Systematic Development of Clinical Practice Guidelines for Prostate Biopsies: A 3-Year Italian Project

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Abstract. *Background: The only available method to detect prostate cancer is prostate biopsy; however, to our knowledge, no evidence-based clinical practice guidelines have been established on this topic. Materials and Methods: A three-year project was elaborated in which experts in the field worked to define the controversies existing in clinical practice regarding prostatic biopsies and then to develop guidelines by means of a systematic search of all the English-language literature using online databases and a consensus conference. Results and Conclusion: The guidelines were formulated to help practitioners in making clinical decisions regarding the appropriate time the patient should undergo prostate biopsy, the type of antibiotic prophylaxis and anaesthesia, the biopsy approach, the method for processing and reporting prostatic needle cores, the biopsy technique, when to repeat a biopsy after a prior negative biopsy, radiotherapy or radical prostatectomy and the accuracy of biopsies in staging prostate cancer.*

According to the latest epidemiological data, prostate cancer has just become the second most common neoplasia, affecting the European male population over 50 years old (1). Presently, the detection of prostate cancer by biopsy is the mainstay of treatment decision but, to our knowledge, no evidence-based literature or following of Consensus Conference guidelines have been introduced in clinical practice (2, 3). The aim of this report was to present the guidelines and the method employed to develop them.

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Materials and Methods

A panel of 32 Italian experts in urology, medical oncology, laboratory medicine, radiotherapy, pathologists and basic researchers set up a study group named "The Italian Group for Developing Clinical Practice Guidelines on Performing Prostate Biopsy". The panel was supported by the Italian Society of Uro-Oncology (S.I.Ur.O), the Italian Society of Urological and Nephrological Ultrasound (S.I.E.U.N), the North-East Uro-Oncology Group (G.U.O.N.E), the Italian Group of Uro-pathology (G.I.U.P) and the Italian Society of Clinical Biochemistry and Molecular Biology (S.I.BIO.C), the Italian Society of Urology (S.I.U), the Italian Group of Biotechnologies in Oncology (A.B.O) and the Italian Urologists Association (AURO.it).

The experts met periodically starting in 2001 for a 3-year period to draft the issues that reflected the sources of uncertainty in performing prostate biopsy (Table I). In 2002, the panel sought the opinions of the Italian practitioners in the field through a feedback survey which was mailed as a structured questionnaire of 49 items representing aspects of the above mentioned controversies. The members of the panel were divided into 7 groups and each one reported evidence on a specific controversial issue (Table II). The panel considered the systematic review of the literature evidence essential to its foundation for making recommendations.

Three research methodologists for clinical trials supported the phases of literature analysis. The seven study groups collected 22,306 articles published in the English-language literature by performing both a computerised search using the Medline database from 1966 to 2004, the EMBASE database from 1982 to 2004, the Cochrane Library database (Issue 4) and a manual search through the reference lists from each article. Subsequently, 699 articles were selected using a systematic weighting and grading of the level of evidence according to the CeVEAS (Centre for the Evaluation of Health Care Assistance Efficacy) scale (Table III) (4).

Table I. *Controversies regarding prostate biopsy.*

The current data are insufficient to:
1. Recommend when the patient should undergo a prostate biopsy.
2. Recommend any use of antibiotic prophylaxis or of anaesthesia for pain relief.
3. Recommend either transrectal digital-guided, or transrectal or perineal approach for performing a prostate biopsy.
4. Recommend a method for processing and reporting prostatic needle cores.
5. Recommend how many cores and from where they should be obtained for an optimal diagnostic yield in relation to the prostate volume and the presence of suspected areas.
6. Recommend repeat prostate biopsies in case of a prior negative biopsy, following radiotherapy or radical prostatectomy in the presence of clinically available parameters (PSA and prostate volume) or the usefulness of performing an extending repeat biopsy.
7. Define the accuracy of biopsies in staging prostate cancer.

Table II. *Group research activities according to each controversial issue.*

Group 1: Indications of prostate biopsy.
Group 2: Use of antibiotic prophylaxis and anaesthesia.
Group 3: Biopsy approach and the related complications.
Group 4: Sampling techniques.
Group 5: Biopsy specimen processing and reporting.
Group 6: The role of prostate biopsy in prostate cancer staging.
Group 7: Indications for repeating biopsy sets.

