www.ncbi.nlm.nih.gov/pubmed/15069422.
9. Shah J, Baston E. Standard of prostate biopsies undertaken by nurse practitioners. Cancer Nurs Pract 2013;12:32–5. http://rcnpublishing.com/doi/abs/10.7748/cnp2013.03.12.2.32.e933.
10. OCEBM Levels of Evidence Working Group. The Oxford Levels of Evidence 1. [Internet]. Oxford Cent Evidence-Based Med Oxford: OCEBM; 2011 [cited 2012 Jan 22]. http://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf.
11. Behrens J, Langer G. Evidence-based nursing - Vertrauensbildende Entzauberung der Wissenschaft [Internet]. Bern, Göttingen, Toronto, Seattle: Verlag Hans Huber; 2004. http://www.socialnet.de/rezensionen/1840.php.
12. Epstein JI, Zelefsky MJ, Sjoberg DD, et al. A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score. Eur Urol 2016;69:428–35. http://www.ncbi.nlm.nih.gov/pubmed/26166626.
13. Patel U, Rickards D. Handbook of transrectal ultrasound and biopsy of the prostate. London, UK: Martin Dunitz Ltd; 2002.

14. Germann W, Stanfield C. Principles of Human Physiology. San Francisco, USA: Benjamin Cummings; 2002.
15. Marieb E, Hoen K. Human Anatomy and Physiology. 8th ed. San Francisco, USA: Benjamin Cummings; 2010.
16. Bray F, Ferlay J, Soerjomataram I, et al. Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. Ca Cancer J Clin 2018;68:394–424. https://onlinelibrary.wiley.com/doi/pdf/10.3322/caac.21492.
17. Jemal A, Siegel R, Ward E, et al. Cancer Statistics, 2009. CA Cancer J Clin 2009;59:225–49. http://doi.wiley.com/10.3322/caac.20006.
18. Parkin DM, Bray F, Ferlay J, et al. Global Cancer Statistics, 2002. CA Cancer J Clin 2005;55:74–108. http://doi.wiley.com/10.3322/canjclin.55.2.74.
19. McCaul KA, Luke CG, Roder DM. Trends in prostate cancer incidence and mortality rates in South Australia, 1977-1993. Med J Aust 1995;162:520–2. http://www.ncbi.nlm.nih.gov/pubmed/7776912.
20. Sarma A V, Schottenfeld D. Prostate cancer incidence, mortality, and survival trends in the United States: 1981-2001. Semin Urol Oncol 2002;20:3–9. http://www.ncbi.nlm.nih.gov/pubmed/11828352.
21. Quinn M, Babb P. Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparisons. BJU Int 2002;90:162–73. http://doi.wiley.com/10.1046/j.1464-410X.2002.2822.x.
22. Potosky AL, Miller BA, Albertsen PC, et al. The Role of Increasing Detection in the Rising Incidence of Prostate Cancer. JAMA 1995;273:548. http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.1995.03520310046028.
23. Legler JM, Feuer EJ, Potosky AL, et al. The role of prostate-specific antigen (PSA) testing patterns in the recent prostate cancer incidence decline in the United States. Cancer Causes Control 1998;9:519–27. http://www.ncbi.nlm.nih.gov/pubmed/9934717.
24. Breslow N, Chan CW, Dhom G, et al. Latent carcinoma of prostate at autopsy in seven areas. Collaborative study organized by the International Agency for Research on Cancer, Lyons, France. Int J Cancer 1977;20:680–8. http://doi.wiley.com/10.1002/ijc.2910200506.
25. Sakr WA, Grignon DJ, Crissman JD, et al. High grade prostatic intraepithelial neoplasia (HGPIN) and prostatic adenocarcinoma between the ages of 20-69: an autopsy study of 249 cases. In Vivo 1994 8:439–43. http://www.ncbi.nlm.nih.gov/pubmed/7803731.
26. Haas GP, Delongchamps N, Brawley OW, et al. The worldwide epidemiology of prostate cancer: perspectives from autopsy studies. Can J Urol 2008;15:3866–71. http://www.ncbi.nlm.nih.gov/pubmed/18304396.
27. Haenszel W, Kurihara M. Studies of Japanese migrants. I. Mortality from cancer and other diseases among Japanese in the United States. J Natl Cancer Inst 1968;40:43–68. http://www.ncbi.nlm.nih.gov/pubmed/5635018.
28. Akazaki K, Stemmerman GN. Comparative study of latent carcinoma of the prostate among Japanese in Japan and Hawaii. J Natl Cancer Inst 1973;50:1137–44. http://www.ncbi.nlm.nih.gov/pubmed/4712588.

