Published in Imaging and Focal Therapy of Early Prostate Cancer,

Ed. T. J. Polasik, Humana Press, 2013, pp 141-151,

Quality Assurance in Prostate Biopsy Sampling, Processing, and Reporting: A New Pathologic Paradigm for Prostate Cancer Diagnosis

David G. Bostwick M.D., M.B.A.

Bostwick Laboratories, Glen Allen, Virginia

Address correspondence to Bostwick Laboratories, 4355 Innslake Drive, Glen Allen, VA 23060; Fax (804) 967-9354; Phone (804) 967-9225; e-mail: bostwick@bostwicklaboratories.com; web site: bostwicklaboratories.com

Abstract

Focal therapy requires accurate patient selection, yet variance in procedures for obtaining, processing, and diagnosing prostate biopsies results in imprecise and often incomparable data. Variance may be minimized by standardization of biopsy procedures by urologists and pathologists. We propose a ten step plan for quality assurance that includes pre-analytical (sampling), analytical (processing), and post-analytical (reporting) improvements that includes the following: (1) Measure the amount of tissue sampled (individual core length, aggregate core length, number of fragments, number of cores collected, and identification of extraprostatic tissue); (2) Improve accuracy of cancer localization (e.g., imaging, 3-D mapping); (3) Compare cancer yield with other urologists; (4) Implement patient biopsy identification system (bar codes or RFID); (5) Compare histotechnologist performance measures (e.g, histotechnologist's skill in processing and cutting prostate biopsies, number of needle cores embedded per cassette, and number of tissue cuts obtained per specimen); (6) Review prior negative slides upon diagnosis of malignancy; (7) Review positive slides from outside institutions; (8) Pathologist skill in biopsy interpretation; (9) Compare laboratory performance measures with national benchmarks; and (10) Use practice protocols and reporting templates.

Key Words: Prostate, biopsy quality assurance, variance, quality control, pathology, central review, sampling

Variance is the enemy of quality. Every effort should be made to decrease or eliminate variance in any healthcare endeavor, including diagnostic anatomic pathology, in order to optimize quality of patient care. Decreasing variance decreases the rate of errors in sampling, processing, and results reporting, and allows valid direct comparison of results between institutions.

Variance is also the nemesis of new treatments that require great accuracy in patient selection such as active surveillance and focal therapy. All agree that these new and controversial approaches should only be used for select patients-- only those who would benefit from such conservative approaches without subsequent harm owing to delayed definitive therapy.[1] Progress in prostate cancer treatment has been hindered by lack of accurate imaging techniques, resulting in surrogates of imaging such as 3-dimensional mapping biopsies (see below). However, this surrogate approach has not yet been widely endorsed, and inaccuracy persists in determination of cancer extent and localization in contemporary practice.

How can we decrease variance and improve the yield of cancer from prostate needle biopsies? Known variables that influence the diagnostic yield of prostate biopsies can be classified as uncontrollable and controllable.[2] Uncontrollable factors include patient- and prostate-related factors such as patient population (e.g., screening population vs. urologic practice), patient symptoms, serum PSA concentration and other laboratory findings, clinical stage, patient age, patient race, prior biopsy findings (e.g., PIN, ASAP), prostate volume, and TRUS and other imaging findings. Controllable factors include biopsy method-related factors that can be modified by the urologist or pathologist to decrease variance and increase the diagnostic yield, and thus deserve additional consideration (Table 1). These controllable factors are the basis of this report and form a ten-point plan for quality assurance in prostate biopsy that involves urologists and pathologists. If variance could be decreased by attending to these factors, there would be a greater level of accuracy in patient selection for focal therapy.

Prostate Biopsy Tissue Sampling (Pre-analytical phase)

QA Factor #1: Measure the Amount of Tissue Obtained to Decrease Variance

The yield of prostate cancer by biopsy is influenced by the amount of tissue collected. For example, in the United Sates, the biopsy side-notch instrument (e.g., Bard, Covington, GA) is used to take biopsy specimens from 10-12 sites. However, in other countries, some practitioners use an end-cut biopsy instrument (e.g., BioPince, Amedic, Sollentuna, Sweden) to take 8-core biopsies.[3] Core length may also be affected by the anatomic site sampled as well as the processing method used in the laboratory (see below).[4-6] Core length of greater than 10 mm is considered by some authors to be the threshold of satisfactory quality for needle biopsies, and shorter biopsies may compromise accurate histological evaluation.[4, 5] Two recent studies found that the mean length of biopsy cores was 12.8 ± 3.5 mm in the United States and 14.1 ± 4.4 mm in Europe.[4, 5]

Iczkowski and colleagues were the first to report on cancer yield as a function of biopsy tissue sampled.[4] Their study of sextant transrectal biopsies from two medical practices revealed a 3.6 fold variance in the length of tissue of single cores, with a trend for prediction of cancer yield, especially at the apex where the cores were shortest. Mean total tissue lengths sampled were 108 +/- 27 mm (range 30 to 275) and 81 +/- 22 mm (range 30 to 228) in each of two urology group practices. They concluded that the amount of tissue sampled by needle biopsy represents an important quality assurance consideration worthy of comparison with national standards.

