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Optimization of Prostate Biopsy: Review of Technique and Complications

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1. OPTIMIZING PROSTATE BIOPSY IN CLINICAL PRACTICE – CORE NUMBER AND LOCATION

a. Cancer Detection Rate

Optimizing prostate cancer detection rates in clinical practice translates into defining the ideal number and location of biopsy cores to maximize clinically significant cancer detection, minimize insignificant cancer detection, and reduce the necessity for repetitive re-biopsy. The recently published AUA recommendations on the optimal technique of prostate biopsy and specimen handling[1] along with an accompanying review article[2] recommended the use of an extended 12 core biopsy strategy, incorporating far lateral and apical samples, for initial prostate biopsy. Historically, comparison of cancer detection rate (CDR) between sextant biopsy protocols and extended-core biopsy protocols (involving 10–12 cores) have demonstrated a trend of increasing CDR with greater core number (Table 1).[3] Although increasing the cores from 6 to 12 results in a significant increased in CDR, increasing the number of cores to 18 or 21 (saturation biopsy) as an initial biopsy strategy does not appear to result in a similar increase.[4] De La Taille et al. (n=303) found that the CDRs using sextant, extended 12-core, 18-core, and 21-core biopsy schemes were 22.7%, 28.3%, 30.7%, and 31.3%, respectively.[5] Diagnostic yield improved by 24.7% when the number of cores increased from 6 to 12, but only by 10.6% when the number of cores increased from 12 to 21. In their review of the diagnostic value of systematic prostate biopsies, Eichler et al noted taking more than 12 cores did not significantly improve cancer yield.[6]

With regard to core location, the AUA white paper highlights the need to sample both apical and far-lateral regions as these appear to increase CDR, but notes that transition-zone sampling does not improve prostate CDR at initial extended biopsy. In a study by Babaian et

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al. evaluating an 11-core biopsy strategy in 362 patients, the CDR was 34% among 85 men undergoing primary biopsy.[3] Among 9 cancers identified uniquely at non-sextant sites, 7 were identified by anterior-horn (far lateral) biopsies and 2 by transition-zone biopsies. Because the entire apex is composed of peripheral zone, biopsies performed at the apex or lateral apex might not sample the anterior apex. Biopsy cores directed at the anterior apex exclusively contribute to cancer detection in 4–6% of men.[7] Moreover, additional extreme anterior apical cores (one on each side) have achieved the highest rate of unique cancer detection (p=0.011).[8] Transition-zone biopsies, as part of an initial diagnostic strategy, have generally demonstrated a low rate of exclusive cancer detection (2.9%) [9], although in some series CDR did improve with transition zone sampling (p=0.023).[4]

b. Likelihood of clinically significant/insignificant prostate cancer

Among the growing concerns of prostate cancer over-detection, a potential drawback of increasing core numbers at the time of initial biopsy is the increased likelihood of detecting insignificant prostate cancers. Few reports have shown a higher detection rate of clinically insignificant prostate cancer with extended biopsy schemes as compared to sextant,[10] while the majority of studies found no significant differences in the detection rate of insignificant cancers between sextant and extended biopsy schemes.[11] In a large database study (n=4,072), Meng and colleagues found that increasing the number of biopsy cores did not result in the identification of a disproportionate number of lower-risk tumors.[11] However, increasing the number of cores beyond the extended biopsy strategy does appear to increase the rate of indolent cancer detection. Haas et al. showed that an extended-biopsy 18-core strategy increased the detection rate of insignificant prostate cancers by 22%.[12] Far lateral and apical directed biopsy cores do not appear to increase the detection of insignificant cancers while the cancer detection rate of the transition zone sample is already low.[2]

c. Negative predictive value/avoidance of repeat biopsy

Sextant biopsies have false-negative rates of 15–34% based on CDR at the time of repeat biopsy and computer simulation.[13,14] Levine and colleagues first evaluated the use of a 12-core biopsy, using 2 consecutive sets of sextant biopsy in a single sitting. They demonstrated an increase in cancer detection to 31% overall, with only 21% being detected on the first sextant alone.[14] Other researchers have demonstrated that prostate CDRs on repeat biopsy vary as a function of the extent of the initial biopsy.[15] If a prior negative biopsy utilized a sextant scheme, the CDR was 39% with a repeat extended biopsy, whereas if a prior negative biopsy utilized an extended scheme, the CDR of the repeat biopsy decreased to 21–28%. Use of repeat saturation (20 to 24 cores) biopsy after initial saturation biopsy has been shown to have a CDR of 24%, similar to the CDR of 29% for biopsies following an initial sextant biopsy (p=0.08).[15] The authors from this study concluded that the false-negative rate for repeat prostate biopsies after an initial saturation biopsy is equivalent to that following traditional biopsy and they recommended against saturation prostate biopsy for primary biopsy.

