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Strategies for Repeat Prostate Biopsies

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1. Introduction

Despite urologists increasingly employing more extended prostate biopsy schemes for initial biopsies, the rate of repeat biopsies continues to rise [1]. Advances in technology and improved understanding of prostate cancer have not eliminated the questions surrounding the issue of repeat biopsies. What are the most reliable indications for repeat biopsy? How many biopsy cores should be obtained for optimal diagnostic yield to reduce the incidence of false-negative biopsies? What areas of the prostate should be biopsied to give the best diagnostic results? What is the best time interval between repeat biopsies? To how many repeat biopsy sessions should a patient be subjected?

Indications for repeat biopsy

Indications for repeat biopsies include sustained or worsening elevation of total serum PSA or other PSA parameters. Repeat biopsy has more recently been incorporated as part of active surveillance protocols to monitor patients with low-risk disease for reclassification to aggressive disease. The histology from the initial biopsy may also encourage repeat biopsy if high grade prostatic intraepithelial neoplasia (HGPIN) or atypical small acinar proliferation (ASAP) are identified. Risk factors such as family history of prostate cancer and African American race have not been evaluated as potential indications for repeat biopsy but often impact urologists attitudes toward encouraging patients to undergo repeat biopsy. Patient anxiety about the possibility of prostate cancer is another common but difficult to quantitate indication for repeat biopsy.

Prostate specific antigen as an indication for repeat biopsy

An elevated or rising PSA level is the most common indication for repeat prostate biopsies. A PSA level over 4.0ng/ml is generally accepted as an indication for initial biopsy while some urologists will biopsy for a PSA over 2.5ng/ml or adjust the acceptable upper limit of normal PSA for the patient's age. For repeat prostate biopsies after an initial set has been free of cancer, a PSA greater than 10.0ng/ml is agreed upon as a clear indication for the need for repeat biopsies while repeat biopsies are not felt to be strongly indicated for a PSA less than 4.0ng/ml [2-4]. PSA levels between 4.0 and 10.0 ng/ml present a significant range in which the indications for repeat biopsy are less obvious. Other PSA parameters can facilitate the decision to perform repeat biopsies. These include the percent-free PSA, PSA velocity (PSAV), PSA density (PSAD), and PSA density of the transition zone (PSAD-TZ).

Percent free PSA

The majority of serum PSA is attached either alpha1-antichymotrypsin or alpha2-macroglobulin. The remainder of the serum PSA that is not bound to these molecules is referred to as the "free" PSA and is decreased in the serum relative to the proportion of bound PSA in patients with cancer. The percentage of the total PSA (the bound and free PSA combined) that consists of the free PSA portion is termed the "percent free PSA." The percent free PSA has good utility in predicting cancer presence, specifically in men with PSA levels of 4 to 10 ng/ml. Catalona et al. demonstrated percent free PSA cutoff of less than 25% corresponded with the highest cancer detection rate and the least number of unnecessary biopsies [5]. Djavan et al. recommend a percent free PSA of less than 30% as one of the most accurate predictors of a positive repeat biopsy result [2]. Morgan et al. demonstrated that a percent free PSA less than 10% was a strong predictor for prostate cancer on repeat biopsy even after two negative prior biopsies with sensitivity and specificity of 91 and 86%, respectively [6]. Lee et al. report percent free PSA less than 10% yielded 90% and 91% specificity in the one repeat biopsy and greater than one repeat biopsy groups, respectively (57).

PSA density (PSAD)

PSAD is calculated by dividing the PSA value by the prostatic volume. This calculation targets the problem of PSA elevation caused by benign prostatic hyperplasia and, when elevated, has been shown to correlate with the existence of cancer. Keetch et al. evaluated density to assist in determining the need for a repeat biopsy [7]. Using a value of 0.15 ng/ml/cm3, they reported missing 35% of the cancers. However, in conjunction with a PSAV>0.75 ng/ml/yr, they had a detection rate of 46% on repeat biopsy, vs only 13% when both values were below the suggested cutoff. Djavan et al. evaluated PSAD, but showed increased utility when it was related to transition zone volume only, known as the PSA density of the transition zone (PSAD-TZ) [2]. Using a value of 0.13 and 0.26 ng/ml/cc for PSAD and PSA-TZ, respectively, they report sensitivities of 74 and 78% and specificities of 44 and 52%, respectively. Calculating the PSAD-TZ has the potential for a high rate of error due to the need for high resolution ultrasound equipment and an experienced sonographer since the margins of the transition zone are not as clearly demarcated as those of the entire prostate [3].

