



Performance of Needle Biopsy of the Prostate for Men with Suspected or Established Prostate Cancer

Recommendation Report

A special report developed by the Surgical Oncology Program at
Cancer Care Ontario in conjunction with the Prostate Biopsy Expert Panel

Report Date: September 2017

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Section 1: Purpose & Scope

Background

Needle biopsy of the prostate is an integral procedure in the diagnosis and care of men with all stages of prostate cancer. Assessing prostate needle biopsy practices in Ontario was identified as a priority by the Prostate Cancer Champions at two workshops in 2008 and 2009. A provincial survey conducted by the Surgical Oncology Program (SOP) on current prostate needle biopsy practices showed that there is some variation in practice across the province. The Prostate Cancer Champions agreed that a document outlining best practice was necessary.

This document addresses “best practices” for prostate needle biopsies and provides guidance on the spectrum of prostate needle biopsy practices, including patient preparation, biopsy techniques, specimen submission to the laboratory, processing of the biopsy specimen, information to include on the requisition and pathology report, and operational issues. Indications for prostate needle biopsy are outside the scope of this document.

Research Questions

1. Who should order prostate needle biopsies?
2. What is the optimal pre-biopsy preparation and peri-biopsy management for patients having a prostate needle biopsy, including: patient consent, management of patients on antiplatelet and anticoagulant medication, bowel preparation, antibiotic prophylaxis and analgesia?
3. What is the optimal prostate needle biopsy technique?
4. How should the biopsy specimen be submitted to the laboratory?
5. What is the optimal pathology processing technique and reporting?
6. What expertise should individuals have who perform prostate needle biopsy?
7. What are the necessary facility requirements to perform prostate needle biopsy?

Target Population

Men with suspected prostate cancer and those with prostate cancer who are being followed in an active surveillance program.

Intended Users

Providers involved in any aspect of prostate biopsy practices, including urologists, radiologists, radiation oncologists, pathologists and individuals responsible for ensuring necessary resources.

Report Rationale

- Reduce variability in practice across Ontario
- Optimize needle biopsy technique and processing
- Improve patient care

Section 2: Recommendations

1. Ordering of Prostate Biopsy

- 1.1 Prostate needle biopsy should only be ordered by a physician with expertise and current knowledge in:
 - Appropriate indications for prostate biopsy
 - Evaluating the risks and benefits of the biopsy and can counsel patients accordingly
 - Confirming appropriate timing and safe preparation for the biopsy taking into consideration appropriate antibiotic prophylaxis, infections, prior complications, recent antibiotic exposures and instrumentation, other medications (such as anticoagulants) and patient's general medical condition
 - Management options based on the results of the biopsy
- 1.2 If the prostate needle biopsy is performed by someone other than the ordering physician, the ordering physician needs to provide the appropriate and sufficient clinical information to ensure safe and appropriate techniques are used for the specific patient.

2. Pre- and Peri-biopsy Management

2.1 Consent

- 2.1.1 Prior to prostate needle biopsy, verbal (documented in the patient chart) and written consent regarding the biopsy procedure should be obtained. Pre-op discussions should include the clinical relevance of PSA/DRE findings, purpose of the biopsy and risk factors for prostate cancer.
- 2.1.2 Potential complications and side effects must be adequately reviewed to ensure that the patient understands the risks prior to prostate needle biopsy. Complications that should be mentioned include (but are not limited to):
 - Infection of the urinary tract and possible sepsis
 - Bleeding
 - Urinary retention
 - Risk of hospitalization due to complications
- 2.1.3 Patients should be instructed to seek prompt medical attention if symptoms suggestive of possible serious complications from prostate needle biopsy develop. If the requisitioning physician is not available, patients should be advised to promptly report to the nearest emergency room and report that they have recently undergone prostate needle biopsy.

2.2 Anticoagulation Management

- 2.2.1 ASA and non-steroidal agents do not need to be discontinued prior to prostate needle biopsy.
- 2.2.2 Anticoagulants such as warfarin, clopidogrel, rivaroxaban and dabigatran should be discontinued prior to prostate needle biopsy. Appropriate bridging therapy may be required depending on the original indication for anticoagulation and if so, the prescribing physician should be consulted.

- *Qualifying statement: Although there is a lack of evidence regarding the risk of post biopsy hemorrhagic complications in patients taking these anticoagulants, it is perceived that if a bleeding complication did occur it might be serious.*

2.3 Bowel Preparation

2.3.1 Use of enemas is optional based on physician preference.

- *Qualifying statement: There is some evidence that enemas can lead to reduction in bacteremia, however, a RCT showed no difference in clinical sepsis rate³³. Nevertheless, some physicians prefer that patients receive enemas to improve ultrasound visualization.*

2.4 Antibiotics

2.4.1 All patients should receive antibiotic prophylaxis prior to prostate needle biopsy. In the absence of a drug allergy, fluoroquinolone antibiotic prophylaxis is recommended.

- *Qualifying statement: If possible, antibiotic prophylaxis regimens should be established with knowledge of local hospital antibiograms and review of cultures of septic cases. If these are not available and there is no known allergy, fluoroquinolone antibiotic prophylaxis is recommended. The role of rectal swabs in choosing appropriate antibiotic prophylaxis is still unclear.*

2.4.2 For patients with an allergy to fluoroquinolone alternative antibiotics may include a second generation cephalosporin or an aminoglycoside.

2.4.3 Patients with risk factors for antibiotic resistance should be identified, counseled and should receive broader coverage prophylaxis. This may include the addition of a cephalosporin or aminoglycoside. This should be decided at each center based on local resistance data and preferably with local or regional infectious disease specialist input.”Risk factors for antibiotic resistance include:

- Antibiotic use (particularly fluoroquinolone) within 3 months prior to biopsy
- Recent international travel (particularly to Asia)
- Diabetes
- Immunosuppression due to medications, prior transplant or medical conditions
- Sepsis after prior biopsy
- Hospital workers or co-habitants of hospital workers
- Recent hospital admission

- *Qualifying Statement: Alternative antibiotic prophylaxis should be established with knowledge of local hospital antibiograms and review of cultures of septic cases. Consultation with an infectious disease specialist may be considered. The role of rectal swabs in choosing appropriate antibiotic prophylaxis is still unclear.*

2.4.4 Single-dose oral antibiotic prophylaxis is sufficient and should be administered at least one hour prior to the biopsy procedure.

- *Qualifying statement: There is a lack of evidence regarding the outcomes following multi-dose vs single-dose antibiotics.*

2.5 Analgesia

- 2.5.1 Prostate needle biopsy performed with a periprostatic local anesthetic block is strongly recommended. Intrarectal local anesthesia (IRLA) can be considered in addition to periprostatic local anesthetic.