Mondet and colleagues undertook a prospective study of 339 consecutive ten-core extended standardized biopsies performed by two urologists over a period of 22 months.[7] Measures of biopsy quality included mean length, amount with identified capsular or periprostatic tissue, and mean number of fragments. Initially, there were significant differences noted, but a progressive decline in variance and improvement in quality occurred as the urologists reviewed feedback on their performance. The authors concluded that systematic scoring of biopsy quality prompted the urologists to improve their practices.

A study from Verona, Italy of 509 consecutive fourteen-core transperineal biopsies from Verona, Italy revealed mean length of 14.14 +/- 4.35mm; all cores were longer than 10mm.[5] Mean length did not correlate with patient age, PSA concentration, digital rectal examination findings, or prostate volume. The percentage of fragmented cores and the rate ofcores without prostatic tissue were 3% and 0.4%, respectively, significantly lower than results reported with transrectal biopsies.[6]

A recent report from Reis and colleagues analyzed the incidence of core fragmentation, and found that the number of core fragments obtained by biopsy was 21.54 (+/- 3.56) compared to 24.08 (+/- 4.77) examined by the pathologist.[8] They concluded that core fragmentation may adversely affect stage and grade consideration.

Urologist skill and standardization of collection and processing of biopsies significantly reduced variance in prostate biopsy quality in the REDUCE clinical trial (prevention of prostate cancer by dutasteride), thereby optimizing cancer detection and yield.[9] Biopsy quality was found to be a useful comparative measure in urologic practice, and the authors concluded that this should be part of all urologists' quality assurance program. They compared biopsy quality among study sites worldwide , and found significant differences between geographic regions in three measures of quality (aggregate core length, number of cores obtained, and mean length of individual cores). For example, entry biopsies from Australia contained 60% more tissue than those from Central/Eastern Europe. Also, there was 1.2-fold difference between South America and Central/Eastern Europe in number of cores and a 1.6-fold difference between Australia and Africa in mean length of individual cores at entry. In an attempt to decrease variance in biopsy quality, they instituted a uniform 10-core biopsy collection at year 2 and trained investigators to standardize the biopsy procedure so that data would be comparable and valid in determining the efficacy of dutasteride for preventing prostate cancer. Biopsies obtained after this protocol-required standardization and investigator training showed a significant increase in all measures of biopsy quality when compared with entry biopsies, with less variance (greater uniformity) among all regions. Even the region with the greatest amount of tissue at entry (Australia) benefitted, with an increase of 24% at year 2. However, there was still a 1.1-fold difference (South America and Africa vs. Australia) in aggregate length and a 1.1- fold difference (South

America vs. Australia) in mean length of individual cores at year 2, despite efforts at standardization and collection of the same number of cores.

QA Factor #2: Improve accuracy of cancer localization (e.g., imaging, 3-D mapping)

A serious unresolved issue confronting advocates of active surveillance and focal therapy is determination of the location(s) of cancer in the prostate; the corollary to this problem is determination of the extent or volume of cancer. Prostatic imaging continues to improve, but is still considered suboptimal for individual patients, and is beyond the scope of this report. Three-dimensional mapping biopsy has been proposed as a surrogate.

Earlier studies compared number and location of biopsies with cancer yield, with varying results. Eskew et al.[10] developed a 5-region, 13-core biopsy strategy which improved the cancer detection rate by 37%. However, this 13-core biopsy was associated with increased complications, such as gross hematuria. Presti et al.[11] developed a 10-core biopsy strategy including sextant biopsies and biopsies from the lateral mid and lateral base from both right and left sides, increasing cancer detection by 16% when compared with sextant biopsy. Subsequently, Presti et al.[12] demonstrated that a 12-core biopsy scheme slightly improved the cancer detection rate compared to a 10-core scheme. These and results from many other reports have resulted in migration from sextant biopsy to more extended biopsy schemes (10 or more biopsies) by most urologists in the United States.

Mapping of biopsies is critical for management and treatment of prostate cancer, but localization of the cores is often inaccurate and prone to variance in practice. Mozer et al. used a registration algorithm to represent the location of biopsies in a reference 3-dimensional ultrasonographic volume in planning TRUS biopsies.[13] Overall, there was 71% success in hitting the planned targets, with substantial variability that depended on their location (100% success rate in the middle and right parasagittal prostate versus 53% in the left lateral base). Substantial improvement was observed as the operator received feedback from the system, resulting in median biopsy tissue length improvement from 90 mm to 121 mm.

Scattoni et al. found that the most beneficial biopsy scheme varied according to the clinical characteristics of the patients.[14] They detected prostate cancer in 47% of patients

(46.8%) with 24-core biopsies, and found that 16-cores was optimal for those with negative digital rectal exam, prostate volume of 60 cm3, and age 65 yr, whereas 14-cores was most advantageous for those with a negative rectal exam, volume of 60 cm3 or >60cm3, and age > 65 yr or a negative rectal and PV >60 cm3. They concluded that 10-core sampling permitted detection of 95% of cancers in patients with a positive rectal examination. It should be noted that this and other biopsy-only studies underestimate the true likelihood of cancer owing to the inability to examine the entire prostate gland.