29. Moradi T, Delfino RJ, Bergström SR, et al. Cancer risk among Scandinavian immigrants in the US and Scandinavian residents compared with US whites, 1973-89. Eur J Cancer Prev 1998;7:117–25. http://www.ncbi.nlm.nih.gov/pubmed/9818773.
30. Bailar JC, Mellinger GT, Gleason DF. Survival rates of patients with prostatic cancer, tumor stage, and differentiation--preliminary report. Cancer Chemother reports 1966;50:129–36. http://www.ncbi.nlm.nih.gov/pubmed/5948715.
31. Gleason DF, Mellinger GT, Arduino LJ, et al. Prediction of Prognosis for Prostatic Adenocarcinoma by Combined Histological Grading and Clinical Staging. J Urol 1974;111:58–64. https://www.sciencedirect.com/science/article/pii/S0022534717598894?via%3Dihub.
32. Epstein JI, Allsbrook WC, Amin MB, et al. The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. Am J Surg Pathol 2005;29:1228–42. http://www.ncbi.nlm.nih.gov/pubmed/16096414.
33. Epstein JI, Egevad L, Amin MB, et al. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: Definition of Grading Patterns and Proposal for a New Grading System. Am J Surg Pathol 2016;40:244–52. http://www.ncbi.nlm.nih.gov/pubmed/26492179.
34. Gleason DF. Histologic grading of prostate cancer: a perspective. Hum Pathol; 1992;23:273–9. http://www.ncbi.nlm.nih.gov/pubmed/1555838.
35. Humphrey PA, Moch H, Cubilla AL, et al. The 2016 WHO Classification of Tumours of the Urinary System and Male Genital Organs-Part A: Renal, Penile, and Testicular Tumours. Eur Urol 2016;70:93–105. http://www.ncbi.nlm.nih.gov/pubmed/26935559.
36. Epstein JI. New prostate cancer grade group system correlates with prostate cancer death in addition to biochemical recurrence. Br J Cancer 2016;114:1069–70. http://www.ncbi.nlm.nih.gov/pubmed/27167449.
37. Sobin L, Gospodarowicz M, Wittekind C. TNM Classification of Malignant Tumours [Internet]. 7th ed. Sobin L, Gospodarowicz M, Wittekind C, editors. New York: 2009. https://www.ncbi.nlm.nih.gov/nlmcatalog/101511218.
38. Eastham JA, Riedel E, Scardino PT, et al. Variation of Serum Prostate-Specific Antigen Levels. JAMA 2003;289:2695. http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.289.20.2695.
39. Stephan C, Klaas M, Müller C, et al. Interchangeability of measurements of total and free prostate-specific antigen in serum with 5 frequently used assay combinations: an update. Clin Chem 2006;52:59–64. http://www.ncbi.nlm.nih.gov/pubmed/11148190.
40. Roobol MJ, Steyerberg EW, Kranse R, et al. A Risk-Based Strategy Improves Prostate-Specific Antigen-Driven Detection of Prostate Cancer. Eur Urol 2010;57:79–85.
41. Roobol MJ, Verbeek JFM, van der Kwast T, et al. Improving the Rotterdam European Randomized Study of Screening for Prostate Cancer Risk Calculator for Initial Prostate Biopsy by Incorporating the 2014 International Society of Urological Pathology Gleason Grading and Cribriform growth. Eur Urol 2017;72:45–51. http://www.ncbi.nlm.nih.gov/pubmed/28162815.
42. Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med 2018;378:1767–77. http://www.nejm.org/doi/10.1056/NEJMoa1801993.