PSA velocity (PSAV)

PSAV is determined by taking the difference between two PSA values and dividing by the time interval between the two levels in years. PSAV has found more utility as a tool to predict recurrence in patients already diagnosed with prostate cancer but has been employed as a predictor of biopsy outcome as well. In a comparison to other PSA parameters, Borboroglu et al found that a PSAV of greater than 0.75 ng/ml/yr was the only statistically significant risk factor for prostate cancer detection on biopsy [8]. However, the European Randomized Study of Screening for Prostate Cancer failed to show clinical utility for either PSA velocity or PSA doubling time [9]. Vickers et al. reported that prostate specific antigen velocity was statistically associated with cancer risk but had low predictive accuracy (AUC 0.55, $p<0.001$) (55). PSA doubling time (PSADT) is another measure of PSA change over time but has similarly demonstrated more utility in the prediction of prostate cancer aggressiveness than as an indication for repeat biopsy.

Many investigators have now come to the conclusion that no single PSA parameter is adequate to indicate the need for repeat biopsies. Keetch et al. determined that using only

PSAV greater than 0.75 ng/ml/yr would miss a large number of cancers and recommended combining the PSAV other parameters [7]. Djavan et al. recommend the combination of a percent free PSA of less than 30% and/or a PSAD-TZ greater than or equal to 0.26 ng/ml/cc as the most accurate predictor of a positive repeat biopsy result in patients with PSA levels between 4 and 10 ng/ml [2]. Busby and Evans recommend a combination of total PSA, percent free PSA, PSAD, and PSAV based on analysis of the published data on each of these parameters [3]. Their recommended PSA-based indications for repeat biopsy include any patient with a PSA in the 4-10 ng/ml range and a percent free PSA less than 25%. For patients with a PSA between 4-10ng/ml and percent free greater than 25%, repeat biopsies are recommended if they have a PSAD greater than 0.15ng/ml/cc and a PSAV greater than 0.75 ng/ml/yr, or a PSAV greater than 1 ng/ml/yr, or a PSAD-TZ greater than 0.26 ng/ml/yr. Both Djavan et al. and Busby and Evans recommend repeat biopsy in any patient with a PSA greater than 10 ng/ml, regardless of the other parameters. Busby and Evans qualify this recommendation by stating patients with PSA >10 ng/ml with inflammation noted histologically should have a trial of antibiotics and repeat PSA before considering repeat biopsy.

Repeat biopsy for active surveillance protocols

As PSA-based prostate cancer screening has expanded, some have noted the overdetection of cancer that would not have been detected in the absence of screening programs (51). The risks and benefits of invasive therapy for prostate cancer have been debated. Active surveillance (AS) has become established for low-risk patients to offset or delay the risks of invasive therapy. AS regimens monitor these low-risk patients via repeat prostate biopsies at fixed intervals to assess for those candidates with disease progression who should be offered radical treatment. The optimal parameters for timing of repeat prostate biopsy have not been definitively established (52). The European Randomised Study of Screening for Prostate Cancer (ERSPC) has instigated a prospective observational study, the Prostate Cancer Research International: Active Surveillance (PRIAS). This protocol includes a schedule for follow-up of low-risk prostate cancer patients that begins with a first repeat biopsy at 1 year after diagnosis. Bul et al. report that 21.5% of patients were reclassificatied to higher risk. This reclassification was significantly influenced by the number of initial positive cores, higher PSA density, and PSA doubling time (PSA-DT) < 3years (52).

Van den Bergh et al. reports that PSAV and PSA-DT carry sparse evidence for their role as prognisticators, especially in active surveillance (53). They report some consensus of the unfavorable prognosis of PSA-DT < 3years and the favorable prognosis of PSA-DT > 10 years or decreasing PSA level (53). The best method of calculation, number of measurements, and time interval of measurements remains unknown.