In the past decade, Onik and Barzell introduced the transperineal 3-dimensional mapping biopsy as an additional staging procedure prior to focal prostate cancer therapy.[15, 16] Samples were taken every 5 mm throughout the volume of the prostate using a brachytherapy grid, and each sample was labeled separately as to its grid location. In an early report of 110 patients, all of whom had unilateral cancer on transrectal ultrasound biopsies, 55% were restaged with bilateral cancer; median number of cores taken was 46 (SD +/- 19). In addition, Gleason score increased in 23% of patients. Complications were self-limited. In a subsequent and remarkably similar report, Onik and colleagues studied 180 additional patients with unilateral cancer and restaged 61% with bilateral cancer; Gleason score increased in 23%.[17] Interestingly, 36 patients had negative results from 3D mapping. Subsequent reports have endorsed 3D mapping biopsies to optimize risk stratification for individual patients being considered for focal therapy.[13, 18-25]

QA Factor #3: Compare cancer yield with other urologists (? Too many or too few biopsies)

Are urologists performing too few or too many prostate biopsies? Who decides what the optimum yield of prostate cancer should be? These and other practice parameters should be included in a complete quality assurance program in urology, yet are often lacking. Such thresholds should be established by local, regional, and national benchmarking to decrease variance in practice. A Mayo Clinic study of all men in Olmstead County, Minnesota with a first prostate biopsy performed between 1986 and 1997 revealed that the overall cancer yield of 36% was essentially unchanged across periods ($p = 0.6$); however, by age, cancer yield decreased from 29% to 21% (1980 to 1986 versus 1993 to 1997) for men 50 to 59 years old but increased from 38% to 45% for those 70 to 79 years old.[26] The SEER database in the PSA era (through

2001) revealed an overall cancer yield of 32%; the yield increased with age (26% for men aged 65-69 years, 31% for men aged 70-74 years, 35% for men aged 75-79 years, and 41% for men aged 80 years and older.[27]

According to an European Uropathology consensus group, the frequency of ASAP (atypical small acinar proliferation suspicious for but not diagnostic of malignancy should be less than 3% (good) or less than 5% (fair).[28] They also suggested a threshold of less than 3% false negative diagnoses of prostate cancer after review, but we disagree, and believe that the false negative rate should be 0%. What urologist wants to be told that 3 of every 100 patients initially reported to have benign findings on biopsy actually had cancer?

Our laboratory maintains an on-line comparative analysis of prostate biopsy diagnoses for clients that is automatically updated daily.[29] This allows the individual urologist to compare his/her results with themselves or others (de-identified national data from our other clients), stratified by diagnosis (Table 2). For Dr. X (de-identified), the findings reveal that his cancer yield rate is consistently below the national database, suggesting that he may be more aggressive in undertaking biopsies than other colleagues. These data are limited and cannot account for practice differences in patient selection, demographics, etc., so they must be interpreted with caution.

Processing (Pre-analytical and Analytical phases)

QA Factor #4: Implement patient biopsy identification system (bar codes or RFID)

Patient specimen switching is a common and avoidable problem, involving about 0.5% of cases[30], and may occur at any step of the workflow process in the urology clinic and pathology laboratory. The potential for patient harm is especially high in diagnostic anatomic pathology given the impact on care by each definitive diagnosis; the most significant resulting damage is to the patient who receives an erroneous diagnosis and potentially irreversible treatment (or the lack thereof) as a result. To protect patients from errors, quality control initiatives must consider every step of this process, regardless of whether the error was caused by a clinician ornurse, laboratory professional, or a non-laboratory provider. Such steps for patient identification errors

include the pre-analytical phase in the clinician's office during which the biopsy is taken, the analytical phase in the laboratory during which the tissue is received, processed, and diagnosed, and the post-analytical phase in the laboratory and elsewhere during which the diagnostic report is delivered and the pathology slides and cassettes are stored. The recent Laboratory National Patient Safety Accreditation Program of the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) required that each laboratory "…establishes processes to maintain specimen identity throughout the pre-analytical, analytical, and post-analytical processes."[31] Process improvement methods include the use of 2-dimensional bar codes and radiofrequency identification (RFID) tags (DG Bostwick, manuscript in preparation). The potential for biopsy mismatches in clinical practice is an under-recognized problem that requires rigorous attention to details of chain of custody and consideration of more widespread DNA identity testing.

QA Factor #5: Compare histotechnologist performance measures (e.g, histotechnologist's skill in processing and cutting prostate biopsies, number of needle cores embedded per cassette, and number of tissue cuts obtained per specimen)

There is variation between laboratories in the number of serial sections obtained from prostate tissue blocks for routine examination; we routinely obtain 6 sections on each of two slides, yielding a total of 12 sections.[2] The first three sections and last three sections are placed on one slide and submitted for routine hematoxylin and eosin staining; the intervening 6 sections are placed on another slide and saved for additional stains or special studies such as immunohistochemistry or digital image analysis for DNA ploidy analysis. In our experience, recutting the block for additional levels is useful in about half of cases, with usually no more than 4 additional slides before the tissue specimen is exhausted. Most biopsy specimens consist only of tissue from the peripheral zone, seldom including the central or transition zones unless the operator has specifically targeted those locations.