At the end of this phase, the seven groups organised a Consensus Conference supported by the above mentioned Italian Scientific Societies (5), which took place in Bologna in February 2005 in the presence of the panel members, a 'Jury', whose members were not involved in the original developing phase, as well as 180 practitioners in the field of prostate biopsy, coming from all Italian regions. The Jury panel was composed of 12 experts in medical oncology, forensic medicine, radiology, biochemistry, family practice medicine, ethics, radiotherapy, medical decision-making/clinical guideline development and patients' rights. During the one-day conference, a pre-selected speaker for each of the workgroups presented a summary of their findings to the Jury (in preparation for the conference, the Jury had received the final evidence-based report made by the panel) who carefully analysed the draft evidence-based report and argued every statement in a round-table discussion. At the end of the meeting, the outcomes of the guidelines were determined and reflect the consensus of the Consensus Conference Jury, resulting from a literature review and discussions of the implications of both favourable and unfavourable statements (6).

Guideline Presentation

All the final guidelines guidelines are summarised in Tables IV to XII (7).

Table III. *CeVEAS (Centre for the Evaluation of Health Care Assistance Efficacy) scale.*

Evidence levels	
I	Evidence obtained from several randomised clinical trials (RCT) and/or systematic reviews of multiple RCTs.
II	Evidence obtained from at least one well-designed RCT.
III	Evidence from nonrandomised cohort studies with concurrent or historical controls or meta-analysis of these studies.
IV	Evidence obtained from retrospective studies such as case-control series or their meta-analysis.
V	Evidence obtained from case-series without controls.
VI	Evidence from expert opinion or expert committees as indicated in guidelines or consensus conferences or opinions of members of working groups responsible for the guidelines.
Recommendations grades	
A	The particular procedure or diagnostic test is strongly recommended; existence of evidence of good quality, not necessarily of level I or II.
B	Doubts whether the particular procedure or intervention should be recommended, but it needs to be considered with attention.
C	Substantial uncertainty whether or not to recommend the procedure or the intervention.
D	The procedure or intervention is not recommended.
E	The procedure or intervention is strongly not recommended.

Table IV. *Indications for prostate biopsy.*

1.Prostate biopsy is recommended to obtain a histological diagnosis of prostate cancer.
2.Prostate biopsy is recommended when the diagnosis leads to a treatment that will improve both patient's quantity or quality of life (level III grade A recommendation) and when:
A. The total PSA is above 4 ng/ml (level III grade A recommendation)
• Total PSA cut-off may be lowered to 2.5 ng/ml when men present a familiarity for prostate cancer (at least one first degree relative of 60 years old or younger affected by prostate cancer) and/or abnormal digital rectal examination and/or low PSA ratio (<10%) (level III grade B recommendation).
• With total PSA range between 4 and 10 ng/ml (so-called "gray zone") the use of the ratio of free to total PSA (PSA ratio) may improve patient selection for biopsy (level III grade B recommendation).
• In evaluating patients treated for at least 3 months with Finasteride or Dutasteride, total PSA values must be doubled or values discharged and considered as only pre-treatment values (level III grade A recommendation).
B. Total PSA values are above 10 ng/ml (level III grade A recommendation).
C. There is an abnormal digital rectal examination (level III grade A recommendation).
D. There is a significant total PSA increase (PSA velocity) over time (data according to level III and grade C evidence).
• There are conflicting data about PSA density and complexed PSA in improving total PSA sensitivity and specificity (level III grade C recommendation).
3. Trans-rectal ultrasound (TRUS) by itself cannot rule out the presence of prostate cancer (level III grade A recommendation).

Table V. *Recommendations for the use of antibiotic prophylaxis and of anaesthesia for pain relief when performing a prostate biopsy.*

1. Antibiotic prophylaxis could be avoided when a transperineal approach is performed because of the low rate of infectious complications (lower than 1%) (level III grade A recommendation).
2. Antibiotic prophylaxis performed prior to a transrectal biopsy is able to reduce post biopsy infectious complications (level III grade A recommendation).
3. The antibiotic administration should be initiated only twelve hours before the biopsy and should be continue for two or three days maximum (level IV grade A recommendation).
4. The use of fluorquinolone or cotrimoxazolo as antibiotic prophylaxis prior to biopsies is widely recommended (level III grade A recommendation).
5. Patients with bio-prosthetic heart valves or valve dysfunction must be treated with antibiotic prophylaxis to provide protection against endocarditis.
6. An enema is not recommended to reduce the development of post TR biopsy infection, but rather as a hygienic standard (level IV grade A recommendation).
7. Local anaesthesia is mandatory before performing a transperineal biopsy, but it is recommended prior to a TR biopsy (level I grade A recommendation).
8. Local anaesthesia with lidocaine gel in the rectum it is not efficacious in the pain relief of TR biopsy (level II grade E recommendation).