Repeat biopsy for high grade prostatic intraepithelial neoplasia

High Grade Prostatic Intraepithelial Neoplasia (HGPIN) is characterized by prostatic glands in which the epithelial cells exhibit the nuclear enlargement and prominent nucleoli characteristic of prostatic adenocarcinoma, yet with a preserved basal cell layer. While the presence of a basal cell layer excludes the diagnosis of invasive cancer, HGPIN is thought to be a precursor to invasive adenocarcinoma [10]. Evaluating pathology trends on 62,537 initial prostate needle core biopsies submitted by office-based urologists, processed at a single pathology laboratory, isolated high grade PIN was diagnosed in 4.1% of the biopsies

[11]. In a referral academic practice employing extended field biopsies for initial prostate tissue sampling, 22% of cases exhibited isolated HGPIN [12].
After sextant biopsies showing HGPIN, 80% of patients demonstrated cancer on repeat biopsy [13]. With extended biopsy schemes showing HGPIN, the rate of cancer detection on repeat biopsies was only 23% [14]. This decreased cancer detection rate after extended biopsy schemes is probably due to the better sampling and increased likelihood of identifying co-existing cancer and HGPIN on the initial extended biopsy procedure.
Low grade prostatic intraepithelial neoplasia does not carry the same risk of concomitant cancer. Zlotta et al. found that low grade PIN was associated with subsequent cancer on repeat biopsies in 10.7% of patients with a PSA was between 4 and 10ng/ml and in none of the cases when PSA was ≤4ng/ml [15]. Low grade PIN is not considered an indication for repeat biopsy unless other factors such as an elevated PSA increase the suspicion of prostate cancer. In fact, the notation of the presence of low grade PIN has been discouraged from being mentioned in pathology reports.
Most experts strongly recommend repeat biopsy for any patient with HGPIN on initial biopsy [3,16]. If HGPIN is again identified on repeat biopsy but no cancer diagnosed, follow-up PSA and examination in 6 months is recommended.

Repeat biopsy for atypical small acinar proliferation

Atypical Small Acinar Proliferation (ASAP) is a focus of small glands that have the cytologic appearance of malignancy; however, the presence or absence of the basal cell
layer is equivocal [17]. Rather than a pre-malignant lesion, this finding is felt to often represent invasive cancer that is simply difficult for the pathologist to clearly identify due to issues such the plane of sectioning. In patients with ASAP, cancer found on repeat biopsy is most likely to be in the same region of the prostate as was the ASAP. Repeat biopsy samples in patients with ASAP are found to have cancer in approximately 40–50% of cases [13]. Zhou et al. affirmed these findings with the report that of patients diagnosed with ASAP, 51.0% were diagnosed with prostate cancer on repeat biopsy (56). This rate has not changed in the era of extended biopsy schemes.
ASAP is considered an absolute indication for repeat biopsy [3,16]. Negative repeat biopsies require close follow-up.

Impact of prostate volume on repeat biopsies

Prostate volume is an important parameter when deciding whether or not to perform a repeat biopsy. Rietbergen et al. found that the most important factor responsible for failure to diagnose these cancers at the primary screening was a large prostate volume in the European Randomized Study for Screening for Prostate Cancer [18]. One explanation is the possibility that these patients' increased PSA levels are primarily due to the volume of prostatic hyperplasia. The lower biopsy yield in larger prostates has also been attributed to undersampling since a proportionally smaller amount of tissue is sampled relative to the total prostate volume. The potential for undersampling in large prostates is compounded by the fact that larger glands tend to harbor smaller volume tumors [19].
Remzi et al. showed that there were increased numbers of cancers discovered on repeat biopsy for those with prostate volume 20-80 cc and for those whose TZ volume was 9-40 cc [20]. Beyond these size limits, they discourage repeat biopsy unless there is very strong suspicion of cancer based on other characteristics. Basillote et al. also demonstrated increased false-negative rates in patients with increased prostate volumes [21]. Using

extended biopsy schemes for initial biopsies, Ung et al. found no increased prostate cancer detection rates in larger volume prostates [22]. However, Sajadi et al found a much lower cancer detection rate with repeat "saturation" biopsies in large prostates compared to smaller glands (57% positive biopsy rate in glands less than 37cc and only 7% for larger glands) [23].