Prostate biopsies are particularly difficult to embed and cut because they are small and tend to fragment and curve. Flat embedding of the biopsy cores enhances the amount of tissue that is examined by the pathologist. Laboratories that process prostate biopsies with other tissues of differing density and consistency (for example, breast biopsies with abundant fatty tissue) usually handle all specimens the same way, which often results in prostate biopsies that are

overstained or too thick to interpret. Similarly, over-stained sections (the most common problem in our consultation practice) contain obscured nuclear chromatin without recognizable nucleoli. These problems are compounded in biopsies with small foci that are suspicious for malignancy.

Multiple needle biopsies submitted in one or two containers tend to entangle and fragment and may be difficult to embed in a single plane during processing unless the histotechnologist is experienced and careful. The resulting loss of tissue surface area makes a definitive diagnosis difficult in many cases, and results in equivocal pathology reports. If multiple cores are embedded in one cassette, all must be separated from each other. We recently compared single core vs. 3-core embedding per block, and found that the yield of suspicious foci (PIN and ASAP) and cancer was identical, indicating that vials can be thoughtfully combined without compromising patient care; different colored inks are used to differentiate the sites (DG Bostwick, H. Kahane, manuscript in preparation, 2011).

Reporting (Post-Analytical Phase)

QA Factor #6: Review Prior Negative Slides Upon Diagnosis of Malignancy

Cytopathologists in the U.S. are required to routinely review all previously negative cervical pap smears received within five years prior to the new diagnosis of high grade squamous intraepithelial lesion or gynecologic malignancy. Patel and Layfield applied this standard to all prior negative prostatic needle biopsies following a new diagnosis of prostatic adenocarcinoma; in a five-year retrospective study, they found a false negative rate of 0.68% (2 of 87 cases initially diagnoses as benign that contained diagnostic foci of cancer).[32] We concur with their suggestion that this process should be included in a quality assurance program in prostate biopsy interpretation.

QA Factor #7: Review Positive Slides from Outside Institutions

Routine systematic review of all diagnostic slides from outside institutions is a requirement of the College of American Pathologists, yet adherence to this standard is imperfect.[33] Frable undertook a structured literature review of discrepancies throughout

anatomic pathology, and found major error rates ranged from 1.5% to 5.7% globally for institutional consults.[34] Error rates were less, 0.26% to 1.2% for global in-house prospective review and 4.0% for in-house and retrospective blinded review. Error rates also varied by anatomic site: skin, 1.4%; prostate, 0.5%; and thyroid, 7.0%.

In an early study of the 535 needle biopsies initially diagnosed on the outside as carcinoma, seven (1.3%) were reclassified as benign upon pathology review prior to radical prostatectomy (false positive rate of 1.3%).[35] The authors updated their findings a decade later, and found an identical level of false positive diagnosies; in addition, there were significant discrepancies in the number of positive cores and maximum percent of cancer positive in a core (discrepancy, 9% each).[36]

A root cause analysis of biopsy misdiagnoses prior to prostatectomy revealed three antecedent events that were contributory: (1) a second (concurring) pathologist did not provide a written opinion; (2) a single pathologist reviewed and signed the final report; and (3) a pathologist did not review the case and reconfirm the diagnosis prior to surgery.[37]

QA Factor #8: Pathologist skill in biopsy interpretation

Pathologists with special interest in urologic pathology have a higher level of accuracy in biopsy interpretation and Gleason grading. This seems reasonable given the fact that the generalist pathologist must deal with a multitude of pathologic conditions arising in the 24 major organs in the body, whereas the specialist urologic pathologist can focus his or her effort on only 4 organs (prostate, bladder, kidney, and testis). Inter-observer reproducibility of Gleason grading among urologic pathologists was considered ‘‘acceptable,’’; the greatest differences of interpretation result from low-grade cancer, cancer with small cribriform pattern, and cancer whose histology was on the border between Gleason patterns.[38, 39] In one report, the false negative rate (missed prostate cancer) was 0.6–1.0%, and the false-positive rate (over-diagnosis of prostate cancer) was 0.3%. These numbers indicate a small but significant error level that could be largely but completely avoided by secondary pathology review.[40]

Central pathology reviews for clinical trials afford an unique systematic unbiased prospective measure of processing and reporting variance. These reviews and second opinions consist of systematic slide review by a pathologist with a special interest and expertise in the specific organ system under study. Central review is commonly employed in the setting of a clinical trial to decrease variance, but the utility in routine practice of pathology has also been studied, and virtually always results in improved accuracy of diagnosis and decreased variance in results reporting. The pathologist undertaking secondary review may or may not have access to the primary report.

Utilization of a single facility decreased variance in tissue handling, processing, and yield, according to previous reports.[4, 6, 39] Variance was decreased with year 2 and 4 biopsies in the REDUCE trial by uniform fixation, processing, embedding, cutting, and staining in the central laboratory, as well as use of standardized diagnostic terminology and reporting by a single pathologist.[39, 41] Also, review of entry biopsies by central pathology revealed misinterpretation in about 4% of cases, a similar incidence to previous observations by us and others (data not shown).[42] It appears that using a central laboratory for processing and review of study biopsies in clinical trials ensures accurate diagnosis.