3. Biopsy Technique

3.1 Pre Biopsy Imaging

- 3.1.1 DRE and transrectal ultrasound should be used to examine suspicious regions and determine prostate volume before removing cores.
- 3.1.2 Multiparametric MRI should not be used routinely in patients prior to first biopsy.
- Pre-biopsy multiparametric MRI mapping and MRI-ultrasound fusion technologies may be considered in selected patients, such as patients on active surveillance who have discordant findings or patients with a prior negative biopsy and high suspicion of cancer.

3.2 General Biopsy Technique

- 3..1 Prostate needle biopsy should be performed under TRUS guidance. Biopsy should not be performed solely via digital guidance. Biopsy may be performed via the transperineal route for select indications, including in men without an anus (after abdomino-perineal resections), for saturation biopsy or to decrease the risk of urosepsis. Transperineal prostate needle biopsy techniques have been shown to reduce sepsis rates but require resources for general or spinal anesthesia.
- 3..2 An end fire probe is preferred for guiding prostate needle biopsies. Biopsy should be performed with an 18-gauge needle biopsy gun.
- 3..3 Prostate needle biopsy cores should be kept as intact as possible during transference.
- 3..4 For the initial prostate needle biopsy:
- The peripheral zone should be systematically sampled including medial and lateral samples at the base, mid and apex on each side. Consideration should be given to sampling other areas including suspicious areas found by TRUS and/or DRE and/or multiparametric MRI.
 - 10-12 cores should be obtained as well as additional cores from suspicious areas. With large glands over 60 cc, an additional 2-4 cores may be considered.
- 3..5 For the repeat prostate needle biopsy:
- Generally, 10-12 cores from the areas sampled at the initial biopsy should be re-sampled. 2-4 additional cores from the transition zone and midline base peripheral zone can be considered.
 - If multiparametric prostate MRI (mpMRI) and qualified interpretation are available, then pre-biopsy mpMRI may be considered to help localize sites for more intensive sampling at repeat biopsy. At this time, note that clinically indicated biopsies should performed even if the mpMRI interpretation suggests that 'no significant lesion is seen' since not all significant lesions can be detected by mpMRI.
- *Qualifying statement: Alternate biopsy protocols (i.e. saturation biopsy) can be considered in special situations, such as in the setting of rising PSA and two or more negative biopsies with no access to MRI or staging in preparation for focal therapy. However, the role of saturation biopsy is not clearly defined.*

3.3 Submission to the Laboratory

- 3.3.1 Containers should be labeled with patient identifiers and core sites. Patient identifiers should be confirmed by the patient to ensure there are no misidentification errors.
- 3.3.2 Ideally individual biopsy cores should be submitted to the laboratory in separate containers. However, 2 cores per container is acceptable if the cores are from the same site.
 - *Please refer to Appendix A for a definition of prostate sites and how they should be labeled.*
- 3.3.3 Cores taken from specific sites should be processed and placed in separate, site-labeled containers in 10% neutral buffered formalin.
- 3.3.4 The pathology requisition form should contain, at a minimum, the following clinical information:
 - DRE results
 - PSA results
 - Prostate volume
 - Clinical stage
 - TRUS and MRI findings
 - Whether the patient is on 5-alpha-reductase inhibitor (5-ARI) therapy
 - Whether patient already has a diagnosis of prostate cancer and therapy he has received (i.e. active surveillance, radiation or hormone therapy, focal therapy)
 - Whether the patient had a previous diagnosis of bladder cancer

4 Pathology

4.1 Processing

- 4.1.1 It is preferable to submit 1 core per paraffin block but 2 non-fragmented cores per paraffin block is acceptable.

4.2 Sectioning

- 4.2.1 Each paraffin block should be cut carefully and examined at multiple levels. Excessive trimming should be avoided.
- 4.2.2 Serial sections or deeper levels may be cut from the paraffin block when required to assess additional H&E sections and/or for confirmatory immunohistochemical staining. Intervening unstained sections between the initial levels may be used for these purposes.

4.3 Immunohistochemical (IHC) staining

- 4.3.1 IHC should not be used as an initial screening tool to identify malignant or atypical/suspicious foci. Prostate cancer diagnoses should be made based on H&E criteria.
- 4.3.2 IHC should be used in specific situations when H&E features are suspicious for malignancy. Immunohistochemical stains such as 34βE12, p63, CK 5/6 and AMACR may be used individually or as cocktails. The indications for use of IHC on prostate biopsies has been extensively reviewed in a recent consensus paper from the International Society of Urological Pathologists (ISUP).

4.4 Necessary information in a pathology report

- 4.4.1 Terminology and items to be included in biopsy reports should be based on the College of American Pathologists checklist.
- 4.4.2 Biopsy reports should include specimen level information in narrative or synoptic form and case level data in synoptic form.

4.4.2.1 Specimen level data (in narrative form):

- Histologic type of carcinoma
- Gleason score (primary +worst), if applicable
- Grade group/ISUP grade
- Number of involved cores/number of cores in that particular specimen container
- % involvement of each positive core and/or linear extent in mm in that particular specimen container
- Comment on the following if present in that particular specimen container:
 - Intraductal carcinoma
 - Periprostatic fat involvement
 - Perineural invasion
 - Treatment effects
 - Should any positive core/core fragment measure < 6 mm in total length, a comment should be made to indicate the mm of adenocarcinoma in relation to the total core/fragment length.

4.4.2.2 Reports for all positive sets of site-directed biopsies should include a case-level synoptic summary with the following information to be used in conjunction with specimen level information listed in 4.4.2.1:

- Gleason score/10 (Primary + Worst)
- Grade group/ISUP grade
- An estimate of the percentage of Gleason pattern 4 and/or 5 tumour (expressed as a the percentage of all the adenocarcinoma sampled in a set of positive biopsies)
- Number of involved cores/number of cores taken
- Total extent of involvement relative to all prostate tissue present in the set of biopsies
- Intraductal carcinoma, if present
- Involvement of periprostatic fat, if present
- Perineural invasion, if present
- Any treatment effects, if present

5 **Human Resources and Training**

5.1 **Physician performing prostate biopsy**

5.1.1 TRUS biopsy should only be performed by physicians who have received adequate training in ultrasound and biopsy techniques. This can be achieved through formal residency or fellowship training programs in urology or radiology, organized mentoring including evaluation in practice setting with a colleague that performs ultrasound and prostate biopsy regularly or accredited professional certifying programs. A physician should demonstrate competency in ultrasound examinations and perform a minimum of 12 successful mentored TRUS biopsies to be considered proficient in the ultrasound evaluation and biopsy technique.

- *Qualifying statement: Training requirements for ultrasound proficiency are out of the scope of this document.*

- 5.1.2 TRUS biopsies should be performed by physicians who perform them regularly. In centres where the volume of prostate needle biopsies performed is low, dedicating one or two individuals to perform all prostate biopsies or referral to a regional cancer centre is recommended.