Although it has been demonstrated that T1c cancers are present more frequently in the transition zone than T2 cancers, the yield of routine transition zone biopsy remains low.[9,16,17] Because relatively few cancers are found uniquely in the transition zone, it is

unlikely that repeat biopsies would be avoided by routine transition-zone sampling. No difference has been seen in the number of men requiring a repeat biopsy when evaluating the role of transition-zone sampling on initial and repeat biopsy.[17] Sampling the anterior apical peripheral zone on repeat biopsy identified 36.0% with cancer exclusively in the anterior apical peripheral zone cores. The CDR from the anterior apical peripheral zone sites was significantly higher in the repeat biopsies than in the initial biopsies ($p<0.01$), suggesting a predominance of missed cancers in this location.[18] Apical cores and extreme anterior apical cores have been shown to increase unique cancer detection and minimize the potential for misdiagnosis and need for repeat biopsy.[8] Few studies have evaluated the NPV of far-lateral sampling of the prostate. However, lateral sampling appears to improve clinical NPV because several cancers are identified only in the lateral sample.

d. Pathology concordance between biopsy and radical prostatectomy

Several studies have demonstrated that extended biopsy schemes improve biopsy concordance with prostatectomy specimens. Concordance rates of prostate cancer grade, when an extended biopsy scheme is used, are as high as 85%, compared to 50% with a sextant biopsy.[19–21] Upgrading of the Gleason score has been shown to be significantly less likely with the extended scheme (17% vs. 41% for the sextant scheme, $p<0.001$).[20] Similarly, 14% of the prostate cancers detected using extended biopsy schemes have been shown to be under-graded compared to 25% of cancers detected using sextant schemes ($p=0.01$).[21] The results of biopsy schemes involving saturation biopsies (more than 12 cores) appear to have a higher concordance rate with results from prostatectomy (59%) than a scheme involving fewer than 12 cores (47%, $p=0.05$).[22]

Apical and laterally directed sampling improves the ability to predict pathological features on prostatectomy, while the concordance of transition-zone biopsies with radical prostatectomy pathology is poor. In a study evaluating individually labeled, preoperative apical core biopsies and corresponding prostatectomy specimens, Rogatsch et al. determined the positive predictive value for identifying the tumor location correctly was 71.1%, while the lack of cancer in the apical biopsy had an negative predictive value of 75.5%.[23] Cancer concordance of transition-zone biopsies and prostatectomy specimens range from approximately 20–40%.[24] The role of lateral sampling of the prostate was evaluated by Singh et al. who showed that laterally directed cores were independent predictors of pathological features at prostatectomy.[25]

2. INFLUENCE OF BIOPSY TECHNIQUE

a. Transrectal

i. End-fire vs Side-fire cancer detection rates—Currently, two different approaches are used for transrectal prostate sampling including an end-fire or side-fire configuration of the biopsy probe (Figure 1). Evidence from retrospective studies has initially suggested that an end-fire configuration results in a greater prostate cancer detection rate than a side-fire configuration. In a study of 2674 patients, Ching et al[26] evaluated 2,674 patients who underwent prostate biopsy and showed a prostate CDR for end-fire versus side-fire probes of 45.8% versus 38.5%, respectively. Similar results were shown by Paul et al[27] in a study of

2625 subjects (31.3% vs 21.5%). Ching et al also found that the use of an end-fire probe on repeat biopsy significantly increased prostate cancer detection (odds ratio [OR] 1.59, 95% confidence interval [CI]: 1.03–2.46).[28] It has been hypothesized that improved cancer detection with the end-fire approach may be due, in part, to a better ability to sample the apex, lateral regions, and the anterior gland due to its needle angle.

Although both of the aforementioned studies included large numbers of patients, they were retrospective, and the number of cores and biopsy schemes were not standardized. To address this concern, Rom and colleagues performed a prospective randomized multicenter study comparing prostate cancer detection rates of end-fire and side-fire transrectal ultrasound probe configurations. The prostate cancer detection rate did not differ between the end-fire and side-fire probe (34.3% vs 34.4%, p=0.972).[29] Recently, Raber et al confirmed these findings in a study comparing end-fire and side-fire configurations in 1705 patients undergoing first biopsy and re-biopsy.[30] No significant difference was found between the two probes in the first biopsy and re-biopsy sets (38% vs 36.5%, P= 0.55; 10.8% vs 9.3%, p=0.7). The side-fire transrectal probe has been associated with a better patient tolerance profile.[30,31]

ii. Computerized templates for prostate biopsy—Computerized templates offer a biopsy strategy with reliable sampling of the same locations in the prostate each time. Available platforms typically convert 2-dimensional ultrasound data to a 3D model or image of the prostate. This technique takes into account the variability in prostate volume and shape, and allows reproducible sampling through accurate needle placement, in a known and recorded location. Furthermore, in theory, such a biopsy should allow better negative accuracy through reproducible spatial sampling of all essential areas of the gland. If an initial biopsy is negative for cancer, subsequent biopsies can be arrayed in such a way as to sample different regions of the prostate, which could potentially reduce sampling error. While such schemes do not increase cancer detection, they allow more reproducible sampling, which increases positive predictive value with regard to cancer location. This has potential value in monitoring or treatment planning.