In practical terms, large prostates can often result in an initial biopsy that shows no malignancy. At least one set of repeat, extended biopsy of moderately enlarged prostates in patients with persistent concern about cancer appear justified. For extremely enlarged prostates (over 80 cc) the utility of repeat biopsies is unclear.

Repeat biopsies and inflammation

Prostatic inflammation often causes an increase in serum PSA levels. While the pathogenesis of inflammation-related PSA elevation is not completely understood, it is theorized to result from either leakage of PSA from epithelial cells into the serum or through stimulation of PSA production by epithelial cells through inflammatory-mediated substances [24, 25]. Nadler et al. noted that prostate inflammation and volume were the most important factors resulting in PSA elevations in those without prostate cancer [26]. Okada et al. found that histologically evident acute inflammation was the only independent determinant of serum PSA in those with prostates smaller than 25 cc [24]. While inflammation may inflate total PSA, it does not appear to influence the percent-free PSA [27]. To further complicate matters, we have demonstrated that the histologic finding of inflammation increases with sequential repeat biopsies [1]. Abouassaly et al have shown that the presence of inflammation can increase likelihood of the histologic diagnosis of ASAP, creating another avenue by which inflammation can stimulate the performance of unnecessary repeat biopsies [28]. Although it has not been clinically validated, interval antibiotic administration to correct PSA elevation secondary to histologic inflammation may help PSA reach its true baseline [3].

Time interval to repeat biopsies

Patients at high risk for existing cancer should undergo repeat biopsy without delay, recommendations vary between 2 and 6 weeks [2, 3]. High risk patients include those with ASAP or HGPIN. Others fitting this high-risk category include patients without inflammation on initial biopsy whose PSA is >10 ng/ml or with both a PSA between 4 and 10 ng/ml and percent free <10%. Other risk factors such as family history of prostate cancer and African American race have not been studied in relationship to the interval between initial and repeat prostate biopsies.

For patients who are not at high risk, a repeat PSA in 3 to 6 months to allow for calculation of PSAV has been recommended. While many patients will be relieved to postpone repeat biopsy for a few months, many will find the wait very anxiety-provoking. There is certainly no contraindication to more expeditious repeat biopsy in a very anxious patient.

Patient preparation

Patient preparation for repeat biopsies is a duplicate of the preparation used for initial biopsy in many facilities. Most urologists have the patient give themselves an enema before the procedure [29]. While taking aspirin or non-steroidal anti-inflammatory drugs is not an absolute contraindication to prostate biopsy, avoiding these medications for at least 10 days prior to the procedure is preferable. Some of the more aggressive extended biopsy schemes are performed under general anesthesia or with monitored sedation. Without the systemic

control of discomfort, periprostatic injection of local anesthetic is strongly recommended before subjecting an patient to extended biopsy schemes [30].
A short course of an oral fluoroquinolone antibiotic is the most common preparation [29]. Since these patients have already had a course of antibiotics for their prior biopsy and may have taken an even longer course of antibiotics if treated for prostatic inflammation, the possibility of resistant bacteria should be considered [31]. Pre-procedure urine culture, extended oral antibiotic coverage, or additional prophylaxis with an intravenous or intramuscular injection of an aminoglycoside should be considered.

Location and number of repeat biopsy cores

Hong et al. demonstrated that prostate cancer detection rates on repeat biopsy vary as a function of the extent of the initial biopsy [32]. If the prior negative biopsy was a sextant scheme, the cancer detection rate was 39% with a repeat extended biopsy, whereas if the prior negative biopsy was an extended scheme, the cancer detection rate was 28%. In general, areas not sampled on initial biopsy have higher rates of cancer detection when those areas were sampled on repeat biopsies. Therefore, repeat biopsy schemes typically consist of extended biopsy schemes designed to sample the areas of the prostate incompletely sampled by the initial biopsy. Repeat biopsy techniques also target those anatomic areas of the prostate where malignancy is more likely to reside. Repeat extended biopsy schemes consist of the classic sextant biopsy pattern plus various combinations of anteriorly directed biopsies that are designed to sample the transition zone, posterolateral sampling which includes the anterior horn of the peripheral zone, and anterior apical biopsies.