5.2 Pathologist assessing prostate biopsy specimen

- 5.2.1 Prostate needle biopsy specimens should be read by a pathologist with an interest in prostate cancer and who is aware of the CAP guidelines and follows them.
- 5.2.2 Prostate needle biopsies should be read by pathologists in a setting where there is an appropriate quality assurance program for prostate interpretation. Quality assurance (QA) reviews should be carried out by the pathologist most responsible for the case in conjunction with 1 or more pathologists with experience in prostate biopsy reporting. If a secondary pathology review is done, the referring pathologist should be made aware of the results of the review. The results of the review (and the identity/institution of the reviewing pathologist) should be reported in addendum to the report initially issued by the referring pathologist.

6 Facility Requirements

- 6.1 In hospital biopsy facilities need to meet provincial and hospital requirements regarding ultrasound examinations and biopsy procedures. Outpatient facilities need to meet provincial CPSO-IHF requirements (<http://www.cpso.on.ca/uploadedFiles/policies/guidelines/facilities/Diagnostic-Imaging-CPP-FS.pdf>)
- 6.2 The technical aspects of TRUS should be conducted in accordance with accepted and established standards, such as the published by the AUA-AIUM. (<http://www.aium.org/resources/guidelines/urology.pdf>)

Section 3: Methods

1) Literature Search

A multidisciplinary Working Group of content matter experts developed a set of research questions (Appendix B). The Evidence Search and Review Service (ESRS) at CCO were then engaged to perform the literature review.

The Evidence Search and Review Service (ESRS) at CCO performed an initial literature review. They searched for peer reviewed publications within Ovid Medline (1946 to June Week 4 2013) and Ovid EMBASE (1947 to June 2013). In addition, an updated literature review was conducted in Medline by the Surgical Oncology Program for relevant peer reviewed articles published between 2013 and 2017. Searches were limited to English language and the year 2000 onwards.

A broad search for high-quality clinical guidelines and reports related to the sub-questions was also performed. Cancerview Canada and the Agency for Healthcare Research and Quality (AHRQ) Guideline Resource Centre were searched in addition to broad searches of Google and Google Scholar.

Screening

References were screened independently by multiple reviewers (JL, HG, and GS). Those studies that did not meet the inclusion criteria were excluded based on title and abstract. Where it was not possible to exclude articles based on title/abstract alone, full-text versions were assessed for inclusion. When the final collection of potentially relevant articles was identified, a second set of reviewers who were experts in the subject matter (RM, AE, and RS) screened the articles for relevance. Where the article was not deemed relevant by the expert in the field, it was excluded from the final synthesis.

In general, articles were excluded if they met one or more of the following criteria:

- a) Articles not published in English
- b) Articles not relevant to prostate biopsies
- c) Articles not relevant to the respective section
- d) Articles which are not evaluative (i.e. commentaries, editorials, conference proceedings, etc.)

Based on the volume of findings results were further limited. Systematic reviews & meta-analyses which were published after 2000 were included. Original research articles were considered for inclusion if they were published after 2010. Given the context-sensitive and inherently qualitative nature of a number of the sub-questions in this review, articles were considered 'systematic reviews' if the authors outlined explicit methods for systematic searching, identification, and collection of information from previously published original research (includes systematic reviews of both qualitative and quantitative research). Additionally, a number of sub-sections had a very limited pool of available studies. In the case where a section had less than two high quality articles per sub-question, limits on all articles regardless of study type were expanded to 2000 onwards.

Results

The search strategy identified a total of 8757 published articles. After reviewing titles and abstracts a total of 406 articles were considered for inclusion in this review. A list of titles and abstracts underwent a second screening by experts in the field who excluded an additional 182 articles based on relevance. The remaining articles were read in full, and 89 articles were included in the final report.

2) Clinical Feedback

A multidisciplinary Working Group was established to provide input into the report at all phases of development. The Working Group consisted of 4 urologists, 1 radiologist and 2 pathologists, all with expertise in performing, processing or reporting of prostate needle biopsies. The Working Group provided feedback in a number of ways during development of the document, including via email, teleconference calls and attending several in-person meetings.

The Working Group used the evidence identified from the literature search and expert consensus to develop a set of initial recommendations. A draft copy of the recommendations and supporting evidence was then reviewed by a multidisciplinary Expert Panel at a half day in-person meeting in Toronto. The Expert Panel included representatives from urology, radiology and pathology. Please refer to Appendix C for full membership of the Working Group and Expert Panel. Following the in-person meeting the Working Group made modifications to the draft recommendations based on the input from the Expert Panel members.

The document then underwent an external review process to solicit feedback from experts in the topic area who were not involved in the development of the document. The external review process involved two steps:

1. **Targeted Peer Review** phase, where 4 physicians (one urologist, one radiologist and two pathologists) were asked to perform a detailed review of the document and comment on areas for improvement in the recommendations or from the methodological point of view. Overall, responses were very positive and the document was viewed as relevant and methodologically sound. Several minor wording suggestions and expansion of recommendations were made, and these were incorporated into the document at the discretion of the Working Group. In addition, there were comments regarding the cost impact of some of the recommendations and the potential implementation barrier this may pose, however, the role of the guideline is not to address cost issues and therefore cost implications were not included in the report.
2. **Professional Consultation** phase, in which the document was distributed to urologists, pathologists and radiologists across the province for an opportunity to provide high-level feedback on the report before it was finalized.

The completed document was approved by the Expert Panel.

Section 4: Key Evidence

1. Ordering of Prostate biopsy

No evidence was identified outlining which physician should be responsible for ordering the prostate needle biopsy. This recommendation is based on consensus of the Working Group and Expert Panel.

2. Pre- and Peri-biopsy Management

2.1 Consent

Several guidelines, based mainly on consensus, outline the elements that should be included in informed consent and discussed with the patient^{1; 2; 3; 4}. General recommendations/best practices for necessary elements that should be included in the informed consent discussion are: PSA and DRE findings, purpose of biopsy, risk factors for prostate cancer including ethnicity, risk of clinically diagnosed insignificant prostate cancer, false positives, potential need for repeat biopsy and potential risks of the procedure itself.

The main adverse events that can occur post-procedure include infection (including drug-resistant E.coli infections); hematuria; hematospermia; rectal bleeding; retention of urine; orchitis; prostatitis; sepsis; fever; and dysuria. Zaytoun et al retrospectively evaluated 1438 patients who had TRUS guided prostate biopsies and reported the rate of infection to be 2.2%; urinary retention 0.8%; hematuria 4.4% and rectal bleeding 1.5%⁵.

