How to Biopsy
Transperineal Versus Transrectal, Saturation Versus Targeted, What's the Evidence?

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KEYWORDS

• Transperineal prostate biopsy • Transrectal prostate biopsy • Targeted prostate biopsy • Saturation prostate biopsy • Template prostate biopsy • MRI • Prostate cancer

KEY POINTS

- Transrectal biopsy has an increasing rate of infection because of increasing multiresistant rectal flora. Targeted prophylaxis with prior rectal swab and/or other methods must be used because standard quinolone prophylaxis is no longer adequate.
- Transperineal biopsy has a near-zero risk of sepsis. A single dose of first-generation cephalosporin only is recommended as prophylaxis, obviating concerns over increasing antibiotic resistance.
- MRI-targeted biopsy increases detection of significant prostate cancer over standard 12-core biopsy.
- It remains unknown if one method of MRI-targeted biopsy is superior to another for detection of significant prostate cancer.
- Combined targeted and template biopsy provides maximal detection of significant prostate cancer, at the cost of increasing detection of indolent disease.

INTRODUCTION

Prostate biopsy remains the gold standard for the diagnosis of prostate cancer (PC).[1] In the workup to determine if a man has PC, the biopsy is the first test along the diagnostic pathway that is truly invasive. In the present era of patient-centered care, it is of utmost importance that this invasive test is performed with optimal comfort, safety, and diagnostic accuracy.

Depending on how it is performed, however, prostate biopsy can cause pain, can miss or undergrade clinically significant cancer, and pose a risk of serious complications. The currently accepted minimum standard for prostate biopsy is to take 10 to 12 random cores transrectally with ultrasound guidance.[2] Although periprostatic infiltration of local anesthesia is the minimum standard in transrectal (TR) biopsy analgesia, it often fails to provide adequate cover, causing unnecessary pain, anxiety, and embarrassment to patients,[3] which has stimulated recent and current studies to improve the patient's biopsy experience.[4,5] This untargeted sampling method has also been shown to miss significant prostate cancer (SPC) up to nearly 30% of the time.[6] As a result, men are often subjected to multiple sets of biopsies until the

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clinician is either satisfied there is no cancer, or that SPC is eventually found. Each of these invasive procedures puts patients at risk of complications, the most morbid of which is sepsis.[7] It is these shortcomings of traditional biopsy methods that have been cited as part of the reason for both the US and Canadian Preventive Services Taskforces'[8,9] recommendations against prostate-specific antigen (PSA) screening, because of harms outweighing benefits.

Multiparametric MRI, with its now standardized acquisition and reporting system (PIRADS),[10] has garnered much interest as a way of relatively reliably *seeing* SPC for the first time, and therefore, significantly increasing diagnostic accuracy.[11] When positive, MRI allows for targeted biopsies, which can be performed in a variety of ways (see later discussion) instead of, or in addition to, random biopsies. The burgeoning evidence of MRI's utility, as discussed elsewhere in this issue, has caused it to gradually work its way into official guidelines in specific clinical contexts.[1,2,12]

However, assessing MRI's accuracy is hampered by the constantly shifting definition of SPC, which is becoming increasingly restricted over time.[11] The confusion is evidenced by at least one study that has examined MRI accuracy using 4 different definitions of SPC,[13] and the recent PROMIS study even used Gleason score $\geq 4 + 3 = 7$ and cancer core length ≥ 6 mm.[14] This changeable definition is due to the combination of a growing recognition that Gleason pattern 3 is practically never metastatic,[15] and to current targeted biopsy methods now allowing regular detection of the longest cores of highest-grade tumor present in the gland.[14,16,17] This should be taken into account in the comparisons of diagnostic accuracy of the current array of biopsy methods discussed later.

Transperineal (TP) biopsy is also finally receiving increasing attention as a method of avoiding the risk of sepsis associated with TR biopsy.[18] This risk has been well documented as increasing in recent years because of the increase in multidrug resistance in rectal flora.[7] To date, TP biopsy has typically been performed under general anesthesia and is therefore a painless procedure; however, this has major implications for health resource use. Alternative methods for reducing the sepsis risk in TR biopsy have therefore also been advanced and are discussed later. A comparison of TP biopsy to the TR route in relation to diagnostic accuracy is also discussed later.

Multiparametric MRI and TP biopsy have added a vast array of options for prostate biopsy. The spectrum spans from the traditional hand-held random TR biopsy to now robotic MRI-targeted TP biopsy via just 2 skin punctures.[19] MRI and TP biopsy have the potential to minimize inaccuracy and risk to patients in the diagnostic workup of PC. These are critical advances in clinical practice that help to reverse the risk:benefit ratio, because harms must be outweighed when testing for PC.

PATIENT SAFETY AND COMFORT

Prostate biopsy, when performed optimally, provides clinicians with arguably the most important information for making management decisions in PC: tissue. However, it is an invasive procedure. It can cause pain, anxiety, and embarrassment,[3] as well as hematuria, hematochezia, hematospermia, erectile dysfunction, lower urinary tract symptoms (LUTS), and urinary retention.[7] Apart from hematochezia, both TR and TP biopsy can cause all of the above side effects to varying degrees. However, there is another complication risk where the choice of biopsy approach may have by far the most profound impact: infection. Infection can manifest from a simple urinary tract infection, epididymoorchitis, or bacterial prostatitis, through to life-threatening sepsis.

Potential side effects of prostate biopsy include the following:

- Pain
- Anxiety
- Embarrassment
- Hematuria
- Hematochezia
- Hematospermia
- Erectile dysfunction
- LUTS
- Urinary retention
- Infection/sepsis

TR biopsy has always been subject to the risk of sepsis. By passing the biopsy needle from the fecally contaminated rectum to the sterile prostate, the procedure contravenes the basic surgical principle of sterile technique. However, it is quick and convenient because it is usually performed under local anesthesia. In the past, sepsis risk has been kept low by covering the contamination by prophylactic broad-spectrum antibiotics. The drug family of choice remains quinolones.[3]

However, it is now clear that TR biopsy sepsis rates are increasing, in line with the increase in multi-drug-resistant and particularly quinolone-resistant rectal flora.[18] In a Canadian population-based study of more than 75,000 patients, Nam and colleagues[20] reported an increase from 0.6% to 3.6% of postprostate biopsy hospital admissions for infection over 10 years to 2005. In another