Directed biopsies

Directed biopsies were the initial approached used in conjunction with prostate ultrasound for prostatic sampling. With this approach, biopsies are taken only from areas that were suspicious on the ultrasound images and/or digital rectal examination. This method was far superior to the previously utilized digitally directed "blind" biopsies, however, with the current predominance of non-palpable isoechoic prostate tumors, biopsy sites limited to either sonographically hypoechoic lesions or areas of palpable abnormality have limited utility [1]. Most current extended biopsy schemes include any region in which an abnormality-directed biopsy would sample but an occasional directed biopsy in conjunction with the performance of an extended biopsy scheme may be useful in selected patients. . In addition, patients with ASAP should have additional cores obtained from the region of the ASAP [14]. This is in contrast to patients who are found to have HGPIN, where the finding of cancer on repeat biopsy is equally likely throughout the gland [14]. Some investigators have found a slight increase in cancer detection rates on repeat biopsies in the area from which the original biopsy containing HGPIN was taken [33,34]. These authors recommend that additional biopsies should be performed in the area previously harboring HGPIN.

Sextant biopsies

The sextant biopsy scheme, a method of obtaining spatially separated biopsies from each sextant of the prostate, was designed to improve the odds of sampling clinically inapparent tumors. These biopsy sites were originally described in mid-lobe parasagittal plane at the apex, mid-gland and base bilaterally. Although far superior to directed biopsies, sextant biopsies maintain a false negative rate between 15% and 34% based on repeated biopsies and computer simulations [1]. While sufficient for histologic confirmation of the presence of

cancer in patients with very abnormal digital rectal examinations and elevated PSA levels, use of sextant biopsies alone is generally considered inadequate for routine initial or repeat biopsies [2,3,16]. "Extended" biopsy is the terminology typically used to refer to greater than six biopsy cores taken in the sextant fashion. Despite falling out of favor as the sole approach to prostate sampling, sextant biopsies in conjunction with additional biopsies as part of an extended biopsy scheme continue to contribute significantly to the successful detection of prostate cancer [35].

Lateral biopsies

Pathologic analysis of radical prostatectomy specimens suggests that small prostate cancers occur in the posterolateral portion of the gland. These cancers are still in the peripheral zone where most prostate cancers reside, but are in the portion of the transition zone that wraps anteriorly and laterally. This area is occasionally termed the "anterior horn" in the literature. Stamey initially described the concept of targeting this area of the prostate with laterally placed sextant biopsies [36]. Eskew et al. introduced the first extended biopsy scheme for routine cancer detection and included the use of lateral biopsies [37]. The 5 regions included the standard sextant biopsies in the mid-lobe parasaggital plane bilaterally as well as two biopsies from lateral aspect of the prostate and three biopsies from the midline. Of the 119 patients studied, 48 (40%) were found to have prostate cancer on the biopsy, of which 17 (35% of cancers identified) were only detected in the additional non-sextant sites. Through analysis of the cancer detection yield of each individual biopsy site, Presti et al. first popularized the 10-core biopsy scheme combining routine mid-lobar sextant biopsies plus lateral biopsies on each side for routine use in all patients [38]. This technique perfected the concept of extended biopsies proposed by Eskew et al by determining the number and location of biopsies that resulted in the maximum cancer detection rate for the minimum number of biopsies performed. Lateral biopsies of the peripheral zone at the base and mid gland were added to the routine sextant biopsy regimen for a total of 10 systematic biopsies of the peripheral zone. Mian et al. utilized a 10-biopsy schema including the six sextant biopsies and two biopsies from each of the anterior horns of the peripheral zone [39]. This resulted in cancer detection in 33% of initial biopsies in 939 men. Babaian et al first introduced the use of extended biopsy schemes for repeat biopsies in 278 patients with prior negative prostate biopsies [40]. This 11-core strategy included sextant, lateral and anterior transition zone biopsies bilaterally.