Discussion

The probability of a positive prostate biopsy and the detection of organ-confined cancer is proportional to total PSA values. An abnormal digital rectal examination (DRE) is an indication for prostate biopsy, since it alone yields a 18% risk of a subsequent positive biopsy. It has been reported that 14% to 30% of men with a positive DRE and a total PSA between 1 and 4 ng/ml will have prostate cancer (8). The free/total PSA ratio (F/T PSA) may be used as an additional test in men with a total PSA between 2.5 and 10.00 ng/ml to increase its specificity. Reported cut-off values range between 10% to 30% (depending on the assay) with a consensus to use the 25% or the 20% cut-off in younger populations (8). The widespread use of the age-related PSA is still limited to selected patients and/or in addition to total PSA and PSA ratio. There is not enough evidence to support a total PSA cut-off value of 2.5 ng/ml for the general population, considering the high risk of unnecessary negative biopsies and cancer over-detection, but this cut-off may be advisable for men with a family history of prostate cancer (8).

Since PSA values may vary significantly with time and assay and its measurement may be jeopardized by other factors affecting PSA levels (*e.g.* exercise, diet, drugs, intercourse) the PSA velocity and doubling time are of limited value in supporting indications for biopsy. The PSA

Table VI. *Recommendations for biopsy approaches and related complications.*

1. Either the transrectal echo-guided and the transperineal approach are comparable in terms of diagnostic efficacy, complications and patient pain or discomfort, while the digitally-guided approach is no longer recommended.
2. The transperineal approach is reasonably preferred over the transrectal approach if rectal diseases such as ulcerative colitis or radiation-induced proctitis are suspected, or if risks of septicaemia are great (level V grade B recommendation).

Table VII. *Recommendations on sampling techniques (number and site of prostatic biopsies).*

1. Optimal sampling should include more than six cores (level III grade A recommendation).
2. Doubling the sextant scheme by the transrectal approach is not sufficient to improve the diagnostic accuracy (level II grade A recommendation).
3. The optimal sampling technique should include eight to twelve cores more peripheral-laterally directed (level III grade A recommendation).
5. Focused biopsies on hypoechoic areas (data according to V level and grade C of evidence) or on suspected areas detected at the echo-color Doppler (level V grade D recommendation) if at least ten cores are taken are not recommended.
6. Evidence supports the sampling of a number of cores in relation to the prostate volume (level III grade A recommendation).
7. Sampling from the transitional zone (level III grade A recommendation) or the central part of the prostate (level IV grade A recommendation) is reasonably indicated in the presence of a prior negative biopsy or of a high PSA level.

Table VIII. *Recommendations on biopsy specimen processing and reporting.*

1. Bioptic specimens should be provided to the pathologist with a complete and adequate clinical report of the patient.
2. Biopsy specimens should be handled and collected with the pre-embeded or *sandwich* technique (level III grade A recommendation).
3. Prostate biopsy should be performed with a biopsy needle of 18 guage (level III grade A recommendation).
4. A needle sample noch length of ≥15 mm is recommended (level III grade A recommendation).
5. The length of the specimen should be checked macroscopically if the length is small or appears less than 10 mm long, one more biopsy core should be obtained from the same sampling site (level V-VI grade A recommendation).
6. At the pathological analysis, tissue should include at least one prostatic gland to be considered representative (level II grade A recommendation).
7. Biopsy specimens should be collected and labelled separately per side (right and left) and area (*i.e.* base, mid, apex, transizion zone) and core specimens of the same area should be collected in the same container (level V grade A recommendation).
8. Marking of one extremity of the specimen (rectal or proximal) to allow for biopsy orientation (level VI grade C recommendation) is not recommended.

Table IX. *Indications on the role of prostate biopsy in predicting prostate cancer staging.*

1. PSA level, clinical stage (cT) and Gleason Score assigned to positive cores taken during prostate biopsy are recommended as pre-operative parameters (level V grade A recommendation).
2. The number of positive cores, the percentage or length of tumour (mm) in each positive core, the presence of diploidic DNA and the microvascular density are statistically significant in the prediction of pathological stage, but still need further clinical investigations (level IV grade A recommendation).
3. The use of nomograms as predictive models may improve the diagnostic accuracy of extraprostatic extension up to 90% (level IV grade A recommendation).