Currently computerized biopsy systems have been studied for purposes of systematic biopsy: TargetScan® and Artemis. 3D transrectal prostate mapping with TargetScan® performed with an endorectal ultrasound probe has been studied in 2 series. In a retrospective multicenter review, a comparative analysis of 140 TargetScan® biopsies and 23 associated prostatectomy specimens demonstrated pathologic concordance in 52%.[32] In a single institution study, a simulation on 20 radical prostatectomy specimens showed that TargetScan® biopsy correctly identified cancer in 16 (80%) of the glands. This technique was reproducible between different operators as demonstrated by an 85% biopsy core concordance.[33]

Artemis® is a 3D imaging and navigation system that converts 2D monochromatic ultrasound images to an enhanced 3D color image allowing manipulation, planning, and management of the prostate biopsy process (Figure 2). While capable of performing a computer-directed template biopsy, as in the case of TargetScan®, Artemis® is distinct in that spatial-tracking of the arm provides exact recording of the location of the biopsy core.

This allows the user to return to the previous biopsy site at a later setting if considering surveillance or re-biopsy. Natarajan, et al, completed Artemis® biopsy in 180/218 men. In the tracking study, they were able to return to the same needle position with a recorded error of 1.2 mm +/− 1.1 mm.[34]

b. MRI-guided prostate biopsy

While conventional biopsy has relied upon improving sampling through increasing numbers of cores, an alternative approach is to reduce sampling error through localization. Recent improvements in multiparametric magnetic resonance imaging (MRI) have allowed accurate localization of prostate cancer.[35,36] A number of investigators have evaluated the impact of pre-biopsy MRI followed by targeted biopsy on cancer detection. The use of MR-targeted biopsy has been studied in the setting of previous negative biopsy,[37] men with no history of previous biopsy,[38] and, most recently, those on active surveillance.[39,40]

Among men undergoing repeat biopsy, 54% of men were found to have cancer only identified on the MR-targeted cores. Cancers in this setting are most often found in the anterior prostate or apex.[7] Among men presenting with no previous history of cancer, pre-biopsy MRI appears to have the potential to stratify the risk of prostate cancer through the application of a suspicion score.[41,42] In a study of 555 men, Haffner, et al demonstrated that MR-targeted biopsy identified fewer cancers overall when compared to systematic biopsy (236/302 vs 290/ 302, respectively), but detected a comparable number of clinically significant cancers (236/249 vs 237/249).[43] All cancers detected by MR-targeted approach were deemed significant. In addition, more cancer was identified per core, suggesting the potential for more accurate risk stratification. A number of subsequent studies have shown similar results[44] suggesting a potential to utilize MRI not only to improve cancer detection, but also to reduce over-detection of indolent disease. The ability to improve risk stratification through better sampling of cancer has also been suggested by several studies evaluating the impact of MR-targeted biopsy in active surveillance patients.[45–47]

3. REPEAT PROSTATE BIOPSY

a. Indications

i. HGPIN, ASAP, rising PSA—There is no consensus regarding the need for repeat biopsy in men with previous negative sampling. Potential indications include abnormal histology, rising PSA, or persistence of an elevated PSA. Historically, men diagnosed with isolated high grade intraepithelial neoplasia (HGPIN) were recommended to undergo immediate repeat biopsy given the high likelihood of concordant occult cancer, but, upon the implementation of extended core biopsy in clinical practice it was noted that the likelihood of cancer detection upon immediate repeat biopsy was small.[48] The recent EAU, AUA and NCCN guidelines reported that the presence of HGPIN diagnosis no longer represents an indication for immediate repeat biopsy.[49] Epstein and Herawi have asserted that the prostate cancer risk at repeat prostate biopsy after HGPIN diagnosis (22%) is similar to the risk of cancer detection after an initial benign biopsy.[50] Additionally, prospective trials have failed to demonstrate an association between the presence of HGPIN at initial prostate biopsy and subsequent prostate cancer at repeat prostate biopsy.[51,52] However, studies by Benecchi et

al.[53], and Netto and Epstein[54] have identified the presence of HGPIN as a risk factor in their analyses and included HGPIN in their repeat prostate biopsy nomograms.

The number of HGPIN foci appears to be an important prognosticator and influences the suggested management protocols. For example, Godoy et al[55] and Merrimen et al[56] have found that isolated HGPIN does not warrant any further prostate biopsy. Similarly, data from the Cleveland Clinic has shown that upon comparison of men with multifocal and isolated HGPIN on initial saturation biopsy, an 80% and 0% likelihood of prostate cancer on repeat prostate biopsy was observed, respectively.[57] These findings, taken together, demonstrate that a single focus may have limited clinical significance, with minimally increase risk of prostate cancer development. Multifocal HGPIN, however, more than doubles the risk of de novo prostate cancer development. The NCCN guidelines recommend that for patients with multifocal HGPIN (≥2 cores) on an extended pattern biopsy, repeat biopsy be performed within the first year.