Nguyen and colleagues studied biopsies from 602 consecutive patients, and found that pathology review by a urologic pathologist changed the Gleason score by at least 1 point in 44% of cases (upgrades[81%] were more common than downgrades[19%]).[43] Patient risk category consequently changed in about 10% of men (from low risk to intermediate or high risk in 8.2%, and intermediate or high risk to low risk in 0.9%). Similar discrepancies in Gleason scores were observed in a brachytherapy cohort of 1323 men in which Gleason score increased in 22% and decreased in 2%, with an impact in clinical management in 15%; the authors concluded that specialty pathology review was essential.[44] Second opinion review of all urologic malignancies from Southern Illinois University revealed disagreement with the original diagnosis in 10% of cases, of which 8% were classified as major, and 2% were classified as minor.[45]

A recent study of second opinions for prostate biopsies showed a higher rate of discordance than concordance (57% vs. 43%), although the cases were selected for second opinion query owing to their recognized diagnostic difficulty.[46]

Central review of radical prostatectomy specimens in the TAX 3051 trial (androgen deprivation with or without docetaxol after radical prostatectomy) showed a 30% disagreement with Gleason score (75% upgraded; 25% downgraded), 30% disagreement with stage (91% upstaged; 9% down-staged), 11% disagreement with margin status, and 1% disagreement with lymph node involvement.[47] They also found changes in progression-free survival estimates in 13% of patients, rendering them study eligible and thus improving trial accrual. A multi-institutional study of more than 2000 prostatectomies with central specialty pathologist review found 45% disagreement, with 26% under-grading and 19% over-grading. Disagreement was 17% for extra-prostatic extension, 2% for seminal vesicle invasion, !% for lymph node involvement, and 12% for positive surgical margins.[48] Similar results were obtained in another study utilizing the International Society of Urologic Pathology 2005 Modified Gleason Scoring System.[49]

.

QA Factor #9: Compare laboratory performance measures with national benchmarks

In the past decade, the College of American Pathologists has expanded the use of its Q-probe system, a system that benchmarks utilization and practice patterns to provide feedback to individual practices as well as create a foundation for assessing the appropriateness of care in the future.[50] The CAP Q-probe database is a rich expanding data source with regular publications throughout the field of pathology.

Two organizational efforts have specifically focused on urologic pathology practice. The European Network of Uropathology (ENUP) was recently organized by the Uropathology Working Group of the European Society of Pathology to rapidly disseminate professional information about uropathology, such as guidelines, consensus documents, meetings, and courses.[51] Other goals include organizing research collaborations and setting up mechanisms for survey studies of practice patterns. ENUP has recruited a total of 374 individual members from 338 pathology laboratories in 15 Western European countries. E-mail is used for all communication, and studies are carried out through interactive Web sites.

Similarly, the International Society of Urological Pathologists (ISUP), formed almost 20 years ago to create agreement and standards for practice, has conducted numerous consensus conferences in the past decade, and closely collaborates with members of the ENUP. These

efforts in urologic pathology are laudatory, but more evidence-based guidelines rather than simple expert opinion agreements are needed. For example, the ISUP introduced a new Gleason grading system six years ago, termed the ISUP 2005 Modified Gleason Grading System, but no formal literature review was undertaken.[52] Critics of the new system, including this author, noted that there was remarkably little or no data upon which to make the changes suggested; dissenters continue to use the original or classic Gleason system (DG Bostwick, personal communication, 2005). Further, some of the initial proponent s of the new system have abandoned it (L. Egevad, personal communication, 2009), and others simply report cancer grade in biopsies as "Gleason score" without qualification that they are using the modified system. These activities actually create more harm than good for patients, clinicians, and pathology colleagues alike, and should be avoided.

QA Factor #10: Use practice protocols and report templates (e.g., Cancer checklists of the CAP)

Numerous attempts have been made in recent years to decrease variance in surgical pathology cancer case reporting. One of the most ambitious in the United States, advocated by the Cancer Committee of the College of American Pathologists and subsequently endorsed (and now required) by the American College of Surgery (ACS) Commission on Cancer (CoC) is a series of practice protocol Cancer Checklists with required elements such as grade, stage, histologic subtype, etc.[53, 54] Likewise, the European network of uropathology has issued similar guidelines.[28]

In a recent study of 2125 cancer reports from 86 medical centers, Idowu and colleagues found that 69% of surgical pathology cancer reports included all the required elements.[33] Centers with systems in place to track errors had a higher incidence of completeness than those lacking such as system (88% versus 68%). The most common missing elements were extent of invasion and status of the resection margin. These findings suggest that pathology reporting can be improved, probably through educational initiatives.

The rapid expansion of electronic medical records in recent years should have a significant positive effect on accuracy and completeness of cancer registry data. Penberthy and colleagues determined the accuracy and impact of automated software to capture and process

billing data to supplement reporting of cancers diagnosed and treated in a large community urology practice.[55] They found that automated processing of billing data from community urology practices captured an additional 12% of missing prostate and bladder cancer surveillance data with minimal effort to their urology practice.