The most serious complication is urosepsis. In the Zaytoun et al series, the rate was 0.2%⁵. Adibi et al reviewed a series of eight reports and found that the hospital readmission rate for infection following a TRUS biopsy ranged from 0.3-2.4%. In all of these studies antibiotic prophylaxis was given, most often with a fluoroquinolone⁶. Ontario data from 1996-2005, which included over 75,000 patients, found a 1.9% hospital readmission rate of which 72% were for infection. In this study, the mortality from prostate biopsy was 0.09%⁷. Because of the low but potentially life threatening risk of sepsis after TRUS biopsy, it is recommended that patients should be informed of the signs of infection to watch for, what action to take and relevant contact details⁴.

2.2 Anticoagulation Management

Guidelines of the European Association of Urology (2010)⁸, European Association of Urology Nurses (2011)², NHS Screening program (2006)⁴ and Society of Interventional Radiology (2012)⁷³ recommend that low-dose aspirin is not a contraindication for biopsy. However, the CUA recommends that ASA be stopped 7-14 days before the procedure⁹. A recent systematic review and meta-analysis which included 3218 patients found that patients taking aspirin were more likely to experience hematuria (OR 1.36; 95% CI: 1.13-1.64). However, the increased risk was due mainly to minor bleeding. There was no significant difference in the occurrence of rectal bleeding and hematospermia¹⁰. Similarly, a study of 530 men undergoing extended needle biopsies, of which 152 were taking aspirin on a daily basis, found no significant differences in the rate of hematuria (64.5% vs. 60.6%, p=0.46), rectal bleeding (33.6% vs. 25.9%, p = 0.09) or hematospermia (90.1% vs. 86.9%, p = 0.45). The only difference observed was the mean duration of bleeding was longer by approximately one day¹¹. Although the CUA recommends that ASA be stopped prior to biopsy, it is the opinion of the Expert Panel, and in-line with the rest of the evidence, that ASA and non-steroidal agents do not need to be discontinued prior to biopsy.

The CUA also recommends that anticoagulants (e.g. warfarin) should be stopped 4-5- days prior to biopsy. Bridging therapy with IV heparin or low molecular weight heparin may be considered depending on the risk of thrombotic events. This recommendation was based on consensus as there is a lack of high-level evidence⁹. The NHS Screening Program also recommends that warfarin should be stopped prior to biopsy with conversion to IV heparin when necessary⁴. In addition, the Italian Prostate Biopsies Group recommends stopping the use of anticoagulant or antiaggregant drugs 7 days before biopsy, when possible⁷⁹. However, in a small study of 49 patients who continued using warfarin there was no significant difference in the severity of bleeding in patients taking warfarin versus those taking aspirin and those taking no anticoagulants¹². Chowdhury et al reported on 902 patients who underwent a TRUS biopsy. Of those, 68 were taking warfarin, 216 low dose aspirin, 1 was on both, and the remaining 617 patients were on no anticoagulants. There was no significant difference in the proportion of patients who experienced hematuria (27.9% vs.33.8% vs. 37%) or rectal bleeding (13.2% vs. 14.4% vs. 11.5%). Regression analysis showed a significant association between increasing number of biopsy cores but no association with use of blood thinners¹³. However, given the small numbers of patients and the low risk of bleeding it is not possible to determine with certainty if there is no difference in the risk of severe bleeding.

The CUA, NHS Screening Program and Society of Interventional Radiology also recommend stopping clopidogrel prior to biopsy^{4; 9; 73}. In addition, the CUA recommends stopping ticlopidine 14 days before TRUS biopsy based on experience of interventions to other sites⁹. Raheem et al reported on bleeding rates in 91 patients on anticoagulation/antiplatelet therapy and 98 control patients and found no significant difference in any bleeding parameter¹⁴. Again, however, this study is limited by the small sample size.

2.3 Bowel Preparation

Guidelines from EAUN, NHS Screening program, and CUA recommend that cleansing enema before biopsy is not required. There is limited evidence and these recommendations are based on consensus^{2; 4; 9}.

Supporting this recommendation is a before and after study which included 190 patients who were on clear liquids the day prior to biopsy and 217 patients who followed a bowel cleansing protocol (clear liquids the day prior to biopsy plus 2 enemas). There was no significant difference in sepsis rates (2.11% vs 0.46%, p=0.189)¹⁵.

Contrary to these results, a Cochrane review which was performed to assess antibiotic prophylaxis combined four studies with a small number of patients and found that the risk of bacteremia was diminished in the antibiotic plus enema group vs antibiotic alone (RR 0.25, 95% CI: 0.08-0.75). There were no other significant differences in any other outcomes¹⁶.

Lindert et al randomized 50 men undergoing TRUS prostate biopsy to one of two groups: pre-operative enema (25 patients) and no enema (25 patients). Post procedure cultures were taken from all patients and they found that the rate of bacteremia was higher in the no enema group compared to the pre-operative enema group (28% vs. 4%, p=0.0003). However, only 1 patient was symptomatic with a positive culture³³.

2.4 Antibiotics

Most guidelines recommend quinolones for prophylaxis but differ in their recommendations for the duration of antibiotics^{2, 4, 8, 9, 17, 18, 80, 81, 83}. The EAUN² and the AUA¹⁷ recommend 1 dose of antibiotics, whereas the EAU¹⁸

recommends a short course less than 72 hours. The NHS Screening Program⁴ and the CUA⁹ recommend starting antibiotics at least 30 minutes before the procedure and continuing for 2-3 days following the biopsy.

A Cochrane review which included 9 trials with a total of 3599 patients analyzed antibiotics vs placebo/no treatment. All outcomes significantly favored antibiotic use including: bacteruria (RR 0.25; 95% CI: 0.15-0.42), bacteremia (RR 0.67; 95% CI: 0.49-0.92), fever (RR 0.30; 95% CI: 0.23-0.64), UTI (RR 0.37; 95% CI: 0.22-0.62) and hospitalization (RR 0.13; 95% CI: 0.03-0.55). Seven trials compared one day vs three day protocols and found that there was a significantly higher risk of bacteruria (RR 2.09; 95% CI: 1.17-3.73) with a one day course but there was no difference in other outcomes. Similarly, when comparing single versus multiple dose protocols, there was a significantly greater risk of bacteruria after single dose prophylaxis (RR 1.98; 95% CI: 1.18-3.33). Finally, there were no significant differences in any outcomes when oral was compared to systemic administration of antibiotics. The authors concluded that there are no definitive data to confirm that long course antibiotics or multiple dose treatment is superior to single dose or short course treatments¹⁶. A meta-analysis based on RCTs by Yang et al found similar results with no substantial differences in outcomes between long-course versus short-course antibiotic treatment and single versus multiple dose treatment except for a greater risk of bacteriuria for short-course treatment and single dose treatment⁸².

While fluoroquinolones have been the drug of choice, there is increasing concern that the risk of fluoroquinolone-resistance is increasing. Populations that may be at risk for harboring fluoroquinolone-resistant E Coli are patients undergoing repeat biopsy^{9,19,83}, those of Asian ethnicity⁹, those who have diabetes⁹, recent fluoroquinolone use^{20,83; 40; 41} and recent travel^{40,83}.