Another critical predictor of cancer risk in men with isolated HGPIN is the interval to biopsy. Studies of serial delayed interval biopsy suggest that repeat biopsy can be performed at longer intervals than 1 year.[48,55] Our group has advocated that serial prostate biopsy every 3 years based upon our early observation of prostate cancer in 26% of men biopsied 3 years after initial diagnosis, and our subsequent demonstration of a similar persistent risk on 6 year biopsy.[48] Among a large cohort of men with isolated HGPIN followed for 3 years as part of the placebo arm of a chemoprevention trial, cancer was demonstrated in 34.7% of men with serial biopsy performed each year.[58]

The natural history of atypical small acinar proliferation (ASAP) is less well defined than that of HGPIN, but, if ASAP is present in the initial biopsy specimen, the risk of diagnosing prostate cancer on subsequent biopsy is significantly increased. Unlike HGPIN, ASAP represents uncertainty regarding the diagnosis of cancer. Studies of repeat biopsy have shown a detection rate for prostatic adenocarcinoma as high as 55% after an initial diagnosis of ASAP[59] and up to 58% when found in combination with HGPIN on initial biopsy.[60] Regardless of PSA values, current recommendations are to rebiopsy all patients with ASAP in their initial biopsy specimen within 3 to 6 months. The typical technique of biopsy is focal saturation to the region of observed atypia.

A rising prostate-specific antigen after a negative prostate biopsy may indicate undiagnosed cancer, while a persistently elevated PSA may draw concern of a missed occult cancer. In the presence of a rising PSA after a negative biopsy a low threshold for repeat biopsy should be entertained. An important consideration is adequacy of the initial prostate biopsy, taking into account the number of cores taken and anatomical sites sampled, areas of under sampling, length of each core, and quality of the tissues sampled. Most studies of repeat prostate biopsy following extended initial prostate indicate that up to 30% of patients have cancers that were not previously identified.[61,62] A repeat biopsy strategy may include focal saturation, extended 21-core, saturation biopsy, or image guidance to improve the detection rate.

b. Technique

i. Focal saturation, 12 core, saturation—When performing repeat biopsies, it is important to recognize that the region of the prostate potentially undersampled in a 12-core biopsy scheme is the anterior apex.[7] The entire apex of the prostate is comprised of peripheral zone and, although extended schemes do sample the apex and lateral apex, additional cores should be taken from the anterior apex on repeat biopsy. Similarly, repeat biopsy should include the transition zone as supported by the European Association of Urology guidelines.[63]

The precise labeling of the initial prostate locations is important to direct rebiopsy in a more concentrated fashion into the region of the initial ASAP.[50,64] Allen et al[64] have demonstrated earlier that the chance of detecting prostate cancer greatly increases by performing a rebiopsy not only of the atypical site but also of adjacent contralateral and adjacent ipsilateral areas. However, Scattoni et al has previously reported that a precise spatial concordance between ASAP and prostate cancer was present in only 33% of the cases, similar to the likelihood of finding prostate cancer in an adjacent or a nonadjacent site.[65]

Contemporary recommendations for the technique of repeat prostate biopsy suggests that a repeated 10- to 12-core extended biopsy scheme remains the most frequently used technique, with additional cores from suspected areas by modern imaging or the anterior and transition zone. As compared to standard extended techniques (10–14 cores), repeat saturation biopsies (20–24 cores) increase the CDR (24.9 % vs. 32.7 %, p = 0.0075).[62]

a. Transperineal saturation biopsy

According to AUA and NCCN guidelines, a saturation prostate biopsy may be considered in men with a prior negative biopsy and persistent suspicion of prostate cancer. The transperineal biopsy technique allows for improved sampling of the apex and anterior zones which are common sites of cancer detection on repeat biopsy. In a series of 92 consecutive men with at least two negative prior transrectal biopsies, most of the tumors detected on transperineal saturation biopsy were found in the anterior zone (83.3%).[66] Transrectal and transperineal prostate saturation repeat biopsies have a similar cancer detection rate.[67]

i. MRI-guided repeat prostate biopsy—MRI-guided repeat biopsy has the potential to reduce the sampling error of the initial biopsy through localization of disease (Figure 3). In a recent meta-regression comparing cancer detection on repeat prostate biopsy, Nelson et al compared transperineal, ultrasound guided transrectal saturation, and MRI-guided biopsy where cancer detection rates were 30.0%, 36.8%, and 37.6%, respectively.[68] Meta-regression analysis showed that MRI-guided biopsy had significantly higher cancer detection than transperineal biopsy. There were no significant differences however between median Gleason scores among the three biopsy strategies. The authors concluded that in the re-biopsy setting, it is unclear which strategy offers the highest CDR. However, MRI-guided biopsies may potentially detect more prostate cancers than other modalities and can achieve this with fewer biopsy cores.