Table X. *Recommendations for repeating a biopsy after a prior negative biopsy.*

It is recommended that a biopsy be repeated after a prior negative biopsy when:
A. The prior sampling is inadequate (less than 6 cores sampled, no prostatic tissue and in the case of very thin or bad readable cores) (grade A recommendation);
B. Total PSA is persistently above 10 ng/ml (grade A recommendation);
C. PSA velocity is above 0.75-1 ng/ml/ year (level III grade A recommendation);
D. ASAP (Atipycal Small Acinar Prolipheration) or HGPIN (High Grade PIN) are found at first biopsy (level III grade A recommendation).
The biopsy should be repeated within 6-12 months (level V grade B recommendation).
A re-biopsy setting should include an increased number of cores relative to the previous biopsy and the sampling of the transition zone; Repeat biopsies following the second biopsy should be considered in selected patients (level V grade A recommendation).
TURP (Tran Urethral Prostate Resection is not considered a re-biopsy method (level V grade B recommendation).

Table XI. *Recommendations for repeating a biopsy after radiotherapy.*

It is not recommended that a biopsy be repeated in the follow-up of patients previously submitted to radiotherapy treatments other than in clinical trials or in patients who are candidates for salvage therapies (grade A recommendation).

Table XII. *Recommendations for repeating a biopsy after radical prostatectomy.*

No evidence-based recommendations exist on if/when/how to repeat a biopsy after radical prostatectomy, but in selected cases a PSA threshold of 0.4 ng/ml, PSA kinetics and unfavourable prognostic factors can help in the decision making (level II/IV grade A recommendation).

density alone or PSA-Dtz (PSA density transitional zone), cannot dictate a prostate biopsy since the result can present variations due to the assay or ultrasound measurement and/or the amount of epithelium *versus* stroma in benign prostatic hyperplasia (BPH) (8). The superiority of cPSA over PSA ratio is not yet proven.

Data from experimental trials with Finasteride (PLESS study; MTOPS study; PCPT study) and Dutasteride (COMBAT study; REDUCE study) support the finding that these drugs reduce total PSA levels by approximately 50% within 3 months (9-11). For non-palpable tumours transrectal ultrasound (TRUS) findings are not contributory for staging but only define the best surgical approach for a patient with BPH and lower urirany symptoms (LUTS). Nomograms and neural networks need validation in a large national general urology trial before introduction in everyday practice (8).

The use of antibiotic prophylaxis in cases of prostatic biopsy is adopted in order to reduce the risk of infections, but should start before transperineal biopsies (12). Bacteremia has been demonstrated 5 min after the procedure but not after 60 min. On the contrary, urine cultures may continue to be positive for days after the procedure (12). To achieve an optimal therapeutic level of antibiotic in the blood, urine and prostatic tissue at the moment of the procedure, the drug should be administered prior to the biopsy. The risk of infection is < 1% when the antibiotic therapy is prolonged for three days and ranges between 1-4% depending on a single or two- (prior and post) dose intake (12).

Local anaesthesia with lidocaine gel in the rectum during transrectal biopsy, was reported to have controversial results *vs.* placebo and to be less efficacious against the pain experience than a 10 mg lidocaine periprostatic injection, but the optimal technique for the injection and dosage still needs to be defined yet (12).

Current data are not sufficient to demonstrate whether the transrectal or transperineal approach offers advantages in terms of detection and complication rate, or which is the more painful after local anaesthesia. Literature data indicate that it is mandatory to perform prostatic local anaesthesia before a transperineal biopsy, while it is only recommended before a transrectal biopsy (13). These procedures are accompanied by a high rate of minor complications while severe morbidities requiring hospitalisation range from 0.9-2.4% (Tables XIII-XIV). No prospective randomised studies documented an increase risk of bleeding after biopsy in patients on anticoagulants and/or antithrombotic agents, even if radiologists and urologists encouraged patients to discontinue the use a week prior to the needle biopsy if it was not contra-indicated (13). Vasovagal episodes described are rare and moderate (13). The transperineal approach is considered safer than the transrectal and is recommended in patients with a compromised immune system. Severe but sporadic