43. El-Shater Bosaily A, Parker C, Brown LC, et al. PROMIS--Prostate MR imaging study: A paired validating cohort study evaluating the role of multi-parametric MRI in men with clinical suspicion of prostate cancer. Contemp Clin Trials 2015;42:26–40. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4460714/.
44. Xue J, Qin Z, Cai H, et al. Comparison between transrectal and transperineal prostate biopsy for detection of prostate cancer: a meta-analysis and trial sequential analysis. Oncotarget 2017;8:23322–36. http://www.ncbi.nlm.nih.gov/pubmed/28177897.
45. Ericson KJ, Wenger HC, Rosen AM, et al. Prostate cancer detection following diagnosis of atypical small acinar proliferation. Can J Urol 2017;24:8714–20. http://www.ncbi.nlm.nih.gov/pubmed/28436357.
46. Merrimen JL, Jones G, Walker D, et al. Multifocal High Grade Prostatic Intraepithelial Neoplasia is a Significant Risk Factor for Prostatic Adenocarcinoma. J Urol 2009;182:485–90. http://linkinghub.elsevier.com/retrieve/pii/S002253470900901X.
47. Stav K, Siegel YI, Beberashvili I, et al. Provision of information leaflet before urodynamic study reduces the pre-examination anxiety level. Neurourol Urodyn 2016;35:805–8. http://doi.wiley.com/10.1002/nau.22799.
48. Wade J, Rosario DJ, Howson J, et al. Role of information in preparing men for transrectal ultrasound guided prostate biopsy: a qualitative study embedded in the ProtecT trial. BMC Health Serv Res 2015;15:80. https://www.ncbi.nlm.nih.gov/pubmed/25889315.
49. McCartney M. Patient information leaflets: a stupid system? BMJ 2013;347:f4748. http://www.ncbi.nlm.nih.gov/pubmed/23900316.
50. Maciolek KA, D.F. J, E.J. A, et al. Systematic Assessment Reveals Lack of Understandability for Prostate Biopsy Online Patient Education Materials. Urology 2017;109:101–6. http://www.elsevier.com/locate/urology.
51. Giguere A, Legare F, Grimshaw J, et al. Printed educational materials: effects on professional practice and healthcare outcomes [Systematic Review]. Cochrane Database Syst Rev 2013;4:4. https://www.ncbi.nlm.nih.gov/pubmed/23076904.
52. Redmond CE, Nason GJ, Kelly ME, et al. Transrectal ultrasound guided biopsy of the prostate: Is the information accessible, usable, reliable and readable? Curr Urol 2014;8:32–7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4483281/.
53. Aron M, Rajeev TP, Gupta NP. Antibiotic prophylaxis for transrectal needle biopsy of the prostate: a randomized controlled study. BJU Int 2000;85:682–5. http://www.ncbi.nlm.nih.gov/pubmed/10759665.
54. Carignan A, Roussy JF, Lapointe V, et al. Increasing risk of infectious complications after transrectal ultrasound-guided prostate biopsies: Time to reassess antimicrobial prophylaxis? Eur Urol 2012;62:453–9. https://www.ncbi.nlm.nih.gov/pubmed/22575912.
55. Loeb S, Vellekoop A, Ahmed HU, et al. Systematic review of complications of prostate biopsy. Eur Urol 2013;64:876–92. https://www.ncbi.nlm.nih.gov/pubmed/23787356.
56. Bruyère F, Malavaud S, Bertrand P, et al. Prosbiotate: a multicenter, prospective analysis of infectious complications after prostate biopsy. J Urol 2015;193:145–50. http://www.ncbi.nlm.nih.gov/pubmed/25063492.
57. Cuevas O, Oteo J, Lazaro E, et al. Significant ecological impact on the progression of fluoroquinolone resistance in Escherichia coli with increased community use of moxifloxacin, levofloxacin and amoxicillin/clavulanic acid. J Antimicrob Chemother 2011;66:664–9. http://www.ncbi.nlm.nih.gov/pubmed/21172788.

58. Loeb S, Carter HB, Berndt SI, et al. Complications After Prostate Biopsy: Data From SEER-Medicare. J Urol 2011;186:1830–4.
http://www.ncbi.nlm.nih.gov/pubmed/21944136.
59. Mottet N, Bellmunt, Briers E, et al. EAU – ESTRO – ESUR – SIOG Guidelines on Prostate Cancer. Edn. presented at the EAU Annual Congress Copenhagen 2018. [Internet]. 2018th ed. Arnhem, The Netherlands: EAU Guidelines Office; 2018.
https://uroweb.org/guideline/prostate-cancer/.
60. Taylor AK, Zembower TR, Nadler RB, et al. Targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound guided prostate biopsy is associated with reduced incidence of postoperative infectious complications and cost of care. J Urol 2012;187:1275–9.
https://www.ncbi.nlm.nih.gov/pubmed/22341272.
61. Ryu JW, Jung S Il, Ahn JH, et al. Povidone-iodine rectal cleansing and targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound-guided prostate biopsy are associated with reduced incidence of postoperative infectious complications. Int Urol Nephrol 2016;48:1763–70.
https://www.ncbi.nlm.nih.gov/pubmed/27495324.
62. Fahmy AM, Kotb A, Youssif TA, et al. Fosfomycin antimicrobial prophylaxis for transrectal ultrasound-guided biopsy of the prostate: A prospective randomised study. Arab J Urol 2016;14:228–33.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4983165/.
63. Patel U, Dasgupta P, Amoroso P, et al. Infection after transrectal ultrasonography-guided prostate biopsy: Increased relative risks after recent international travel or antibiotic use. BJU Int 2012;109:1781–5.
https://www.ncbi.nlm.nih.gov/pubmed/22040349.
64. Berger AP, Gozzi C, Steiner H, et al. Complication rate of transrectal ultrasound guided prostate biopsy: A comparison among 3 protocols with 6, 10 and 15 cores. J Urol 2004;171:1478–81.
http://linkinghub.elsevier.com/retrieve/pii/S0022534705623245.
65. Zaytoun OM, Anil T, Moussa AS, et al. Morbidity Of Prostate Biopsy After Simplified Versus Complex Preparation Protocols: Assessment of Risk Factors. Urology 2011;77:910–4.
http://linkinghub.elsevier.com/retrieve/pii/S0090429510021710.
66. Anastasiadis A, Zapala L, Cordeiro E, et al. Complications of prostate biopsy. Expert Rev Anticancer Ther 2013;13:829–37.
https://www.tandfonline.com/doi/abs/10.1586/14737140.2013.811056?tab=permissions&scroll=top&.
67. Challacombe B, Dasgupta P, Patel U, et al. Recognizing and managing the complications of prostate biopsy. BJU Int 2011;108:1233–4.
https://www.ncbi.nlm.nih.gov/pubmed/21958223.
68. Grabe M, Bartoletti R, Bjerklund Johansen T, et al. EAU Guidelines on Urological Infections [Internet]. 2015.
http://uroweb.org/guideline/urological-infections/.
69. Rosario DJ, Lane JA, Metcalfe C, et al. Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: Prospective evaluation within ProtecT study. BMJ 2012;344 (7840).
https://www.ncbi.nlm.nih.gov/pubmed/22232535.
70. Akduman B, Akduman D, Tokgoz H, et al. Long-term fluoroquinolone use before the prostate biopsy may increase the risk of sepsis caused by resistant microorganisms. Urology 2011;78:250–6.
https://www.ncbi.nlm.nih.gov/pubmed/21705048.