4. PAIN CONTROL

a. Technique of anesthesia

Improvements in anesthesia techniques have allowed urologists to sample a greater number of cores and from different locations in the gland including the ability to perform a saturation biopsy procedure in an office setting.[62] Both rectal and prostatic anesthesia may limit pain during the procedure. Intrarectal local anesthesia has been used both as lubrication in order to reduce friction and protect the mucosa during instrumentation as well as ease the discomfort with introduction of the ultrasound probe. A variety of anesthetic agents have been employed including lidocaine, prilocaine, nifidipine, and dimethyl sulphoxide in various combinations with varied results. A periprostatic nerve block is commonly used in TRUS-guided biopsy where the optimal injection site seems to be localized in the angle between the prostate and the seminal vesicles, which can be easily identified as a hypoechoic area on TRUS. A concentration of 1% lidocaine, 5 ml per side, is sufficient to provide pain relief. Periprostatic nerve block is associated with significantly less pain during biopsy than lidocaine gel or placebo[69] and is superior to intrarectal instillation of anesthetic cream[70] Extensive biopsy protocols may be comfortably performed in office setting using local anesthesia with 22 ml 1% lidocaine injection[71] Despite lack of a standardized dose or optimal technique, periprostatic anesthetic infiltration should be considered the gold standard.[72] Intraprostatic anesthesia has been provided in combination with periprostatic nerve block resulting in improved pain control,[73] but further studies are needed to delineate location, technique and dosages. Historically, the transperineal approach to prostate biopsy has been performed under general anesthesia, but recent studies have demonstrated the combination of pudendal and periprostatic nerve block is well tolerated and improves pain reduction without the need for general anesthesia.[74]

5. COMPLICATIONS

a. Incidence of prostate biopsy complications

According to the AUA clinical guidelines on the incidence, prevention, and complications related to prostate needle biopsy, the most common urological side effects of a prostate needle biopsy include hematuria, rectal bleeding, hematospermia, urinary tract infection, acute urinary retention.[75,76] Erectile dysfunction and vasovagal response have also been noted to occur in patients undergoing prostate biopsy (Table 2).

b. Bleeding complications

Episodes of significant bleeding after prostate biopsy may occur in 1–4% of patients.[77] Recent data suggest that hematuria is noted in 23–84%, rectal bleeding in 17–45%, and hematospermia in 12–93% of men post prostate needle biopsy. However relatively fewer men who underwent a biopsy perceived hematuria (6%), rectal bleeding (3%), and hematospermia as a major/moderate problem (27%).[5,78–80]

i. Prevention of prostate biopsy complications—Current considerations for the prevention of bleeding complications after prostate biopsy include holding anticoagulation, including warfarin, aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), herbal

supplements, and clopidogrel, for 7–10 days prior to the biopsy when it is possible to do so. For those patients with underlying coagulopathy or who are on warfarin, prostatic biopsy should not be performed until the international normalized ratio has been corrected below 1.5. Several studies have evaluated the safety of maintaining anticoagulation during biopsy. From the data it appears that stopping aspirin may be unnecessary, as it does not increase the incidence or severity of bleeding complications.[81–83] Aspirin may, however, prolong the duration of self-limiting hematuria and rectal bleeding.[81,83] Similar trends demonstrating no increased risk of bleeding have been noted in evaluating the safety of continuing warfarin during biopsy.[84,85] Taken together, it appears as though aspirin may be continued during the procedure if there is any concern about the safety of withholding it. Data on stopping warfarin and clopidogrel are limited and the risks between cardiovascular or thromboembolic events when stopping anticoagulation must be weighed against the risk for bleeding and associated complications with continuation.[76]

ii. Influence of technique—In a meta-analysis and review of prostate biopsy results, Shen et al determined there was no significant differences in the incidence of major or minor complications between the tranperineal and transrectal technique.[86] In prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy, Hara et al found no differences in rectal bleeding, hematuria, or hematopsermia between the two techniques.[87] A major consideration is the potential to reduce infection by utilizing a transrectal approach, particularly in view of the increasing rate of infection following biopsy noted in recent years.[88]

iii. Management—Severe rectal bleeding may be managed initially with bed rest, volume resuscitation, and transfusion. If the patient's condition does not improve while under observation, options for management include digital compression, rectal tamponade with a tampon,[89] inflated condom, or inflated foley catheter balloon.[90] Colonoscopy with injection of epinephrine and polidocanol or use of sclerotherapeutic agents, angiography with embolization,[91] transrectal exploration, and suturing are alternative means of stopping rectal bleeding.[92,93] Hematuria may be managed similarly with bed rest, volume resuscitation and transfusion. Cystoscopy or anoscopy with coagulation of bleeding points may be used in more severe cases.