Liss et al performed rectal swabs on 136 men who underwent repeat TRUS biopsy and 33 men who were having an initial biopsy between 2009-2010. In those patients having a repeat biopsy, 22% (95% CI: 15, 29) had cultures positive for fluoroquinolone-resistant bacteria compared to rate of 15% in those having an initial biopsy¹⁹. Zaytoun et al reported that 40 of 1446 patients developed infection after a first biopsy. Of note, 20 of the 40 had urine cultures positive for E coli, and of these 11 had fluoroquinolone-resistant infections⁵. Mosharafa et al found that in 107 patients undergoing TRUS biopsy, prior use of a fluoroquinolone antibiotic increased the risk of developing acute prostatitis. Acute prostatitis developed in 7 of 41 (17.1%) of patients who had used a fluoroquinolone compared with 3 of 66 (4.5%) of patients who had not (P=0.042)²⁰. In a separate study of 316 men undergoing TRUS biopsy, antibiotic use within 4 week prior to biopsy (4/16 vs. 20/300; P=0.025; RR 2.7) as well as recent travel (8/16 vs. 76/300; P=0.04; RR 2.7) were independent risk factors for infection⁴⁰. In addition, Taylor et al assessed the microbial and antibiotic sensitivity in 849 men undergoing prostate biopsy and found that ciprofloxacin use in the past 3 months (P<0.05) increased the risk of harboring resistant microorganisms on multivariate analysis⁴¹.

Overall in the province of Ontario, E coli resistance to ciprofloxacin is estimated to be approximately 20%, but it ranges from 18-27% across the province. There is no consensus on whether rectal swab should be done routinely, but likely should be performed in patients at high risk of antibiotic resistance²¹. This view is supported by the Italian Prostate Biopsies Group to lower the risk of post biopsy sepsis⁷⁹.

There is no consensus in the literature on the preferred antibiotic for prophylaxis in patients who are resistant to ciprofloxacin. Some of the possible combinations that have been recommended are amoxicillin clavulanate, ciprofloxacin plus gentamicin, and Tazobactam/piperacillin (TAZ/PIPC) plus levofloxacin^{22; 23; 24}. There are no studies which have addressed this question in men who are known to have E coli resistance to ciprofloxacin. However, in three studies from the UK where amoxicillin clavulanate was prescribed to determine whether it

decreased the risk of *Clostridium difficile* colitis, ciprofloxacin was found to be superior to amoxicillin clavulanate in preventing septic complications following prostate biopsy^{22; 23; 25}.

Finally, Adibi et al performed a cost-effectiveness analysis comparing fluoroquinolones to an intensive antibiotic regimen in men having a TRUS biopsy. They assumed a 50% risk reduction in admission rates with intensive antibiotics (amikacin 500mg pre-biopsy followed by a 5 day course of ciprofloxacin 500mg/twice a day for 5 days) and found that standard fluoroquinolone was slightly less costly. However, if the risk of admission for quinolone resistant infections was greater than 1.1% or the more intensive antibiotic regimen decreased the rate of admission by 54%, then the 2 regimens were cost equivalent⁶.

2.5 Analgesia

Patient tolerance and comfort during TRUS guided prostate biopsy can be improved by anesthesia/ analgesia. The different methods include: periprostatic nerve block (lateral and apical periprostatic anesthesia), anesthetic gel instillation (lidocaine gel), and sedation with anesthetic agents (general anesthesia, prostatic block with infiltration of local anesthetic agent – administered by qualified personnel).

The EUAN, NCCN, EUA, CUA and ESMO guidelines recommend the use of peri-prostatic nerve block^{2; 3; 8; 9; 80; 81; 84}. A systematic literature review (without meta-analysis) suggested that of the various options periprostatic anesthetic infiltration is the safest, is easiest to perform and is highly effective²⁶. Additionally, two separate systematic reviews with meta-analysis evaluating periprostatic local anesthetic and pain associated with biopsy found that periprostatic block with local anesthetic was significantly associated with reduced pain scores compared with either placebo injection or no injection^{27; 28}. In contrast however, one randomized placebo-controlled, double-blinded study did find that pain experienced during transrectal biopsy of the prostate is mild and was not significantly lowered with periprostatic nerve block. Pain from the injection itself was found to be similar to pain from core biopsies. Overall, the study suggested that pain from TRUS-guided biopsy of the prostate is well tolerated with no anesthesia²⁹.

In addition, the NCCN guidelines recommend that topical lidocaine may be efficacious in reducing pain specifically during probe insertion³. However studies on the use of lidocaine to reduce pain during biopsy are conflicting. A prospective randomized-controlled study to examine the efficacy of lidocaine and tramadol in periprostatic nerve blockage found the mean self-reported patient pain scores were significantly lower in both the lidocaine and the tramadol groups compared with the placebo group ($P < .001$)³⁰. However, a separate RCT concluded that the use of intrarectal lidocaine gel does not seem to affect pain perception during prostate biopsy³¹. A more recent meta-analysis also found that combined modalities show better analgesic efficacy than periprostatic nerve block alone, with lidocaine-prilocaine cream appearing to be the most effective⁹⁰.

A randomized controlled double blind trial to examine the effect of a number of sedative agents found that midazolam, when given in addition to doing a periprostatic nerve block, improves pain control during both probe insertion and penetration of the biopsy needle into the prostate capsule³². This study also assessed the efficacy of tramadol and concluded that it did not provide any additional benefit when given supplementary to periprostatic nerve block³²; however, in a separate study tramadol was effective compared with placebo³⁰.

3 Biopsy Technique

3.1 Pre-Biopsy Imaging

Multiple guidelines (NCCN, DUA, NICE, ESUR, ESMO) recommend that multiparametric MRI may assist in cancer detection in patients with persistent PSA elevation but negative TRUS-guided biopsy to determine if another biopsy is needed^{3; 34; 74; 75; 81; 84}. A recently released Cancer Care Ontario guideline on the role of multiparametric MRI in the diagnosis of prostate cancer recommends that multiparametric MRI should not be standard of care in men with an elevated risk of prostate cancer who are biopsy-naïve, but that it can be considered in patients with a prior negative TRUS biopsy who are still considered to have an increased risk of having prostate cancer⁸⁵. This recommendation is further supported by a systematic review and meta-analysis by Schoots et al who performed a subgroup analysis which showed that MRI plus TRUS biopsy improved the detection of significant prostate cancer in men with a previous negative biopsy, but not in men at initial biopsy⁸⁸.

In patients entering an active surveillance program, multiparametric MRI may be considered prior to beginning of the active surveillance program to help evaluate for unsuspected significant intra-prostatic disease and adverse prognostic factors^{74;75; 89}.