Other issues in quality assurance

Numerous other factors not addressed here should also be considered in a complete quality assurance plan for prostate biopsies, including the role ancillary diagnostic and prognostic laboratory tests such as PCA3, use of nomograms and neural networks in practice to enhance predictive accuracy, considerations of repeat biopsy protocols, and questions regarding the definition of significant and insignificant prostate cancer.

Table 1

Physician-Controlled Factors in Prostate Biopsy Quality: Ten-Step Quality Assurance Plan for Prostate Biopsy Sampling, Processing, and Reporting

Sampling (Pre-analytical phase)

1. Measure the amount of tissue sampled (individual core length, aggregate core length, number of fragments, number of cores collected, and identification of extraprostatic tissue)
2. Improve accuracy of cancer localization (e.g., imaging, 3-D mapping)
3. Compare cancer yield with other urologists (? Too many or too few biopsies; electronic cancer registry reporting)

Processing (Pre-analytical and Analytical phases)

4. Implement patient biopsy identification system (bar codes or RFID)
5. Compare histotechnologist performance measures (e.g, histotechnologist's skill in processing and cutting prostate biopsies, number of needle cores embedded per cassette, and number of tissue cuts obtained per specimen)

Reporting (Post-Analytical Phase)

6. Review prior negative slides upon diagnosis of malignancy
7. Review positive slides from outside institutions
8. Pathologist skill in biopsy interpretation
9. Compare laboratory performance measures with national benchmarks
10. Use practice protocols and reporting templates (e.g., Cancer checklists of the CAP)

Table 2 Comparison of Prostate Biopsy results of a Single Physician (Dr. X*; n=400 cases) with Bostwick Laboratories/ National database (n= 52,480 cases)

Time period	Dr. X-Benign	National Database-Benign	Dr. X-Suspicious*	National Database-Suspicious*	Dr. X-Cancer	National Database-Cancer
Jul-Sep 2010	64.6	54.9	9.8	9.2	25.6	35.9
Oct-Dec 2010	63.8	56.6	7.5	8.4	28.7	35.0
Jan-Mar 2011	68.6	55.0	6.7	9.3	24.7	35.7
Apr-Jun 2011	67.2	55.3	5.0	9.2	27.8	35.5

*Suspicious includes ASAP and PIN. On the website, the physician can separate these out as the database is interactive.

References

[1] Bostwick DG, Waters DJ, Farley ER, Meiers I, Rukstalis D, Cavanaugh WA, et al. Group consensus reports from the Consensus Conference on Focal Treatment of Prostatic Carcinoma, Celebration, Florida, February 24, 2006. Urology. 2007 Dec;70(6 Suppl):42-4.

[2] Bostwick DG, Meiers I. Prostate biopsy and optimization of cancer yield. European urology. 2006 Mar;49(3):415-7.

[3] Haggarth L, Ekman P, Egevad L. A new core-biopsy instrument with an end-cut technique provides prostate biopsies with increased tissue yield. BJU Int. 2002 Jul;90(1):51-5.

[4] Iczkowski KA, Casella G, Seppala RJ, Jones GL, Mishler BA, Qian J, et al. Needle core length in sextant biopsy influences prostate cancer detection rate. Urology. 2002 May;59(5):698-703.

[5] Ficarra V, Martignoni G, Novella G, Cerruto MA, Galfano A, Novara G, et al. Needle core length is a quality indicator of systematic transperineal prostate biopsy. European urology. 2006 Aug;50(2):266-71.

[6] Dogan HS, Eskicorapci SY, Ertoy-Baydar D, Akdogan B, Gunay LM, Ozen H. Can we obtain better specimens with an end-cutting prostatic biopsy device? European urology. 2005 Mar;47(3):297-301.

[7] Mondet F, Boyer C, Oddou JH, Corsois L, Collomb D. [Quality score in pathological report of prostate biopsies improve professional practice]. Prog Urol. 2009 Dec;19(11):825-9.

[8] Reis LO, Reinato JA, Silva DC, Matheus WE, Denardi F, Ferreira U. The impact of core biopsy fragmentation in prostate cancer. International urology and nephrology. Dec;42(4):965-9.

[9] Bostwick DG, Qian J, Drewnowska K, Varvel S, Bostwick KC, Marberger M, et al. Prostate needle biopsy quality in reduction by dutasteride of prostate cancer events study: worldwide comparison of improvement with investigator training and centralized laboratory processing. Urology. Jun;75(6):1406-10.

[10] Eskew LA, Bare RL, McCullough DL. Systematic 5 region prostate biopsy is superior to sextant method for diagnosing carcinoma of the prostate. The Journal of urology. 1997 Jan;157(1):199-202; discussion -3.

[11] Presti JC, Jr., Chang JJ, Bhargava V, Shinohara K. The optimal systematic prostate biopsy scheme should include 8 rather than 6 biopsies: results of a prospective clinical trial. The Journal of urology. 2000 Jan;163(1):163-6; discussion 6-7.