c. Infectious complications

Most infectious complications after prostate biopsy are limited to symptomatic urinary tract infection and low-grade febrile illness, which can be readily treated with oral or intravenous antibiotics; however, post-biopsy sepsis has emerged as a risk of this procedure. The incidence of infectious complications following prostate biopsy in large multi-institutional studies ranges from 0.1%–7%, depending upon the antimicrobial prophylactic regimen used,[88,94,95] with approximately 30%–50% of these patients having accompanying bacteremia.[96,97] The risk of hospitalization for infectious complications in contemporary studies ranges from 0.6–4.1%.[95] The reported incidence of UTI after prostate biopsy typically ranges between 2% and 6%.[98] Bacteremia is frequently accompanied by severe sepsis, which has an overall incidence of 0.1%–2.2% following prostate biopsy.[96] One recent study reported that among post–TRUS biopsy patients hospitalized with *E. coli*

bacteremia, 25% had severe sepsis requiring intensive care unit admission.[99] In terms of repeat prostate biopsy, Loeb et al demonstrated a repeat biopsy session was not associated with a greater risk of infectious (OR 0.81, p = 0.39) or serious noninfectious urological complications (OR 0.94, p = 0.82) compared to the initial biopsy.[100]

i. Prevention—According to the AUA Best Practice Statement, TRUS-guided prostate biopsy, performed through a grossly contaminated field, requires important preventative considerations. There is wide variation in the approach to the preparation of the rectum. Some studies found no benefit to either preprocedural povidine-iodine[96] or sodium biphosphate enemas.[101] However, another study found that a bisacodyl suppository rectal preparation the night before or morning of the procedure decreased infectious complications.[102]

The AUA Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis recommends a Fluoroquinolone or 1st/2nd/3rd generation cephalosporin prior to biopsy.[103] Currently, no conclusive data have been found to support either the use of long-course (3 days) over short (1 day) fluoroquinolone regimens, or multiple vs single dose schedules.[104] Although antibiotic prophylaxis is largely effective in preventing infection, leading to a low incidence of sepsis, recently there have been increasing quinolone-resistant infection resulting from more frequent use of quinolones in the population overall, including at the time of transrectal prostate biopsy.[105] Prebiopsy screening with rectal swabs may allow identification of those men harboring antibiotic resistant organisms in their endogenous gastrointestinal flora prebiopsy, and for whom fluoroquinolone prophylaxis may not be appropriate.[94] This strategy has revealed a prevalence of about 22% of men harboring fluoroquinolone resistant bacteria.[94,106] Taylor and colleagues targeted specific antimicrobial prophylaxis based on rectal swab results.[107] These authors were able to show a non-significant reduction in post-prostate biopsy infections from 2.6% to 0% (p=0.12) and a potential cost savings per infectious complication averted. However, these methods have not been broadly used and the determination of true benefit requires further prospective investigation.

The need for routine urine culture prior to prostate biopsy is unclear; urine culture appears only to be useful in the decision to refrain from prostate biopsy when bacterial growth is evident.[108] The use of urinalysis or urine dipstick prior to prostate biopsy is widespread; however, there are no published studies to document its benefit.

ii. Technique—In a prospective randomized study comparing transperineal and transrectal systematic 12-core prostate biopsy, Hara et al found no differences in the rates sepsis or post-biopsy fevers.[87] Similarly, Miller et al found similar rates of sepsis when comparing the 2 biopsy techniques.[109] Shen et al determined there was no significant differences in the incidence of major or minor complications between the transperineal and transrectal technique in a large meta-analysis.[86]

iii. Management—At present, there are no published guidelines for the management of post–prostate biopsy infections. However, in addition to patient-specific prophylactic regimens, consideration should be given to empiric followed by culture driven antimicrobial

therapy if a patient presents with post-biopsy sepsis. Previous studies have demonstrated that inappropriate empiric therapy of *E. coli.* bloodstream infections is associated with an increased risk of mortality.[110] Broader spectrum empiric antimicrobial coverage should be considered for post–prostate biopsy sepsis compared to that given for other causes of community-onset urosepsis as prostate biopsy was actually a risk factor for bacteremia with multidrug-resistant *E. coli.*[99] Moreover, other individual risk factors that should be considered when choosing appropriate empiric therapy including prior exposure to fluoroquinolones. Initial therapy must cover *E. coli*, the most common pathogen, as well as numerous other organisms. Prior to treatment, a urine culture, and blood cultures if the patient is febrile, should be obtained.

a. Quality of life

ii. Erectile dysfunction—Recent data has suggested an associated between prostate biopsy, lower urinary tract symptoms, and erectile dysfunction. In their randomized trial of 145 men, Klein et al. authors found that prostate biopsy may cause urinary symptoms and erectile dysfunction, regardless of anesthesia or number of cores sampled as shown by a decreased in IIEF-5 and an increase in IPSS scores in their study.[111] Erectile dysfunction was noted in 2.2% of men in a study be Akyol and Adayener possibly due to nerve injury caused by the biopsy needle.[112] However, in a study by Helfand et al, cancer diagnosis appears to have an adverse effect on the erectile function of men undergoing prostate biopsy but no effect on lower urinary tract symptoms.[113] Similarly, serial prostate biopsies appear to have an adverse effect on erectile function in men with prostate cancer on active surveillance but do not affect lower urinary tract symptoms.[114] Several other studies, however, have suggested the effects of the prostate needle biopsy are transient with no significant differences in men with and without prostate cancer.[115,116]