3.2 General Biopsy Technique

Most guidelines recommend that biopsy should be performed under transrectal ultrasound guidance^{1; 2; 3; 4; 8; 9; 17; 34;80; 81; 84}. The transrectal approach should be used unless it is not possible due to specific patient conditions, such as after abdomino-perineal resection^{1; 4; 8; 17}. The Italian Prostate Biopsies Group recommends transrectal and transperineal biopsy with the same level of evidence⁷⁹. The transperineal approach, as opposed to the transrectal approach, should be used in men at high risk of urosepsis⁷⁹ and can be considered in the setting of repeat biopsy⁸⁴. Biopsy can be adequately performed with end fire probes^{4; 80; 86}. When end fire probe biopsy were compared with side fire probe biopsies, Ching et al found a significant difference in the overall cancer detection rate (45.8% vs 38.5%, $p < 0.001$)⁷⁷. Wang et al compared use of an 18G needle to 20G needle and found the 20G needle had a similar cancer detection rate, but led to lower local injury, pain and complications. However, the study was small and a larger more sensitive study is needed to verify results⁸⁶.

With regards to the number of cores to sample at prostate biopsy, the initial report by Hodge et al recommended that 6 cores be taken when performing a prostate biopsy³⁵. Subsequently, other studies have shown that by taking more laterally directed biopsies, the detection rate of prostate cancer can be increased without increasing the morbidity or the detection rate of insignificant cancers. Biopsy strategies which include 10-18 cores are termed *extended prostate biopsy*.

The majority of guidelines recommend sampling up to 12 cores during prostate biopsy^{1; 2; 3; 4; 8; 9; 17; 79; 84}. The EUAN², AUA¹⁷ and DUA³⁴ recommend a minimum of 8 cores be sampled, whereas the NHS Screening Program⁴ CUA⁹, EUA⁸⁰ and ESMO⁸¹ support sampling a minimum of 10 cores. Additional cores should be taken from suspicious areas^{2; 3; 4; 8; 9; 79; 80; 84}.

Chun and colleagues performed a systematic review of the literature, which included 4 studies comparing 10-12 core biopsies to 6 core biopsies. The detection rate increased by 20-35% with the 10-12 core biopsy schemes. Three other studies did not show that the detection rate increased if more than 10-12 cores were taken. One other study, Ravery, did show a benefit to taking 20 cores but was criticized because in the 10 core group, only

two biopsies were taken from the apical and transition zones. Thus, the authors concluded that a minimum of 10 but not more than 18 cores should be taken ³⁶.

Similarly, in a retrospective chart review of 1613 patients, Bittner et al found a significant association between higher number of biopsy cores and longer biochemical progression-free survival (BPFS), overall survival (OS), and cause-specific survival (CSS). With >20 cores the BPFS, OS and CSS were all 100%. When 13-20 cores were removed, BPFS and CSS remained at 100% while OS dropped to 93.4%³⁷.

Other studies have suggested that the relationship between the number of biopsy cores and the resultant cancer detection rate does not correlate linearly. These studies seem to indicate that the optimal scheme varies according to the clinical characteristics of the patients^{38; 39}. Depending on DRE findings, prostate volume and previous biopsy results, taking 14-16 cores may be considered.

The apex and base of the peripheral gland are the most common cancer sites which is where biopsy should be directed. Parasagittal biopsies have been demonstrated to have the lowest probability of prostate cancer at initial biopsy. Furthermore, the vast majority of prostate cancer originates from the peripheral zone vs the transitional and central zone thus the addition of laterally detected biopsies has been shown to yield approx. 5-35% increase in cancer detection rates³⁶.

The EUA^{8; 80}, EUAN², DUA³⁴, NHS Screening Program⁴, AUA¹⁷, NCCN^{3; 84} and Italian Prostate Biopsies Group⁷⁹ guidelines all recommend targeting the peripheral zone during biopsy, as well as laterally directed cores on each side of the prostate. Transition zone biopsies should generally be omitted from the initial biopsy^{2; 4; 3; 8; 9; 42; 80; 84}.

There are conflicting indications for which sites should be sampled on repeat biopsy. One systematic review documented that repeat biopsies should be based on saturation biopsies (number of cores > 20) and should include the transition zone targeting lateral biopsies⁴². Another report based on consensus suggested that repeat biopsy sites should include the initial atypical site, and adjacent ipsilateral and contralateral sites with routine sampling of all sextant sites⁴³. One other review suggested that needles should be directed to a more apico-dorsal location upon repeat biopsy⁴⁴. Multiple guidelines recommend considering sampling anterior areas and transition zone ^{3; 4; 8; 17; 84}.

3.3 Submission to the laboratory

Guidelines for submitting prostate biopsy cores to the laboratory vary widely. There is general consensus that core biopsies taken from different sites should be sent to the laboratory in different vials^{2; 8; 79; 87} and, at a minimum, should be identifiable by left or right side^{4; 34}. The NHS Screening Program also recommends having one set of patient notes and adhesive labels in the procedure room, as well as local policies/procedures in place for labeling and checking to ensure correct patient identification⁴. The ERSPC committee emphasizes the importance of having patient identifiers, clinical information and demographics accompany the prostate biopsies to ensure pathologists have all necessary information to interpret the biopsy results⁸⁷.

Published recommendations also vary concerning the number of cores to be submitted per container, ranging from one to three cores per container^{45; 78; 79; 87}. Limiting the number of cores per container can reduce fragmentation and thereby improve the ability to diagnose, quantify and grade cancer in needle biopsies⁴⁶.

There is limited evidence identified in the literature on what information should be included on the pathology requisition form. This recommendation is based the guidelines of the ERSPC committee⁸⁷ and on consensus of the Expert Panel. The following information should be included: patient age, DRE findings, serum PSA, prostate volume, TRUS and MRI findings, 5ARI therapy and previous diagnosis of prostate cancer and therapy (i.e. active surveillance, radiation or hormone therapy) and purpose of the biopsy (i.e. for primary diagnosis of cancer or follow-up biopsy after a previous diagnosis of cancer).

4 Pathology

4.1 Processing

Very few articles specify how prostate biopsy cores should be fixed and processed. The EAU recommends a maximum of 3 cores per cassette⁸. Similarly, the ERSPC committee recommends that up to 3 cores from the same biopsy site can be embedded in one cassette, provided measures are taken to prevent their curling or floating⁸⁷. Despite this recommendation, it is the opinion of the Expert Panel that there should only be 1-2 cores per cassette. While overnight fixation in formalin is likely to be used by most laboratories, rapid fixation and processing can also be used to facilitate same-day diagnosis. Morales et al compared rapid vs conventional processing of various tissues including prostate on basic histology. They concluded there was no difference in quality - rapid microwave-assisted processing, if done properly, has no negative effects on histologic quality⁷².