Table XIII. *Complications following transperineal biopsy.*

Haematuria	26-42%
Severe haematuria	0.7%
Haemospermia	13-46%
Pelvic hematoma	0.1%
Pain (with anesthesia)	31%
Voiding impairment	2.7%
Urinary retention	2%
Septicemia	0.1-0.7%
Urinary infections	0.0-0.5%
Rectal bleeding	0.0%
Fever	0.5%

Table XIV. *Complications following transrectal biopsy.*

Haematuria	47-74%
Severe haematuria	0.1-0.7%
Haemospermia	19-45%
Pelvic haematoma	0.0%
Pain	36%
Voiding impairment	6.8-7.2%
Urinary retention	1%
Septicemia	0.1-0.2%
Urinary infections	27-32%
Urinary infections (with antibiotic prophylaxis)	0.2-5.6%
Mild rectal bleeding	4.9-22.1%
Severe rectal bleeding	1.2%
Fever	1%

complications due to the transrectal approach can occur in the presence of inflammatory rectum diseases (13). Extra peritoneal haematoma due to Santorini plexus injuries, perineal prostatic tumour seeding and death following either transperineal or transrectal biopsies have been reported previously (13).

The optimal number of cores to be taken has yet to be defined but should include more than 6 cores. Doubling the sextant scheme (Hodge's scheme) during the same biopsy sampling (12 cores) and performing the biopsy on the same site and with the same angle of penetration does not increase the detection rate. There is conflicting evidence supporting the sampling of the peripheral gland more laterally and towards the apex of the prostate (14).

It is widely accepted that hypoechoic lesion-directed cores in association with the standard sextant scheme (Stamey or Hodge's scheme) may increase the detection rate by about 5.0-5.7%, but not in the case of prostate biopsy with a higher number of cores (>10 cores) (14). There is no strong evidence for an increased detection rate with the biopsy of color-power-doppler-visible lesions (14).

There is a significant inverse relationship between the cancer detection rate and prostate volume and it was shown that the yield of sextant biopsy decreases upon increasing prostate volume. The data suggest schemes with more than 6 cores in prostates larger than 45 ml, or with an increasing number of cores, according to the prostatic volume (14). Mathematical models and computer simulations of prostatic biopsies demonstrate the necessity of increasing the number of biopsies according to the prostate volume especially in younger patients (14).

Only in selected cases with a high PSA value (PSA >10 ng/ml) and without clinical suspicion of positive nodules on rectal examination or TRUS, may transitional zone (TZ) biopsies be initially useful if an extended biopsy scheme of the peripheral gland has been adopted. The number of cores that should be taken may range from a minimum of 2 to a maximum of 6, according to TZ volume (14).

The average length of prostatic tissue per biopsy specimens should be >10 mm, measured on a glass slide and the recommended length of the needle sample noch should be ≥15 mm (15). If the length of the specimen released from the needle appears less than 10mm long, one more biopsy core in the same sampling site is recomended. For the pathological analysis, tissue should include at least one prostatic gland as representative (15). The cytological examination of aspirated tissue should be abandoned (15). The best method to handle and collect biopsy specimens is the pre-embedded *sandwich* technique (15).

Biopsy specimens should be collected as single or grouped (no more than 2 or 3) and labeled separately per side (right and left) and area (*i.e.* base, mid, apex, transition zone). It was shown that the simultaneous inclusion of more than 3 biopsies in the same cassette can lead to a loss of a 1.1 cm mean length of assessable tissue (15). The exact labeling and analysis of each specimen outlines the potential importance of knowing the specific location of the biopsy and the cancer extension that may influence the planning of surgery. The inking of one extremity of the specimen to allow biopsy orientation is not recommended, unless this information may influence treatment strategy, *i.e.* before cryosurgery or brachytherapy (15). The role of the urologist/radiologist is to provide complete and adequate clinical information to the pathologist (15).

Once prostate cancer has been diagnosed, the most predictive factors are PSA level, clinical stage (cT) and Gleason Score assigned to the positive cores (16). The role of the peri-neural infiltration (PNI), lymphnode micrometastasis and neuroendocrine differentiation are still controversial (16). Recent studies proposed detection of the presence of proliferation (nuclear cell proliferation antigens, Mib-1 and Ki 67) and/or telomerase activity

Table XV. *The Italian group for developing clinical practice guidelines on performing prostate biopsy.*

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markers on the bioptic core tissue as predictive factors since previous data showed that an increasing level might be associated with local advanced disease with a major risk of progression (16).