Transition zone biopsies

We initially introduced the biopsy technique to sample the anterior prostate, or transition zone, in order to evaluate patients with cancer diagnosed by transurethral resection of the prostate (TURP) for residual/recurrent disease [41]. Anterior biopsies detected residual cancer in 47% of patients in whom cancer was detected by TURP. While routine performance of anterior biopsies was shown to be not warranted, anterior biopsies have been recommended as part of repeat extended field biopsies [32]. Liu et al. evaluated 116 patients who underwent sextant plus transition zone biopsies after prior negative sextant biopsies [42]. Overall, 36 (31.0%) were found to have prostate cancer while 11 (9.5%) demonstrated cancer only in the transition zone. Most investigators suggest 2 cores bilaterally from the transition zone while others recommend 3 biopsies from each side of the prostate in an anterior version of the sextant biopsy scheme [32, 39]. Adjusting the number of anterior biopsies according to the size of the transition zone, spacing them approximately 1cm apart, has also been suggested [43].

Transition zone biopsies should be performed near the midline, as close as possible to the urethra and anterior fibromuscular stroma. Transition zone biopsies are taken by advancing the biopsy needle through the posterior capsule of the prostate, into the peripheral zone to within 2-3 mm of the sonographically evident surgical capsule between the transition zone and the peripheral zone before firing; in prostates that extend far anteriorly (determined by the anteroposterior dimension of the transition zone exceeding 2cm), the needle is advanced through the surgical capsule and into the transition zone in order to sample the anterior-most tissue where transition zone tumors most frequently reside [41].

Midline biopsies

Performance of biopsies in the midline of the prostate has been utilized by some authors [37]. These biopsies have a very low yield compared to sextant, anterior, or lateral biopsies and have not been widely accepted by other investigators [38]. Even proponents of routinely performed extended field biopsies, find that these midline cores provide the least additional information [39,40].

Anterior apical biopsies

The entire apex of the prostate is composed of peripheral zone where it wraps around the caudal extent of the transition zone Although extended biopsy schemes sample the posterior and lateral apex, the anterior apex of the prostate is potentially undersampled. Several investigators have independently recommended that additional cores should be taken from the anterior apex on repeat biopsy [16, 44, 45].

Saturation biopsies

One of the most aggressive biopsy approaches suggested in patients with prior negative biopsies is the "saturation biopsy" technique [46]. The approach was originally described as multiple cores take from each of the 12 midlobe and lateral sextant locations as well as the transition zone. A mean of 23 cores were performed under anesthesia as an outpatient procedure. Subsequent use of a 24-core office-based saturation biopsy approach was described by Jones et al [47]. The utility of saturation biopsies for initial biopsies has been shown to be limited but use as a repeat biopsy scheme, with or without anesthesia may have a role in some patients [23, 48]. In patients who did not tolerate their initial biopsies without anesthesia very well, proceeding with performance of saturation biopsy under anesthesia rather than repeat, less extensive biopsies without anesthesia is often the more humane option.

Transperineal template biopsies

Igel et al. advocate employing the transperineal template apparatus used for brachytherapy seed implants for extensive repeat biopsy sampling [49]. In there follow-up study in which over 80% of patients had had at least 2 prior transrectal biopsy procedures, cancer was detected in 37% of patients [50]. The method seems to be superior in sampling the transition zone as 77% of the cancers in these patients with prior negative transrectal biopsies had cancer in the transition zone biopsies. Some experts question the accuracy of the assumed location of biopsy placement by this method [16].

How many repeat biopsy sessions is enough?

Unfortunately, negative repeat biopsies do not often settle the question of the presence or absence of prostate cancer. Multiple repeat biopsy procedures that reveal no cancer despite a rising PSA cause increasing frustration for the patient and urologist, alike. In men with

serum PSA levels between 4 and 10ng/ml, the European Randomized Study for Screening for Prostate Cancer demonstrated cancer detection rates on biopsies 1, 2, 3 and 4 of 22% (231 out of 1051), 10% (83 of 820), 5% (36 of 737) and 4% (4 out of 94), respectively [2]. The pathological and biochemical features of cancers detected on the first two sets of biopsies were similar but cancers detected on the third and fourth sets had lower grade, stage and volume. Even before the widespread use of extended biopsy protocols, a significant decreased yield after the third set of biopsies was demonstrated [1]. Therefore, after 2 or 3 sets of negative biopsies, further repeat biopsies appeared to be justified in very young, healthy patients where there is a very high suspicion of cancer despite two sets of negative findings [2]. Resnick et al. noted the risk of clinically insignificant disease in those patients diagnosed with prostate cancer on first repeat biopsy, on second repeat biopsy, and on third repeat biopsy of 31.1%, 43.8%, and 46.8%, respectively ($p<0.01$) (54). Conversely, the risk of adverse pathology in the above groups was determined to be 64.6%, 53.0%, and 52.0%, respectively ($p<0.01$) (54).