4.2 Sectioning

Multiple levels should be examined from each paraffin block, as additional sections can reveal areas of carcinoma that were not apparent in original sections⁴⁹. One study suggested that prostate biopsy blocks should initially be cut and examined at three levels⁵⁰; another indicated that each block should be cut at three levels with 5 spacing sections (20 µm in total) between levels⁴⁸. Still another specified embedding 6 tissue cores in 2 separate blocks followed by cutting at 5 levels⁵². When examination of the initial sections reveals atypical or suspicious foci, one study suggested cutting three additional serial sections with no shaving between sections⁴⁸. The additional cutting of suspicious foci can help avoid overgrading⁸⁷. These studies are all supported by the EAU, NHS Screening Program, DUA and ERSPC committee guidelines which recommend blocks be cut at three levels, with additional (deeper) sections considered for suspect glandular lesions^{4; 8; 34; 87}.

4.3 Immunohistochemical Staining

There is general consensus that immunohistochemical and other ancillary stains can be used to support the diagnosis of cancer on prostate needle biopsies^{4; 8; 87}. Immunostaining should only be performed as an additional tool in cases where conventional histology fails to confirm the malignant nature of small foci which are highly suspicious on morphology^{50; 87}. Such stains will typically be used when foci of cancer are small (<1 mm in maximum dimension), although there are other scenarios where the use of these ancillary stains is helpful to clarify the nature of larger atypical foci (*ie: PIN-like carcinoma, pseudohyperlastic carcinoma, atrophic carcinoma, adenosis, etc*)⁸⁷. High molecular weight cytokeratin (34βE12 or cytokeratin 5/6), p63, AMACR/P504S or a cocktail containing up to three stains are useful in confirming prostatic carcinoma which lacks diagnostic, qualitative or quantitative features or that has an unusual morphologic pattern^{54; 76}. The indications for use of IHC on prostate biopsies has been extensively reviewed in a recent consensus paper from the International Society of Urological Pathologists (ISUP)⁹¹.

4.4 Necessary information in a pathology report

Several guidelines contain detailed accounts of information to include in prostate biopsy pathology reports, including Gleason score (primary + worst), number of involved cores and proportion of tumour involvement, presence of extraprostatic extension and the presence of HGPIN^{4; 8; 55; 81; 87; 92; 93; 94}. In Ontario, the College of American Pathologist (CAP) checklists have been adopted for pathological reporting of cancer specimens. For prostate, the CAP reporting requirements include: histologic type; histologic grade/grade group/ISUP grade; tumor quantification; intraducal carcinoma; periprostatic fat invasion; seminal vesicle invasion; lymph-vascular invasion; perineural invasion; additional pathologic findings (including high grade-PIN, adenosis, inflammation, and other)⁵⁶. In addition, the majority of the literature indicates that the number of positive cores should be reported, along with one other measurement (ie percent of overall cancer, percent of each involved core by cancer, total percent of cancer, total millimeters of cancer)^{49; 50; 57; 58; 87}. On the other hand, there is a strong consensus that low-grade PIN should not be reported in needle biopsies. In addition, Gleason scores of 2-5 cannot be reliably diagnosed in the setting of prostate needle biopsies^{8; 59; 60; 61}.

With regards to terminology, there is general agreement that “atypical hyperplasia” is nonspecific and should not be used in pathology reports⁶¹. Nomenclature of prostatic lesions in pathology reports should be uniform and follow current recommendations from the WHO and CAP in addition to other sources⁸⁷. Descriptive terms such as “atypical glands” and “glandular atypia” should be used in a consistent manner so that the urologist can plan appropriate follow-up. Terms such as “probably malignant”, “but benign not excluded” should be avoided, as it may not be clear to the urologist what further action should be taken⁶².

5 Human Resources and Training

5.1 Physician performing prostate biopsy

The EAUN recommends that healthcare practitioners undertaking prostate biopsies be trained by competent practitioners and trained in physical assessment including digital rectal exams (DREs). Experience should include at least 3 years of experience working with prostate cancer patients, and performing a minimum of 20 biopsies satisfactorily without supervision at an acceptable speed. Direct supervision should be undertaken until the healthcare practitioner is deemed competent and final competence should be assessed and signed by a senior urologist².

However, these recommendations refer to non-clinicians and may not be relevant in the Ontario setting where prostate biopsies are generally done by physicians.

Investigators leading the REDUCE trial found significant variance in biopsy quality. As such, the study coordinators instituted a training program including a biopsy guidance manual, as well as a video webcast providing detailed protocol guidance, a streaming video of the biopsy procedure which included use of anesthetic and protocol-required placement of the needle at specified anatomic sites. Following this educational invention there was an increase in the aggregate core length, number of cores and the mean length of individual cores, and significantly less variation between regions⁶³.

Benchikh et al reviewed urology residents performing prostate biopsies in a training program under senior supervision. There was an improvement in biopsy as measured by core length that plateaued after 12 procedures⁴⁷.

The American Institute of Ultrasound in Medicine (AIUM), in collaboration with the AUA, developed training guidelines for physicians who evaluate or interpret ultrasound examinations in urology. These guidelines recommend that physicians performing and/or interpreting diagnostic ultrasound examinations in urology have a thorough understanding of the indications for GU ultrasound examination, an understanding of ultrasound technology and instrumentation, ability to correlate ultrasound findings with complementary imaging and diagnostic procedures, and should have knowledge of the anatomic, physiologic and pathophysiologic characteristics of the anatomic areas being examined. They should also provide evidence of the training and competence needed to perform and/or interpret diagnostic genitourinary ultrasound examinations successfully. The training should include methods of documentation and reporting of ultrasound studies. In addition, it is recommended that a minimum of 50 diagnostic genitourinary ultrasound examinations be performed per year to maintain the physician's skills⁶⁴.

5.2 Pathologist assessing prostate biopsy specimen

In a non-specialized pathology practice, there is a role for intradepartmental consultation by colleagues with experience or expertise in prostate biopsy interpretation for issues of potential clinical significance such as; grading thresholds (Gleason 6 versus 7), minor high-grade components (particularly Gleason pattern 5), the diagnosis of minimal cancer, intraductal carcinoma or extraprostatic extension. There is general consensus that re-evaluation should be performed on all external biopsies prior to definitive surgery^{65; 66; 67}, and in patients with primary Gleason score >6⁶⁸. As well, the literature suggests central pathologic review should be performed by uropathologists with attention to different types of discordance on grading between uropathologists and generalist pathologists^{69; 70; 71}. The EAU and NHS Screening Program also recommend that suspicious or equivocal cases be reviewed by a pathologist with expertise in prostate biopsy interpretation^{4; 8}.