71. Lodeta B, Trkulja V. Septic complications and hospital admissions after transrectal ultrasound-guided prostate biopsy: incidence rates and outcomes in 913 consecutive biopsies. Int Urol Nephrol 2014;46:2335–6.
http://link.springer.com/10.1007/s11255-014-0815-x.
72. Kamdar C, Mooppan UMM, Gulmi FA, et al. Multi-drug-resistant bacteremia after transrectal ultrasound guided prostate biopsies in hospital employees and their relatives. Urology 2008;72:34–6.
http://www.ncbi.nlm.nih.gov/pubmed/18372012.
73. Loeb S, van den Heuvel S, Zhu X, et al. Infectious Complications and Hospital Admissions After Prostate Biopsy in a European Randomized Trial. Eur Urol 2012;61:1110–4.
http://www.ncbi.nlm.nih.gov/pubmed/22244150.
74. Le JD, Tan N, Shkolyar E, et al. Multifocality and Prostate Cancer Detection by Multiparametric Magnetic Resonance Imaging: Correlation with Whole-mount Histopathology. Eur Urol 2015;67:569–76.
http://linkinghub.elsevier.com/retrieve/pii/S0302283814008914.
75. Wegelin O, van Melick HHE, Hooft L, et al. Comparing Three Different Techniques for Magnetic Resonance Imaging-targeted Prostate Biopsies: A Systematic Review of In-bore versus Magnetic Resonance Imaging-transrectal Ultrasound fusion versus Cognitive Registration. Is There a Preferred Technique? Eur Urol 2017;71:517–31.
https://www.europeanurology.com/article/S0302-2838(16)30446-8/fulltext.
76. Schoots IG, Roobol MJ, Nieboer D, et al. Magnetic resonance imaging-targeted biopsy may enhance the diagnostic accuracy of significant prostate cancer detection compared to standard transrectal ultrasound-guided biopsy: a systematic review and meta-analysis. Eur Urol 2015;68:438–50.
https://www.ncbi.nlm.nih.gov/pubmed/25480312.
77. Panebianco V, Barchetti F, Sciarra A, et al. Multiparametric magnetic resonance imaging vs. standard care in men being evaluated for prostate cancer: A randomized study. Urol Oncol Semin Orig Investig 2015;33:17.e1-17.e7.
https://www.ncbi.nlm.nih.gov/pubmed/25443268.
78. Baco E, Rud E, Eri LM, et al. A Randomized Controlled Trial to Assess and Compare the Outcomes of Two-core Prostate Biopsy Guided by Fused Magnetic Resonance and Transrectal Ultrasound Images and Traditional 12-core Systematic Biopsy. Eur Urol 2016;69:149–56.
https://www.ncbi.nlm.nih.gov/pubmed/25862143.
79. Tonttila PP, Lantto J, Paakko E, et al. Prebiopsy Multiparametric Magnetic Resonance Imaging for Prostate Cancer Diagnosis in Biopsy-naive Men with Suspected Prostate Cancer Based on Elevated Prostate-specific Antigen Values: Results from a Randomized Prospective Blinded Controlled Trial. Eur Urol 2016;69:419–25.
https://www.ncbi.nlm.nih.gov/pubmed/26033153.
80. Carey JM, Korman HJ. Transrectal ultrasound guided biopsy of the prostate. Do enemas decrease clinically significant complications? J Urol 2001;166:82–5.
http://www.ncbi.nlm.nih.gov/pubmed/11435829.
81. Vallancien G, Prapotnich D, Veillon B, et al. Systematic prostatic biopsies in 100 men with no suspicion of cancer on digital rectal examination. J Urol 1991;146:1308–12.
http://www.ncbi.nlm.nih.gov/pubmed/1719243.