Complications of repeat prostate biopsy

Prostate biopsy is not entirely free from morbidity, especially in the setting of serial biopsies. In a cohort of greater than 75,000 patients, Nam et al. reported that the risk of post-biopsy hospital admission rates have increased from 1.0% in 1996 to 4.1% in 2005. There is concern for fluoroquinolone resistant infections, and the AUA Best practices statement recommends antibiotic prophylaxis.

In the prospective European Prostate Cancer Detection Study, Djavan et al. report minor or no discomfort was observed in 92% and 89% of patients at first and re-biopsy, respectively (p _ 0.29). Immediate morbidity was minor and included rectal bleeding (2.1% versus 2.4%, p _ 0.13), mild hematuria (62% versus 57%, p _ 0.06), severe hematuria (0.7% versus 0.5%, p _ 0.09) and moderate to severe vasovagal episodes (2.8% versus 1.4%, respectively, p _ 0.03). Delayed morbidity of first and re-biopsy was comprised of fever (2.9% versus 2.3%, p _ 0.08), hematospermia (9.8% versus 10.2%, p _ 0.1), recurrent mild hematuria (15.9% versus 16.6%, p _ 0.06), persistent dysuria (7.2% versus 6.8%, p 0.12) and urinary tract infection (10.9% versus 11.3%, respectively, p _ 0.07). Major complications were rare and included urosepsis (0.1% versus 0%) and rectal bleeding that required intervention (0% versus 0.1%, respectively) (59). Hence, repeat biopsy was recommend repeat after 6 weeks with no significant difference in pain or morbidity.

2. Conclusions

The primary indications for repeat biopsies are a persistently elevated/rising PSA , active surveillance protocols, or suspicious histology on initial biopsies. Variations of PSA measurement may help determine the need for repeat biopsies. Repeat biopsies should include a minimum of 14 cores including parasagittal and lateral sextant biopsies and 2 additional cores obtained from the right and left anterior apex. For patients in whom repeat biopsies fail to identify cancer despite a high clinical suspicion, consideration for repeat 14-core biopsy with additional 4 to 6 transition zone biopsies or a saturation biopsy approach seems warranted. Repeat biopsies after 2 or 3 biopsies fail to reveal cancer have limited yield. There is no significant increase in morbidity for repeat biopsy procedures after six weeks.

Further areas of study include determining any difference in the indications for repeat biopsy in patients with risk factors such as a family history of prostate cancer or African

American patients. Artificial neural networks incorporating the multiple potential indicators of repeat biopsies have yet gain the ease of use necessary for routine clinical care but may have future utility. Advanced sonographic technological such as power Doppler and elastography as well as biopsy needles that provide feedback on tissue characteristics have shown some promise. Additionally, transrectal MRI-guidance or MR spectroscopy for prostate biopsy have also been performed with promising results. Adjustment of biopsy schemes to allow tailoring to individual patient prostate size and shape may also improve yield without continued increase in the total number of biopsies performed

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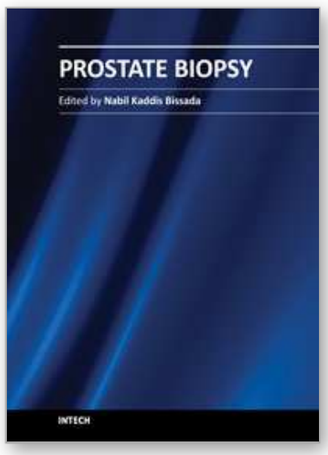

Prostate Biopsy
Edited by Dr. Nabil K. Bissada

ISBN 978-953-307-702-4
Hard cover, 134 pages
Publisher InTech
Published online 02, December, 2011
Published in print edition December, 2011

Prostate Biopsy represents the standard procedure for diagnosing Prostate Cancer. This procedure can be performed transrectally, through perineum or occasionally through the urethra. Although the procedures of Prostate Biopsy are covered in numerous publications, there is still a need for gathering different aspects and methods in one source. Hopefully, this book will help physicians in their effort to provide the best treatment for their patients.

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