[12] Presti JC, Jr., O'Dowd GJ, Miller MC, Mattu R, Veltri RW. Extended peripheral zone biopsy schemes increase cancer detection rates and minimize variance in prostate specific antigen and age related cancer rates: results of a community multi-practice study. The Journal of urology. 2003 Jan;169(1):125-9.

[13] Mozer P, Baumann M, Chevreau G, Moreau-Gaudry A, Bart S, Renard-Penna R, et al. Mapping of transrectal ultrasonographic prostate biopsies: quality control and learning curve assessment by image processing. J Ultrasound Med. 2009 Apr;28(4):455-60.

[14] Scattoni V, Raber M, Abdollah F, Roscigno M, Deho F, Angiolilli D, et al. Biopsy schemes with the fewest cores for detecting 95% of the prostate cancers detected by a 24-core biopsy. European urology. Jan;57(1):1-8.

[15] Onik G, Barzell W. Transperineal 3D mapping biopsy of the prostate: an essential tool in selecting patients for focal prostate cancer therapy. Urol Oncol. 2008 Sep-Oct;26(5):506-10.

[16] Barzell WE, Melamed MR. Appropriate patient selection in the focal treatment of prostate cancer: the role of transperineal 3-dimensional pathologic mapping of the prostate--a 4-year experience. Urology. 2007 Dec;70(6 Suppl):27-35.

[17] Onik G, Miessau M, Bostwick DG. Three-dimensional prostate mapping biopsy has a potentially significant impact on prostate cancer management. J Clin Oncol. 2009 Sep 10;27(26):4321-6.
[18] Ahmed HU, Hu Y, Carter T, Arumainayagam N, Lecornet E, Freeman A, et al. Characterizing clinically significant prostate cancer using template prostate mapping biopsy. The Journal of urology. Aug;186(2):458-64.
[19] Barqawi AB, Rove KO, Gholizadeh S, O'Donnell CI, Koul H, Crawford ED. The role of 3-dimensional mapping biopsy in decision making for treatment of apparent early stage prostate cancer. The Journal of urology. Jul;186(1):80-5.
[20] de la Rosette J, Ahmed H, Barentsz J, Johansen TB, Brausi M, Emberton M, et al. Focal therapy in prostate cancer-report from a consensus panel. Journal of endourology / Endourological Society. May;24(5):775-80.
[21] Patel V, Merrick GS, Allen ZA, Andreini H, Taubenslag W, Singh S, et al. The incidence of transition zone prostate cancer diagnosed by transperineal template-guided mapping biopsy: implications for treatment planning. Urology. May;77(5):1148-52.
[22] Taira AV, Merrick GS, Galbreath RW, Andreini H, Taubenslag W, Curtis R, et al. Performance of transperineal template-guided mapping biopsy in detecting prostate cancer in the initial and repeat biopsy setting. Prostate cancer and prostatic diseases. Mar;13(1):71-7.
[23] Ukimura O, Hung AJ, Gill IS. Innovations in prostate biopsy strategies for active surveillance and focal therapy. Current opinion in urology. Mar;21(2):115-20.
[24] Villers A, Ouzzane A. Word of wisdom. Re: three-dimensional prostate mapping biopsy has a potentially significant impact on prostate cancer management. European urology. Dec;58(6):941-2.
[25] Sullivan KF, Crawford ED. Targeted focal therapy for prostate cancer: a review of the literature. Therapeutic advances in urology. 2009 Aug;1(3):149-59.
[26] Roberts RO, Bergstralh EJ, Peterson NR, Bostwick DG, Lieber MM, Jacobsen SJ. Positive and negative biopsies in the pre-prostate specific antigen and prostate specific antigen eras, 1980 to 1997. The Journal of urology. 2000 May;163(5):1471-5.
[27] Welch HG, Fisher ES, Gottlieb DJ, Barry MJ. Detection of prostate cancer via biopsy in the Medicare-SEER population during the PSA era. Journal of the National Cancer Institute. 2007 Sep 19;99(18):1395-400.
[28] Boccon-Gibod L, van der Kwast TH, Montironi R, Boccon-Gibod L, Bono A. Handling and pathology reporting of prostate biopsies. European urology. 2004 Aug;46(2):177-81.
[29] Bostwick DG. Webdox. 2011 [cited; Available from: https://www.bostwicklaboratories.com/global/services/practice-solutions/webdox.aspx
[30] Marberger M, McConnell JD, Fowler I, Andriole GL, Bostwick DG, Somerville MC, et al. Biopsy misidentification identified by DNA profiling in a large multicenter trial. J Clin Oncol. May 1;29(13):1744-9.
[31] Organizations JCoAoHC. Laboratory National Patient Safety Goals. 2008 [cited; Available from: http://www.jointcommission.org/NR/rdonlyres/32B9933B-5638-4FB0-BEDA-04C3A6BBF398/0/LAB_NPSG.pdf.
[32] Patel J, Layfield LJ. Histopathologic review of previously negative prostatic core needle biopsies following a new diagnosis of adenocarcinoma of the prostate by core needle biopsies: implications for quality assurance programs. Clinical medicine. 2008;1:77-81.
[33] Idowu MO, Bekeris LG, Raab S, Ruby SG, Nakhleh RE. Adequacy of surgical pathology reporting of cancer: a College of American Pathologists Q-Probes study of 86 institutions. Archives of pathology & laboratory medicine. Jul;134(7):969-74.