82. Abughosh Z, Margolick J, Goldenberg SL, et al. A prospective randomized trial of povidone-iodine prophylactic cleansing of the rectum before transrectal ultrasound guided prostate biopsy. J Urol 2013;189:1326–31. https://www.ncbi.nlm.nih.gov/pubmed/23041343.
83. Gyorfi JR, Otteni C, Brown K, et al. Peri-procedural povidone-iodine rectal preparation reduces microorganism counts and infectious complications following ultrasound-guided needle biopsy of the prostate. World J Urol 2014;32:905–9. https://www.ncbi.nlm.nih.gov/pubmed/24682238.
84. Adams R, Floss K, Frank C, et al. The Handbook of Peri-Operative Medicines [Internet]. UK Clinical Pharmacy Association; 2016. https://perioperative.files.wordpress.com/2017/12/handbook-of-2016_perioperative-medicines-v1-september-2016-6.pdf.
85. Culkin DJ, Exaire EJ, Green D, et al. Anticoagulation and antiplatelet therapy in urological practice: ICUD/AUA review paper. J Urol 2014;192:1026–34. http://www.auanet.org/guidelines/anticoagulation-and-antiplatelet-therapy.
86. Kariotis I, Philippou P, Volanis D, et al. Safety of ultrasound-guided transrectal extended prostate biopsy in patients receiving low-dose aspirin. Int Braz J Urol 2010;36:308–16. https://www.ncbi.nlm.nih.gov/pubmed/20602823.
87. Chowdhury R, Abbas A, Idriz S, et al. Should warfarin or aspirin be stopped prior to prostate biopsy? An analysis of bleeding complications related to increasing sample number regimes. Clin Radiol 2012;67:e64–70. https://www.ncbi.nlm.nih.gov/pubmed/22959852.
88. Raheem OA, Casey RG, Lynch TH. Does anticoagulant or antiplatelet therapy need to be discontinued for transrectal ultrasound-guided prostate biopsies? A systematic literature review. Curr Urol 2011;5:121–4. https://www.karger.com/Article/Abstract/327464.
89. Price MJ, Walder JS, Baker BA, et al. Recovery of Platelet Function After Discontinuation of Prasugrel or Clopidogrel Maintenance Dosing in Aspirin-Treated Patients With Stable Coronary Disease. J Am Coll Cardiol 2012;59:2338–43. http://www.ncbi.nlm.nih.gov/pubmed/22698488.
90. Billett HH. Antiplatelet Agents and Arterial Thrombosis. Cardiol Clin 2008;26:189–201. http://www.ncbi.nlm.nih.gov/pubmed/18406994.
91. Oprea AD, Popescu WM. Perioperative management of antiplatelet therapy. Br J Anaesth 2013;111:i3–17. https://linkinghub.elsevier.com/retrieve/pii/S0007091217309273.
92. Lee A, Chia SJ. Contemporary outcomes in the detection of prostate cancer using transrectal ultrasound-guided 12-core biopsy in Singaporean men with elevated prostate specific antigen and/or abnormal digital rectal examination. Asian J Urol 2015;2:187–93. https://www.ncbi.nlm.nih.gov/pubmed/29264144.
93. Gosselaar C, Roobol M, Roemeling S, et al. The Role of the Digital Rectal Examination in Subsequent Screening Visits in the European Randomized Study of Screening for Prostate Cancer (ERSPC), Rotterdam. Eur Urol 2008;54:581–8. http://linkinghub.elsevier.com/retrieve/pii/S0302283808004168.
94. NHS. Consent to treatment - NHS [Internet]. NHS website 2016 [cited 2018 Dec 14]. p. Conditions section. https://www.nhs.uk/conditions/consent-to-treatment/.