6 Facility Requirements

The European Association of Urology Nurses² and the Prostate Cancer Risk Management Programme⁴ (under the auspices of the NHS Screening Program) guidelines provide the most comprehensive list of required equipment/resources necessary to perform a prostate biopsy. These include: a clinic room spacious enough for at least 3 people; examination couch; curtains or a screen; imaging equipment (capable of measuring prostatic volume, providing resolution of the zonal anatomy, and capable of viewing the prostate in both longitudinal and transverse planes); linen skip; clinical waste bin; sharps bin; biopsy gun and needle or single use device (PCRMP recommends the use of dedicated end-fire probes with curved array or biplanar dual side firing transducers); long spinal needles; condoms/sheaths (for ultrasound probe); specimen pots; lubricating jelly; wipes/gauze; gloves; needle guide; emergency equipment including oxygen, suction, cardiac arrest trolley, defibrillator, emergency drugs, anaphylaxis kit, monitoring equipment, and intravenous fluids^{2;27}



ACKNOWLEDGEMENTS

This report was developed by Dr. Rajiv Singal (Chair), MD; Dr. Joseph Chin, MD; Dr. Christopher Morash, MD; Dr. Roland Sing, MD; Dr. John Srigley, MD; Dr. Andrew Evans, MD; Dr. Ants Toi, MD; Leigh McKnight, HBMSc; Dr. Alice Wei, MD; and Dr. Robin McLeod, MD.

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Appendix A – Prostate Site Labeling

Urologists or radiologists performing the biopsies may submit the biopsies in any order using the following standardized terminology depending on the biopsies performed.

It is preferable to include the number of cores obtained from each site (ie: left lateral apex - 1, left medial base nodule – 3, etc)

STANDARDIZED PROSTATE BIOPSY LABELLING AND SUBMISSION		
Specimen #	Site	No. of Cores Submitted
	Right Base Lateral (RBL)	
	Right Base Medial (RBM)	
	Right Mid Lateral (RML)	
	Right Apex Lateral (RAL)	
	Right Apex Medial (RAM)	
	Left Base Lateral (LBL)	
	Left Base Medial (LBM)	
	Left Mid Lateral (LML)	
	Left Mid Medial (LMM)	
	Left Apex Lateral (LAL)	
	Left Apex Medial (LAM)	
	Right Transition Zone (RTZ)	
	Left Transition Zone (LTZ)	
	Nodule (DRE, TRUS)	
	Other e.g. MRI targeted (specify _____)	
	Other (specify _____)	
	Other (specify _____)	

Appendix B – Research Questions

Ordering of Prostate Biopsy

1. Which physicians should be responsible for ordering prostate biopsies?

Pre-op Preparation:

1. Patient consent: What risks should patients be made aware of prior to biopsy?
2. Antiplatelets and anticoagulants: What is the recommended pre-op management of patients on antiplatelets and/or anticoagulants?
3. Bowel preparation: What is the role of bowel preparation prior to prostate biopsy?
4. Antibiotic prophylaxis: What is the recommended regimen(s) for prophylactic antibiotics?
5. Analgesia: What is the recommended use of analgesia when performing prostate biopsy?

Biopsy Technique:


1. Technique: What is the recommended operative technique for performing prostate biopsy?
2. Number of cores: What is the optimal number of cores to remove during biopsy?
3. Sites to sample: Which prostate sites should be sampled during biopsy?
 - a. What sites should be sampled during initial biopsy?
 - b. What sites should be sampled in patients on active surveillance?
 - c. What sites should be sampled on repeat biopsy?
4. Special circumstances: How do special circumstances influence biopsy technique (special circumstances include prostate volume, abnormal ultrasound findings)
5. What needs to be considered when performing a repeat biopsy?
 - a. What sites should be sampled on repeat biopsy?
6. Pathology requisition: What information should be included on the pathology requisition?
7. Specimen submission to lab: What is the optimal way of submitting a biopsy specimen to the lab, specifically:
 - a. Number of cores per bottle
 - b. Labelling of bottles

Pathology:

1. Specimen processing: What is the recommended way to process biopsy specimens in the laboratory?
 - a. How should the prostate biopsy specimen be fixed?
 - b. What is the optimal way to paraffin embed and section these specimens (i.e. number of cores/block and the number of levels cut from each block)?
 - c. What is the role of immunohistochemistry or other ancillary stains during the review of prostate biopsies?
2. Pathology reporting: What is the optimal way to report on prostate biopsy findings?
 - a. What information should be included on the pathology report?
 - b. Is there standardized terminology that should be used on the pathology report?
 - c. What is the recommended timeframe for the pathology report to be provided after biopsy?

Human Resources and Training

1. What training and experience should physicians performing prostate biopsy have?

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- a. What specific elements should be included in the training for physicians performing prostate biopsy?
 - b. How many biopsies should a surgeon/unit complete annually to ensure quality?
 - c. Continuing Education, CME requirements

Facility Requirements

1. What are the minimum resource requirements necessary for a centre performing prostate biopsies?

Appendix C – Working Group and Expert Panel Membership

Name	Discipline	Organization	LHIN
Working Group Members			
Rajiv Singal (Chair)	Surgery	Toronto East General Hospital	Toronto Central (North)
Chris Morash	Surgery	The Ottawa Hospital	Champlain
Joseph Chin	Surgery	London Health Sciences Centre	South West
Roland Sing	Surgery	Halton Healthcare	Mississauga Halton
John Srigley	Pathology	Trillium Health Partners	Central West & Mississauga Halton
Andy Evans	Pathology	University Health Network	Toronto Central (South)
Ants Toi	Radiology	Princess Margaret Hospital	Toronto Central (South)
Robin McLeod	Surgical Oncology Program	Cancer Care Ontario	
Amber Hunter	Surgical Oncology Program	Cancer Care Ontario	
Leigh McKnight	Surgical Oncology Program	Cancer Care Ontario	
Expert Panel Members			
Bishwajit Bora	Surgery	Health Sciences North	North East
Ilias Cagiannos	Surgery	The Ottawa Hospital	Champlain
Arthur Grabowski	Surgery	Rouge Valley Health System	Central East
Rob Siemens	Surgery	Kingston General Hospital	South East
Tariq Aziz	Pathology	Hamilton Health Sciences Centre	Hamilton Niagara
Eric Belanger	Pathology	The Ottawa Hospital	Champlain
Chris Davidson	Pathology	Kingston General Hospital	South East
Madeleine Moussa	Pathology	London Health Sciences Centre	South West
Ken Newell	Pathology	Grey Bruce Health Services	South West
Masoom Haider	Radiology	Sunnybrook Health Sciences Centre	Toronto Central (South)
Nick Schieda	Radiology	The Ottawa Hospital	Champlain
Glenn Bauman	Radiation Oncology	London Health Sciences Centre	South West
Julie Bowen	Radiation Oncology	Health Sciences North	North East
Louis Fenkell	Radiation Oncology	Southlake Regional Health Centre	Central
Himu Lukka	Radiation Oncology	Juravinski Cancer Centre	Hamilton Niagara