i. Urinary retention—Urinary retention requiring temporary catheterization develops in up to 1% of men undergoing transrectal prostate biopsy.[80,117,118] Men with enlarged glands and higher International Prostate Symptom Scores are more prone to develop post biopsy retention.[118] Data suggest that starting higher-risk patients on an alpha blocker prior to prostate biopsy may prevent episodes of urinary retention.[119] Higher rates of acute urinary retention have been noted in men undergoing transperineal prostate biopsy.[120]

ii. Other—Excessive anxiety and discomfort from the endorectal probe may produce a moderate or severe vasovagal response in 1.4% to 5.3% of patients[121,122] and may require termination of the procedure. Placing the patient in the Trendelenburg position and use of intravenous hydration usually resolve these symptoms, with further intervention as clinically indicated

CONCLUSIONS

A 12-core systematic biopsy that incorporates apical and far-lateral cores in the template distribution allows maximal cancer detection, avoidance of a repeat biopsy, while minimizing the detection of insignificant prostate cancers. MRI guided prostate biopsy has an evolving role in both initial and repeat prostate biopsy strategies, potentially improving

sampling efficiency, increasing detection of clinically significant cancers, and reducing detection of insignificant cancers. Hematuria, hematospermia, and rectal bleeding are common complications of prostate needle biopsy, but are generally self-limiting and well tolerated. All men should receive antimicrobial prophylaxis prior to biopsy. Fluoroquinolones or cephalosporins remain the recommended prophylactic antibiotics, although the frequency of quinolone-resistant infections is increasing.

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KEY POINTS

- A 12-core systematic biopsy that incorporates apical and far-lateral cores in the template distribution allows maximal cancer detection, avoidance of a repeat biopsy, while minimizing the detection of insignificant prostate cancers.
- Endfire and sidefire ultrasound probes, along with transrectal and transperineal approaches to prostate biopsy, have similar cancer detection rates and complications.
- MRI guided prostate biopsy has an evolving role in both initial and repeat prostate biopsy strategies, potentially improving sampling efficiency, increasing detection of clinically significant cancers, and reducing detection of insignificant cancers.
- Hematuria, hematospermia, and rectal bleeding are common complications of prostate needle biopsy, but they are generally self-limiting and well tolerated.
- Fluoroquinolones or cephalosporins remain the recommended prophylactic antibiotics, although the frequency of quinolone-resistant infections is increasing

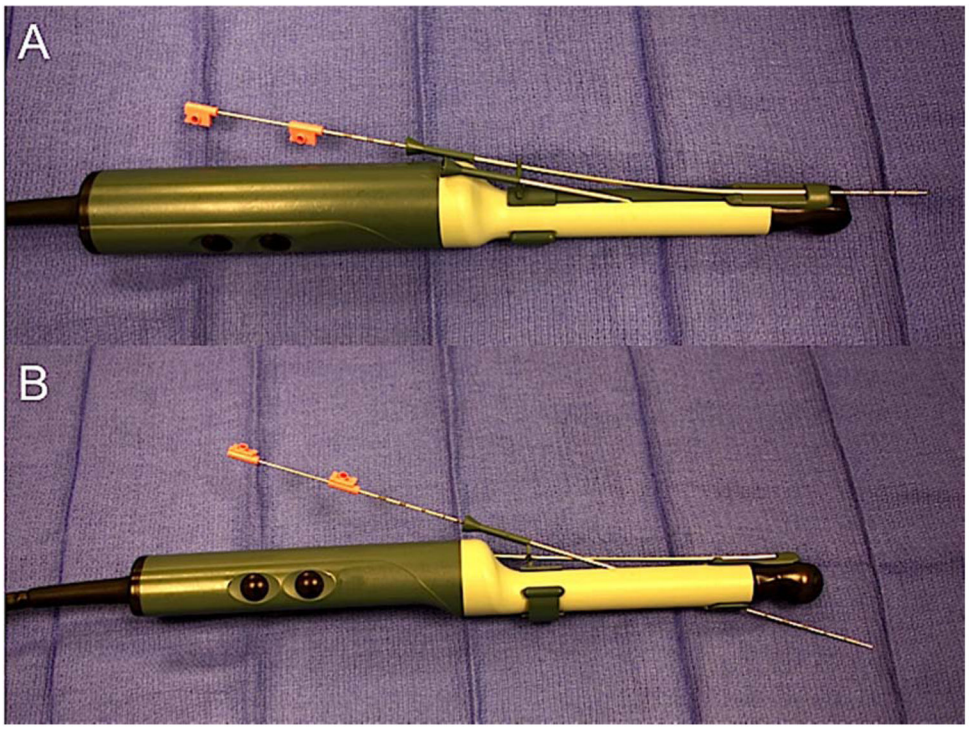

Fig. 1.
End-fire (A) and side-fire (B) configurations of the transrectal ultrasound biopsy probe.