95. Taylor H. Informed consent 1: legal basis and implications for practice | Clinical | Nursing Times. Nurs Times 2018;114:25–8. https://www.nursingtimes.net/roles/nurse-educators/informed-consent-1-legal-basis-and-implications-for-practice/7024574.article.
96. Selley S, Donovan J, Faulkner A, et al. Diagnosis, management and screening of early localised prostate cancer. Health Technol Assess 1997;1:i, 1-96. http://www.ncbi.nlm.nih.gov/pubmed/9414541.
97. Du J, Johnston J, Studd R. Does waiting after peri-prostatic nerve block reduce pain during transrectal ultrasound-guided prostate biopsy? A randomized controlled trial. ANZ J Surg 2017;87:262–5. https://www.ncbi.nlm.nih.gov/m/pubmed/27091235/.
98. Ates F, Dursun F, Malkoc E, et al. Comparison of two different doses of lidocaine on the pain sensation during transrectal ultrasound-guided prostate biopsy. Turkish J Urol 2016;42:145–9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5012440/.
99. Valdez-Flores RA, Campos-Salcedo JG, Torres-Gomez JJ, et al. Prospective comparison among three intrarectal anesthetic treatments combined with periprostatic nerve block during transrectal ultrasonography-guided prostate biopsy. World J Urol 2018;36:193–9. https://www.ncbi.nlm.nih.gov/pubmed/29170792.
100. Anup K, Pawan V, Niraj K, et al. A prospective randomized trial comparing three different analgesic techniques for pain control during transrectal ultrasound guided prostate biopsy: A single center experience. Minerva Urol e Nefrol 2013;65:77–82. https://www.ncbi.nlm.nih.gov/pubmed/23538313.
101. Hodge K, McNeal J, Stamey T. Ultrasound Guided Transrectal Core Biopsies of the Palpably Abnormal Prostate. J Urol 1989;142:66–70. https://www.sciencedirect.com/science/article/pii/S0022534717386639?via%3Dihub.
102. Chen MK, Luo Y, Zhang H, et al. Investigation of optimal prostate biopsy schemes for chinese patients with different clinical characteristics. Urol Int 2012;89:425–32. https://www.ncbi.nlm.nih.gov/pubmed/23075831.
103. Cormio L, Scattoni V, Lorusso F, et al. Prostate cancer detection rates in different biopsy schemes. Which cores for which patients? World J Urol 2014;32:341–6. https://www.ncbi.nlm.nih.gov/pubmed/23184141.
104. Ghafoori M, Velayati M, Ghasabeh MA, et al. Prostate biopsy using transrectal ultrasonography; the optimal number of cores regarding cancer detection rate and complications. Iran J Radiol 2015;12 (2) (no. https://www.ncbi.nlm.nih.gov/pubmed/26060552.
105. Mohammed W, Davis NF, Elamin S, et al. Six-core versus twelve-core prostate biopsy: a retrospective study comparing accuracy, oncological outcomes and safety. Ir J Med Sci 2016;185:219–23. https://www.ncbi.nlm.nih.gov/pubmed/25786623.
106. Ouzaid I, Xylinas E, Campeggi A, et al. Contemporary pathologic characteristics and oncologic outcomes of prostate cancers missed by 6- and 12-core biopsy and diagnosed with a 21-core biopsy protocol. World J Urol 2013;31:869–74. https://www.ncbi.nlm.nih.gov/pubmed/22116600.
107. Chambo RC, Tsuji FH, de Oliveira Lima F, et al. What is the ideal core number for ultrasound-guided prostate biopsy? Korean J Urol 2014;55:725–31. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4231149/.

108. Chun FKH, Epstein JI, Ficarra V, et al. Optimizing performance and interpretation of prostate biopsy: A critical analysis of the literature. Eur Urol 2010;58:851–64. https://www.ncbi.nlm.nih.gov/pubmed/20884114.
109. Leitao T, Alfarelos J, Rodrigues T, et al. A Prospective Randomized Trial Comparing the Vienna Nomogram and a Ten-Core Prostate Biopsy Protocol: Effect on Cancer Detection Rate. Clin Genitourin Cancer 2017;15:117–21. https://www.ncbi.nlm.nih.gov/pubmed/27436153.
110. Lughezzani G, Sun M, Budaus L, et al. Effect of the number of biopsy cores on prostate cancer detection and staging. Futur Oncol 2010;6:381–90. https://www.futuremedicine.com/doi/abs/10.2217/fon.10.4?journalCode=fon.
111. Park HK, Lee KY, Kim KH, et al. Intermediate versus low or high prostate-specific antigen density level: Comparison of cancer detection rate between 12- and 18-core prostate biopsy. Scand J Urol Nephrol 2010;44:391–8. https://www.ncbi.nlm.nih.gov/pubmed/20695726.
112. Ukimura O, Marien A, Palmer S, et al. Trans-rectal ultrasound visibility of prostate lesions identified by magnetic resonance imaging increases accuracy of image-fusion targeted biopsies. World J Urol 2015;33:1669–76. https://www.ncbi.nlm.nih.gov/pubmed/25656687.
113. Yoon BI, Shin TS, Cho HJ, et al. Is it effective to perform two more prostate biopsies according to prostate-specific antigen level and prostate volume in detecting prostate cancer? Prospective study of 10-core and 12-core prostate biopsy. Urol J 2012;9:491–7. https://europepmc.org/abstract/med/22641493.
114. Nomikos M, Karyotis I, Phillipou P, et al. The implication of initial 24-core transrectal prostate biopsy protocol on the detection of significant prostate cancer and high grade prostatic intraepithelial neoplasia. Int Braz J Urol 2011;37:87–93.
115. Abd TT, Goodman M, Hall J, et al. Comparison of 12-core versus 8-core prostate biopsy: multivariate analysis of large series of US veterans. Urology 2011;77:541–7. https://www.ncbi.nlm.nih.gov/pubmed/20817273.
116. Remzi M, Fong Y, Dobrovits M, et al. The Vienna nomogram: validation of a novel biopsy strategy defining the optimal number of cores based on patient age and total prostate volume. J Urol 2005;174:1256–60; discussion 1260–1; author reply 1261. http://www.ncbi.nlm.nih.gov/pubmed/16145388.
117. Lecuona A, Heyns CF. A prospective, randomized trial comparing the Vienna nomogram to an eight-core prostate biopsy protocol. BJU Int 2011;108:204–8. https://www.ncbi.nlm.nih.gov/pubmed/21087452.
118. Irani J, Blanchet P, Salomon L, et al. Is an extended 20-core prostate biopsy protocol more efficient than the standard 12-core? A randomized multicenter trial. J Urol 2013;190:77–83. https://www.ncbi.nlm.nih.gov/pubmed/23313205.
119. Zavaski ME, Korus A, Staff I, et al. Prostate biopsy volume predicts final tumor volume. Conn Med 2014;78:167–72. https://www.ncbi.nlm.nih.gov/pubmed/24772836.
120. Scattoni V, Maccagnano C, Capitanio U, et al. Random biopsy: when, how many and where to take the cores? World J Urol 2014;32:859–69. https://www.ncbi.nlm.nih.gov/pubmed/24908067.
121. Efesoy O, Bozlu M, Cayan S, et al. Complications of transrectal ultrasound-guided 12-core prostate biopsy: a single center experience with 2049 patients. Turkish J Urol 2013;39:6–11. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4548577/.

