Comparative Analysis of Whole Mount Processing and Systematic Sampling of Radical Prostatectomy Specimens: Pathological Outcomes and Risk of Biochemical Recurrence

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Abbreviations and Acronyms

BCR = biochemical recurrence
EPE = extraprostatic extension
LNI = lymph node involvement
PGS = pathological Gleason score
PSA = prostate specific antigen
RP = radical prostatectomy
RRP = retropubic RP
SM = surgical margin
SS = systematic sampling
SVI = seminal vesicle invasion
VUMC = Vanderbilt University Medical Center
WM = whole mount

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Purpose: Whole mount processing is more resource intensive than routine systematic sampling of radical retropubic prostatectomy specimens. We compared whole mount and systematic sampling for detecting pathological outcomes, and compared the prognostic value of pathological findings across pathological methods.
Materials and Methods: We included men (608 whole mount and 525 systematic sampling samples) with no prior treatment who underwent radical retropubic prostatectomy at Vanderbilt University Medical Center between January 2000 and June 2008. We used univariate and multivariate analysis to compare the pathological outcome detection rate between pathological methods. Kaplan-Meier curves and the log rank test were used to compare the prognostic value of pathological findings across pathological methods.
Results: There were no significant differences between the whole mount and the systematic sampling groups in detecting extraprostatic extension (25% vs 30%), positive surgical margins (31% vs 31%), pathological Gleason score less than 7 (49% vs 43%), 7 (39% vs 43%) or greater than 7 (12% vs 13%), seminal vesicle invasion (8% vs10%) or lymph node involvement (3% vs 5%). Tumor volume was higher in the systematic sampling group and whole mount detected more multiple surgical margins (each $p < 0.01$). There were no significant differences in the likelihood of biochemical recurrence between the pathological methods when patients were stratified by pathological outcome.
Conclusions: Except for estimated tumor volume and multiple margins whole mount and systematic sampling yield similar pathological information. Each method stratifies patients into comparable risk groups for biochemical recurrence. Thus, while whole mount is more resource intensive, it does not appear to result in improved detection of clinically important pathological outcomes or prognostication.

Key Words: prostate; pathology, surgical; prostatic neoplasms; prostatectomy; clinical laboratory techniques

PROSTATE cancer remains the most commonly diagnosed, solid nonskin cancer in men in the United States with approximately 186,000 incident cases in 2008.[1] While a large proportion of men with clinically localized prostate cancer undergo surgery,[2] the optimal strategy for pathological evaluation of RP specimens is still debated.

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The aim of RP is prostate removal and cancer cure. RP also provides the opportunity for pathological evaluation, yielding important prognostic information and guiding adjuvant therapy. In addition to preoperative PSA, the strongest predictors of BCR after RP are pathological tumor features, including PGS, SM status, EPE, SVI and LNI.[3,4] Thus, accurate, reliable pathological assessment is of the utmost importance but these goals must be balanced against the resource use of the processing method.

Pathological processing of RP specimens varies by institution and by pathologist. The pathologist has the option of using a WM technique or routine sectioning. In WM the prostate is completely embedded in paraffin and the pathologist evaluates full coronal sections perpendicular to the rectal surface on oversized glass slides cut on specialized microtomes. In contrast, in routine sectioning methods the prostate is quartered in left/right and anterior/posterior dimensions before embedding so that sections can fit in standard size blocks that can be cut on standard microtomes. In routine sectioning all blocks can be embedded and submitted or representative sections can be embedded and submitted, as in SS (fig. 1).

In a step toward standardization the Association of Directors of Anatomic and Surgical Pathology, and the College of American Pathologists published guidelines with required and optional elements for reporting RP pathology.[5–7] Similarly there have been comments at a number of consensus conferences on reporting pathological findings in RP specimens.[8,9] None of these efforts has yielded a definitive recommendation on whether WM or SS is the preferred method. Thus, it remains uncertain whether WM processing provides enough additional information over that of SS to justify the higher resource requirements in routine clinical settings. We determined whether pathological processing method has an impact on pathological and BCR outcomes.

PATIENTS AND METHODS

A total of 3,090 consecutive RPs were done at VUMC between January 2000 and June 2008, including 1,221 RRPs and 1,866 robotic assisted laparoscopic prostatectomies. We focused on the RRP group to avoid confounding due to possible differences in pathological outcomes based on surgical technique and since all robotic cases were evaluated by SS. With institutional review board approval we reviewed the charts of 1,221 patients who underwent RRP and pelvic lymphadenectomy. We excluded 72 men with preoperative hormone therapy or radiotherapy, 12 with no residual tumor (pT0) and 4 with missing data, leaving 1,133 available for analysis. At our pathology department WM was used between January 2000 and May 2003 in 608 cases, and SS was used thereafter in 525.

Specimen Handling and Pathological Examination

The WM protocol was described previously.[10] Briefly, the fresh specimen was weighed, longitudinal and transverse dimensions were measured and the entire surface was inked. The proximal and distal 3 to 5 mm were amputated perpendicular to the urethra and sectioned parallel to the urethra to evaluate the apical and bladder neck margins. These margins were submitted for routine histological preparation and evaluation. Sections from the seminal vesicle junction with the prostate were also submitted. The remaining prostate was sliced in 4 to 5 mm blocks perpendicular to the rectal surface and embedded in paraffin (fig. 2). Sections of each block were cut in 5 μ sections, stained for hematoxylin and eosin, and submitted for histological examination. Tumor areas on each submitted section were outlined on a digitized graphic tablet and National Institutes of Health software was used to calcu-

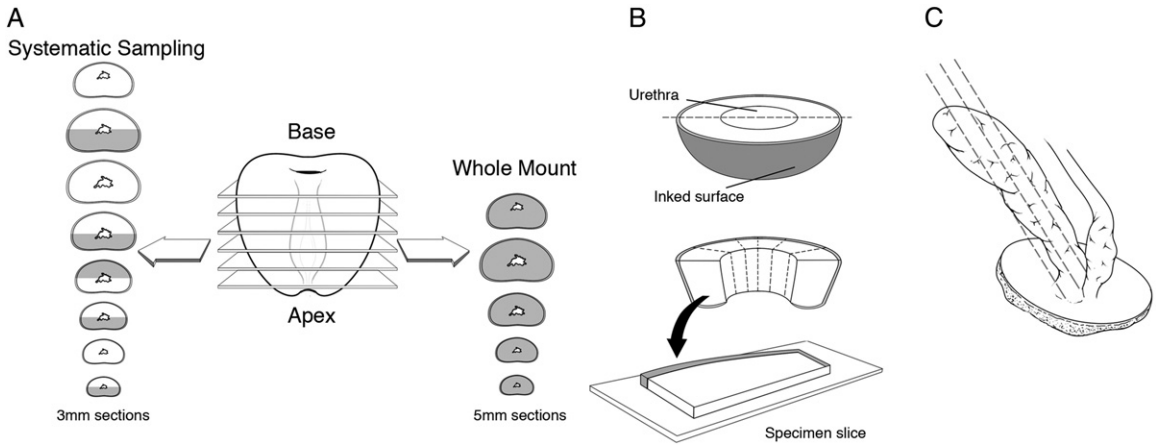

Figure 1. Gross dissection techniques for prostate SS and WM processing. *A,* difference between 2 techniques in slice thickness and amount of tissue submitted (gray areas). *B,* apex and base are sectioned identically in 2 methods and designed to highlight surgical margins (gray areas) for evaluation. *C,* seminal vesicle is sectioned longitudinally in each method through its junction with prostate (dashed lines) to identify seminal vesicle invasion.