The routine seminal vesical biopsy, performed in order to reduce a possible clinical understaging, should be considered only in selected patients with a clinical or echographic suspicion of seminal vesical invasion (16).

It is currently impossible to define a sub-group of patients in which re-biopsy is unnecessary, especially in the case of increasing PSA. For PSA >10 ng/ml, 23% of cancer at the second biopsy was reported (17). PSA derivates are not superior to the free/total PSA in predicting a positive re-biopsy (17). F/T PSA with a cut-off of 30% in combination with PSA density transitional zone (PSA-Dtz) in addition to PSA density (PSAD) and PSA velocity can be used as biopsy predictor factors (17). Most authors suggest repeating biopsies and coring all the gland areas in the presence of high grade prostatic intraepithelial neoplasia (PIN) (HGPIN) and acinar small atypical proliferation (ASAP) at the first biopsy, since both ipsilateral or controlateral carcinoma and a detection rate up to 75% were found at the re-biopsy (17). PSA-D and low grade PIN are useless in the re-biopsy decision making process (17). A 10-11 core scheme and coring of both the peripheral and anterior zone of the gland, showed a higher percentage of positive cores at the re-biopsy than the sextant scheme (17). Performing TZ biopsies in the repeat setting may provide an increased detection rate, especially in the high volume glands (17).

The use of an artificial neuronal network (ANN) as the nomogram developed by the Memorial Sloan Kettering New York Centre for the rebiopsy decision-making could reduce unnecessary re-biopsies by 68%, with a specificity of 68% and a sensitivity of 95%, but unfortunately this model is very complex and needs a validation procedure (17). The saturation re-biopsy of 23 cores on average, after a prior negative biopsy, gave a detection rate of 32% in the case of a high PSA level, 31% in the case of HGPIN and 43% in case of ASAP (17). Important clinical factors can lead to re-biopsy within 6 weeks after the first biopsy without an increase in complications. In the presence of high suspicion of prostate tumour, it is recommended that up to three sets of sextant biopsies can be performed, while the fourth set (4% to 10% positive finding) should be reserved for a sub-group of very high risk patients with HGPIN, ASAP, and high PSA level. The F/T PSA cut-off of </=10% showed a sensitivity of 91% and a specificity of 86% in identifying patients who need a third biopsy set (17). Obviously, increasing the number of biopsies will increase the risk of finding a small size tumour. Trans urethral resection of prostate (TURP) should not be considered a diagnostic tool for prostatic cancer after one or more series of negative biopsies (17).

The positive biopsy rate after radiotherapy treatment ranged from the 29% to 93% (18). A study of the Princess Margaret Hospital Canadian Group shows that PSA might be a better marker than the biopsy histological results (18). The Memorial Sloan Kettering New York Centre data showed that a re-biopsy after radiotherapy should be performed within 2.5 years and that the biopsy positive rate decreased when neo-adjuvant therapy was administered alone, or in combination, and with increasing doses of radiation (18). Biopsy after radiotherapy should not be considered a routine test (18).

The detection of local prostate cancer recurrence after radical prostatectomy still represents a matter of debate. Some authors look at PSA kinetics and unfavourable factors (pre/post-surgery PSA level, the bioptic and pathological Gleason score, number/percentage of positive cores and positive margins, PSA recurrence time and PSA doubling time), while others believe that it is necessary to perform a biopsy of the prostatic fossa. Available studies reported a positive bioptic rate of 54% with approximately 80% in the presence of a palpable lesion or a suspicious lesion at TRUS (19). Furthermore, there is a strong correlation between positive biopsy rate and post-surgery PSA values. In the follow-up of patients who underwent radical prostatectomy, the use of PSA and PSA doubling time was sufficient for clinical practice (19). The baseline PSA, the pathological extracapsular extension of the tumour, the Gleason Score of the surgical specimen and the positive surgical margin are the most important variables predictive of local recurrence risk and are usually employed in planning immediate post-operative external radiation therapy (19).

Conclusion

The guidelines presented are not intended to replace judgment of the physician regarding particular patients or special clinical situations, or to support opportunistic or population-based screening programs, but were developed to help in the clinical decision-making process. In particular, these guidelines provide indications as to when and how to perform a prostate biopsy and should be periodically updated as the literature is made available.

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