122. Carroll PR, Parsons JK, Andriole G, et al. NCCN Clinical Practice Guidelines Prostate Cancer Early Detection, Version 2.2015. J Natl Compr Canc Netw 2015;13:1534–61. http://www.ncbi.nlm.nih.gov/pubmed/26656522.
123. Murray KS, Bailey J, Zuk K, et al. A prospective study of erectile function after transrectal ultrasonography-guided prostate biopsy. BJU Int 2015;116:190–5. https://www.ncbi.nlm.nih.gov/pubmed/25430505.
124. Zani LE, Clark AO, Rodrigues Netto Jr N. Antibiotic prophylaxis for transrectal prostate biopsy [Systematic Review]. Cochrane Database Syst Rev 2011;5:5. https://www.cochrane.org/CD006576/PROSTATE_antibiotic-prophylaxis-for-transrectal-prostate-biopsy.
125. Skills for Health. PB2 - Undertake trans-rectal ultrasound guided biopsy of the prostate [Internet]. Ski Heal 2010 [cited 2018 Oct 16]. p. 1–4. https://tools.skillsforhealth.org.uk/competence/show/html/id/2008/.

11. About the authors

Corinne Tillier (NL), Chair

Qualified as a State Registered Nurse in 1992 and commenced her career at the Cancer Institute of Bordeaux (France). In 2000 she moved to the Netherlands where she worked on oncology wards. In 2005 she received her Diploma in Oncology Nursing. Working as a research nurse she was involved in several studies in onco-urology (prostate carcinoma and renal cell carcinoma).

In 2010 she moved to the Netherlands Cancer Institute (uro-oncology) in Amsterdam and in 2012 earned a Master's in Advanced Nursing Practice (MANP diploma) at the University of Applied Sciences. She now specialises in localised prostate and renal cell carcinoma and penile carcinoma.

She is author and co-author of several scientific publications, an active lecturer throughout Europe and writes columns in the Bulletin Infirmier du Cancer about published results of nursing studies. She is an active member of the Panel of the Dutch Guidelines for Renal Cell Carcinoma and Prostate Carcinoma and a member of the French Association of Oncology Nurses (A.F.I.C.)

Since October 2012 she has been a member of the EAUN and in March 2015 joined the EAUN Board. In March 2016 she became Chair of the EAUN Scientific Congress Office.

Kaljit Kaur (UK)

Qualified and commenced her career in urology as a Registered General Nurse in 2001 and worked in the North East of England until 2017. Her time here began working as part of the inpatient care service and team that she then went on to manage. A change in direction led to her implementation of a nurse-led urology emergency service, in which she worked as a nurse practitioner before deciding to relocate south.

Currently she is a Urology Advanced Nurse Practitioner, specialising in prostate cancer at The Royal Marsden Hospital in London, alongside studying for her MSc Advanced Clinical Practice (Advanced Nurse Practitioner) degree.

More recently her clinical role has expanded within prostate cancer diagnostics and she is currently working across South West London, assisting with the delivery of a rapid access prostate diagnostic project. As part of this work she is currently learning how to perform MRI fusion transperineal prostate biopsies independently. She is a member of EAUN and the British Association of Urological Nurses.