[34] Frable WJ. Surgical pathology--second reviews, institutional reviews, audits, and correlations: what's out there? Error or diagnostic variation? Archives of pathology & laboratory medicine. 2006 May;130(5):620-5.
[35] Epstein JI, Walsh PC, Sanfilippo F. Clinical and cost impact of second-opinion pathology. Review of prostate biopsies prior to radical prostatectomy. Am J Surg Pathol. 1996 Jul;20(7):851-7.
[36] Brimo F, Schultz L, Epstein JI. The value of mandatory second opinion pathology review of prostate needle biopsy interpretation before radical prostatectomy. The Journal of urology. Jul;184(1):126-30.
[37] Piotrowski MM, Bessette RL, Chensue S, Cutler D, Kachalia A, Roseborough JW, et al. Learning to improve safety: false-positive pathology report results in wrongful surgery. Jt Comm J Qual Patient Saf. 2005 Mar;31(3):123-31.
[38] Allsbrook WC, Jr., Mangold KA, Johnson MH, Lane RB, Lane CG, Amin MB, et al. Interobserver reproducibility of Gleason grading of prostatic carcinoma: urologic pathologists. Human pathology. 2001 Jan;32(1):74-80.
[39] Allsbrook WC, Jr., Mangold KA, Johnson MH, Lane RB, Lane CG, Epstein JI. Interobserver reproducibility of Gleason grading of prostatic carcinoma: general pathologist. Hum Pathol. 2001 Jan;32(1):81-8.
[40] Oxley JD, Sen C. Error rates in reporting prostatic core biopsies. Histopathology. Apr;58(5):759-65.
[41] Iczkowski KA, Bostwick DG. Sampling, submission, and report format for multiple prostate biopsies: a 1999 survey. Urology. 2000 Apr;55(4):568-71.
[42] Bostwick DG, Ma J. Over-diagnosis of high-grade prostatic intraepithelial neoplasia: a prospective study of 251 cases. BJU Int. 2007 Nov;100(5):1036-9.
[43] Nguyen PL, Schultz D, Renshaw AA, Vollmer RT, Welch WR, Cote K, et al. The impact of pathology review on treatment recommendations for patients with adenocarcinoma of the prostate. Urol Oncol. 2004 Jul-Aug;22(4):295-9.
[44] Thomas CW, Bainbridge TC, Thomson TA, McGahan CE, Morris WJ. Clinical impact of second pathology opinion: a longitudinal study of central genitourinary pathology review before prostate brachytherapy. Brachytherapy. 2007 Apr-Jun;6(2):135-41.
[45] Wayment RO, Bourne A, Kay P, Tarter TH. Second opinion pathology in tertiary care of patients with urologic malignancies. Urol Oncol. 2009 Jun 11.
[46] Jara-Lazaro AR, Thike AA, Tan PH. Diagnostic issues in second opinion consultations in prostate pathology. Pathology. Jan;42(1):6-14.
[47] Netto GJ, Eisenberger M, Epstein JI. Interobserver variability in histologic evaluation of radical prostatectomy between central and local pathologists: findings of TAX 3501 multinational clinical trial. Urology. May;77(5):1155-60.
[48] Kuroiwa K, Shiraishi T, Ogawa O, Usami M, Hirao Y, Naito S. Discrepancy between local and central pathological review of radical prostatectomy specimens. The Journal of urology. Mar;183(3):952-7.
[49] Kuroiwa K, Shiraishi T, Naito S. Gleason score correlation between biopsy and prostatectomy specimens and prediction of high-grade Gleason patterns: significance of central pathologic review. Urology. Feb;77(2):407-11.
[50] 2011 [cited; Available from: www.cap.org/apps/cap.portal?
[51] Egevad L, Algaba F, Berney DM, Boccon-Gibod L, Griffiths DF, Lopez-Beltran A, et al. The European Network of Uropathology: a novel mechanism for communication between pathologists. Analytical and quantitative cytology and histology / the International Academy of Cytology [and] American Society of Cytology. 2009 Apr;31(2):90-5.

[52] Epstein JI, Allsbrook WC, Jr., Amin MB, Egevad LL. The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. The American journal of surgical pathology. 2005 Sep;29(9):1228-42.

[53] Srigley JR, Humphrey PA, Amin MB, Chang SS, Egevad L, Epstein JI, et al. Protocol for the examination of specimens from patients with carcinoma of the prostate gland. Archives of pathology & laboratory medicine. 2009 Oct;133(10):1568-76.

[54] Hassell L, Aldinger W, Moody C, Winters S, Gerlach K, Schwenn M, et al. Electronic capture and communication of synoptic cancer data elements from pathology reports: results of the Reporting Pathology Protocols 2 (RPP2) project. Journal of registry management. 2009 Winter;36(4):117-24; quiz 63-5.

[55] Penberthy LT, McClish D, Agovino P. Impact of automated data collection from urology offices: improving incidence and treatment reporting in urologic cancers. Journal of registry management. Winter;37(4):141-7.