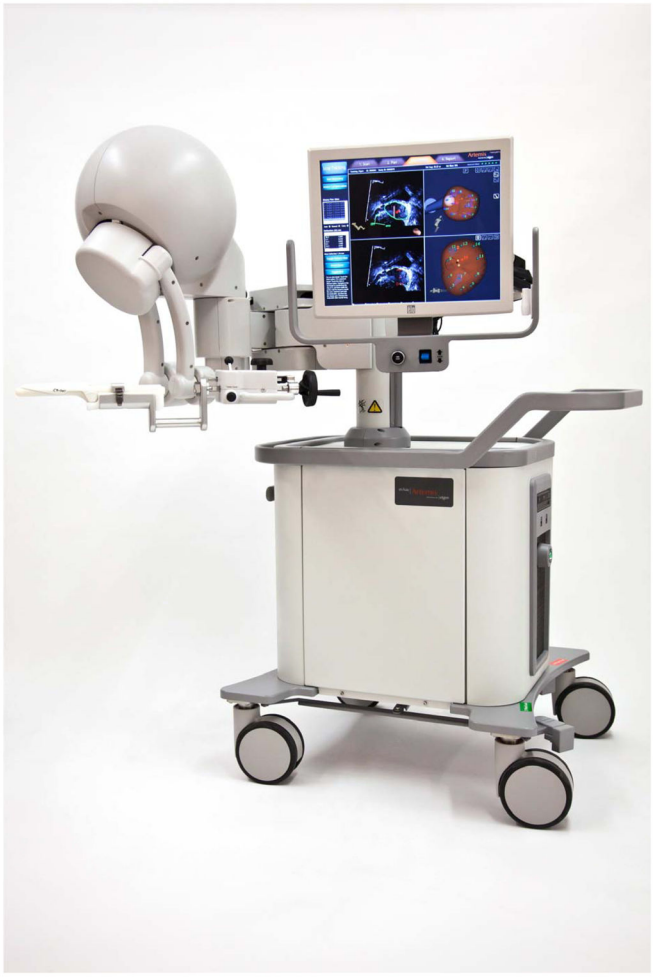

Fig. 2.

Artemis 3D imaging and navigation system. Courtesy of Eigen, Grass Valley, CA; with permission.

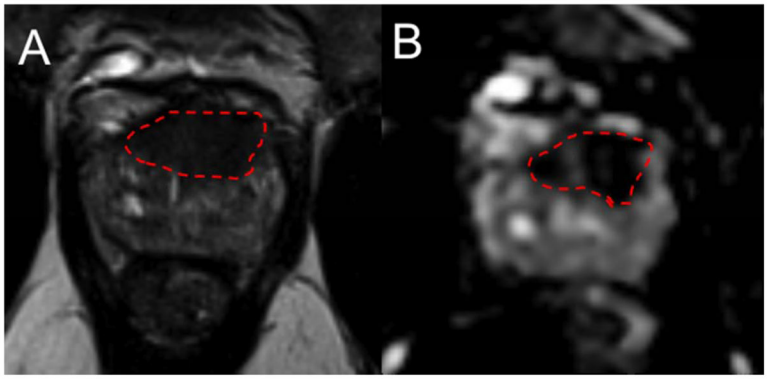

Fig. 3.

MRI-guided repeat prostate biopsy after a negative 12-core template biopsy. MRI demonstrated a left anterior mid-to-apex transition zone lesion that appeared to intimately involve anterior fibromuscular stroma (suspicion score 4/5) on T2 weighed imaging (A) and apparent diffusion coefficient map (B). Targeted biopsy revealed Gleason score 3+4=7 prostate cancer in 2 of 2 cores, 20–70% of each core.

Table 1

Cancer detection rates by number of prostate biopsy cores

	Cancer Detection Rate				
No. prostate biopsy cores	6	10–12	18	20–21	24
Study					
Eskew et al	26.1%	40.3%*			
Naughton et al	26%	27%			
Presti et al	33.5%	39.7%			
Babaian et al	20%	30%			
Elabbady et al	24.8%	36.4%			
Gore et al	31%	43%			
Philip et al	23%	32%			
Shim et al	22%	28%			
Scattoni et al		38.5%	39.9%		
De La Taille et al	22.7%	28.3%	30.7%	31.3%	
Pepe et al		39.8%	39.8%		49.0%**
Jones et al		52%			45%
Guichard et al		38.7%	41.5%	42.5%	
Ploussard et al	32.5%	40.4%		43.3%	

* 13 core extended biopsy strategy

** 29 core saturation biopsy strategy

Data from Refs 3–5,19,123–132.

Table 2

Incidence of prostate biopsy complications

Complication	Incidence
Hematuria	23–84%
Rectal bleeding	17–45%
Hematospermia	12–93%
Urinary tract infection	2–6%
Bacteremia	0.1–2.2%
Hospitalization	0.6–4.1%
Erectile dysfunction	2.2%
Urinary retention	1–7%
Vasovagal response	1.4–5.3%

Data from Refs 5,78–80,95,96,98,112,117,118,120–122.