Philip Cornford (UK)

Trained in London and Liverpool and was appointed Consultant Urological Surgeon in 2001. Currently he is the Clinical Director at the Royal Liverpool University Hospitals where he leads the combined Urology, Nephrology and Transplantation service. He is also Honorary Senior Lecturer at the University of Liverpool. His clinical practice has focused on urological malignancy, and he has also actively contributed to research on the molecular mechanism behind the development of androgen independent prostate cancer growth and recruiting to a number of clinical trials.

He is also a member of the BAUS Specialist Advisory Committee in Urology, Vice-Chair of the EAU Prostate Cancer Guidelines Panel and a member of the EAU Guidelines Office Board.

Gijs De Lauw (NL)

Qualified as a State Registered Nurse in 2003 and commenced his career as a paediatric nurse at the Radboud University Medical Center (Radboudumc) in Nijmegen, Netherlands. In 2006 he started to study at the University of Utrecht for a Degree in Nursing Science that he obtained in 2009.

After a short period of working as a scientist he started to work at the Department of Urology at Radboudumc, where he started his training Master Advanced Nursing Practice (MANP) to become a nurse practitioner.

In his daily practice he works with patients who have been diagnosed with prostate cancer. He plays a critical role in the screening of patients and is independently performing (fusion) biopsies of the prostate.

In September 2018 he will go back to school to start further training to become a physician assistant.

Janette Kinsella (UK)

Qualified as a Registered Nurse in 1996 (UK), she has more than 20 years' experience in Uro-Oncology as a staff nurse, nurse specialist, advanced nurse practitioner and more recently Nurse Consultant. She is current chair of the urology pathway vanguard group for Royal Marsden Partners (South, south-west, north-west London).

Her clinical practice includes new patient diagnostics using a transrectal and transperineal prostate biopsy (with MRI Fusion) approach. She also established a urology survivorship clinic (pre-hab to re-hab) service at The Royal Marsden Hospital, (NHS England innovation award) which is now accessed by patients across the UK .

She completed an MSc in Developing cancer nursing practice at Kings College London in 2009 winning the Wilson Barnett prize for best dissertation. She is currently completing a PhD thesis on prostate cancer active surveillance at Kings College London.

She is extensively published on all aspects of prostate cancer from diagnostics to survivorship and teaches worldwide (both nurses and physicians) on diagnostics and nurse-led care.

Ingrid Charlotte Klinge Iversen (NO)

Qualified as a State Registered Nurse in 1992 (Oslo) and commenced her career at Kristiansund Hospital on the North West coast of Norway. She is now working as a urotherapist in an outpatient clinic at the same hospital.

She has some experience in reading scientific articles and writing academic procedures, as the professional development nurse in the clinic for 2 years and from two further education qualifications: Specialist Nurse in Rehabilitation (Ålesund) and Urotherapy (Bergen).

As a urotherapist her main responsibilities include patient observation through different urological tests and taking medical histories, and guiding patients to cope better with their illnesses. She follows up paediatric and adult patients who have different bladder dysfunctions. She assists urologists with prostate biopsy, and follows up patients who have undergone radical prostatectomy for prostate cancer.

She leads a 2-day course every 6 months for patients who have or have had prostate cancer.

Hanneke Lurvink (NL)

Has worked for EAU since 2006. She was appointed coordinator for all EAUN activities in 2006. She has assisted the EAUN Working Groups for all eight EAUN Guidelines since 2007 with editorial work, finding the right illustrations, copyright issues, literature search, data extraction and retrieving full-text papers, contributing to the design of flowcharts, and playing an important role in the planning and keeping of deadlines. She is a member of the Guidelines International Network.

Tiago Santos (PT)

Qualified as Registered Nurse in 2012 in Portugal and started his career in a rehabilitation unit. In 2014 he moved to the Champalimaud Center for the Unknown, a reference oncology centre in Lisbon, and started as the responsible nurse for the urology outpatient clinic. He continues to work at Champalimaud Center for the Unknown while he finished his Master Degree and Specialty in Rehabilitation Nursing in 2018.

In his daily practice he plays a major role as the reference nurse for patients who are being investigated and those who already have a diagnosis of urological cancer. He follows up patients and performs all the nursing interventions required. The interventions are mostly provided to prostate cancer patients, mainly in the areas of urinary continence and sexual rehabilitation. He assists urologists with prostate biopsy and performs follow-up for early identification of potential complications.

He is also involved in research programmes about quality of life after radical prostatectomy and active surveillance. Since 2015 he has been an EAUN member. In 2017 he was invited to give a presentation at the 18th International Meeting of the EAUN.

Giulia Villa (IT)

Registered Nurse, Master Degree in Nursing Sciences. Nurse Coordinator at the Urology Department, San Raffaele Hospital, Milan, Italy. She has worked in the field of urology since 2005 and as a lecturer since 2008.

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She is involved in developing several research projects in urology related to bladder cancer, prostate cancer and urinary tract infection.

Special interests: bladder and prostate cancer, urinary diversion, urinary tract infection, self-care, and fast-track surgery.

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