RECOMMENDATIONS FOR THE REPORTING OF PROSTATE CARCINOMA

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ASSOCIATION OF DIRECTORS OF ANATOMICAND SURGICAL PATHOLOGY

(Updated September 2006, Version 1.4)

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Introduction for ADASP reporting Guidelines

It has been evident for decades that pathology reports are very variable even within a single institution. Standardization of reporting is the optimal way to insure that information necessary for patient management, prognostic and predictive factor assessment, grading, staging, analysis of outcomes and tumor registries are included in pathology reports.

The ADASP has chosen a pathologist expert in each field to assemble a group from within the pathology community (with clinician input if desired) to write specific cancer protocols. These were then approved by the ADASP council and subsequently by the membership. The American College of Surgery (ACS) Commission on Cancer (COC) accredits cancer centers in the USA. Recently, the COC decided to require elements, deemed as essential by the CAP, to be described in all pathology reports in their accredited cancer centers as of January 2004. Importantly they do not require that the specific CAP protocols or synoptic reports be utilized. ADASP has updated all of its protocols to comply with the COC requirements in the form of uniform checklists. The checklists use the staging criteria sited in the American Joint Committee on Cancer (AJCC) 2002 staging manual (sixth edition) but include a variety of other references listed in each of the checklists. Moreover, the checklists are formatted for ease of use. They may be used as templates for uniform reporting and are designed to be compatible with voice-activated transcription.

The different elements in these revised ADASP Diagnostic Checklists have been divided into Required and Optional. The term Required in this context only signifies compliance with the COC guidelines. ADASP realizes that specimens and practices vary and it will

not be possible to report these elements in every case. However, ADASP hopes that pathologists will find these checklists to be useful in daily clinical practice, while facilitating compliance with the new COC requirements.

The checklists are in standard PDF file format, and may be easily downloaded from the ADASP website. They are not to be reproduced, altered or used for commercial purposes without consent from ADASP.

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Editor, ADASP Practice Guidelines.

I. Features the Association recommends to be included in the final report because they are generally accepted as being of prognostic importance, required for therapy and/or traditionally expected.

A. Gross Description

1. Description of Specimen Received - Fresh, in formalin, intact, cut, margins inked or not, etc.

2. Specimen Labeling - Labeled with (name, number), designated as prostate, and procedure [core biopsy, transurethral biopsy, transurethral resection, enucleation, radical prostatectomy, radical cystoprostatectomy, other]

3. Size - The overall size of the excised specimen should be measured in three dimensions: TURP specimens should be weighed; needle biopsy cores should be counted, and measured in length (state if multiple small fragmented cores w/o need for measuring),

4. Additional Organs Attached - (e.g. seminal vesicles, vasa deferentia, bladder neck in radical prostatectomy specimens).

5. Tumor Description

- Presence of lesion (s) or absence of lesion (s)
- Location of the lesion (s) (e.g., in radical prostatectomy: posterior, posterolateral, lateral, anterior and apex, mid, base)
- Size of the lesion (s) (greatest diameter if radical prostatectomy)
- Consistency of the lesion (s) (e.g. firm, fleshy)

6. Lymph Nodes - Number and appearance of lymph nodes if received

7. Frozen Section - Whether a frozen section was performed and the diagnosis that was made

B. Diagnostic Information

1. Histological Type -

___ Adenocarcinoma (acinar, not otherwise specified)

___ Prostatic duct adenocarcinoma

___ Mucinous (colloid) adenocarcinoma

___ Signet-ring-cell-like carcinoma

___ Adenosquamous carcinoma

___ Small cell carcinoma

___ Sarcomatoid carcinoma

___ Undifferentiated carcinoma, not otherwise specified

___ Other (specify): _____

2. Histological Grade. All acinar adenocarcinomas should be graded using the Gleason grading system. Ductal adenocarcinomas are typically assigned a Gleason score 4+4=8 yet are diagnosed as “ductal adenocarcinoma (Gleason score 4+4=8)” to convey the unique clinical and pathological features of this tumor. There is no consensus as to the grading of mucinous carcinomas. Approximately one-half of urological pathologists grade them as Gleason pattern 4 (e.g. Gleason score 4+4=8 if pure mucinous tumor). The remaining experts grade the tumor based on the underlying tumor architecture, mentally subtracting away the mucin. Regardless of the method used to grade mucinous carcinomas, the majority of these tumors end up being assigned a Gleason score 4+4=8.

True signet-ring-cell carcinomas containing vacuoles of mucin that are primary in the prostate are exceedingly rare. Rather, there exists signet-ring-cell-like carcinomas, which contain clear vacuoles without mucin. These tumors are graded by their underlying architecture. Small cell carcinomas are not graded as they have unique clinicopathological features and most importantly are treated differently than Gleason pattern 5 adenocarcinoma. The carcinomatous component of sarcomatoid carcinoma and adenosquamous carcinoma should be assigned a Gleason score.

For all types of specimens (needle, TURP, enucleation, radical prostatectomy), when there is a minor secondary component (<5% of tumor) and where the secondary component is of higher grade, the latter should be reported. For instance, a case showing >95% Gleason pattern 3 and <5% Gleason pattern 4 should be reported as Gleason score 3+4=7. Conversely, if a minor secondary pattern is of lower grade, it need not be reported. For instance, where there is >95% Gleason score 4 and <5% Gleason 3, the score should be reported as Gleason score 4+4=8. These aggressive cases with only a few glands of Gleason pattern 3 should be distinguished from cases with a more prominent secondary Gleason pattern 3 which are assigned a Gleason score of 4+3=7.
In needle biopsy specimens, it is recommended that separate Gleason scores be assigned for each specimen container. This is most critical for the situation where the grade for the tumor in one container is Gleason score 4+4=8 and the others are of lower grade. In these cases, the tumor behaves according to the highest grade (e.g. Gleason score 4+4=8) and not the composite (overall) score which would be lower. Further support for assigning separate Gleason scores for different containers is that the Gleason grade factored into

currently existing tables and nomograms (e.g. Partin tables, Kattan nomograms), which predict the stage and prognosis of prostate cancer, utilized the highest Gleason score in a case and not the composite (global) score. Providing a global or composite score reflecting the overall Gleason score in the entire specimen is optional.

In needle biopsy specimens where more than two patterns are present and the worst grade is neither the predominant nor the secondary grade, the predominant and highest grade should be chosen to arrive at a score (e.g. 75% pattern 3, 20% pattern 4, and 5% pattern 5) is assigned a Gleason score 3+5=8. It is assumed that a minor component of high grade cancer on needle represents a sampling artifact, where it is likely that there will be a significant amount of the high grade cancer in the prostate.

In TURP or enucleation specimens where one cannot identify separate tumor nodules, only one Gleason score is assigned. In radical prostatectomy specimens, each dominant tumor nodule is assigned a separate Gleason score. It is not necessary to assign a separate score to each small, multifocal, low grade cancer focus in the setting of a larger higher grade dominant nodule. In the case where there is no dominant tumor nodule, it can be stated that there are multifocal tumor nodules with a comment as to their grades. In TURP, enucleation, and radical prostatectomy specimens, the Gleason score is based on the primary (most common) and secondary (next most common) pattern. If there is a third pattern or if the second pattern occupies less than 5% of the specimen, then this pattern is reported as a tertiary pattern.

3. Tumor Extent. In core biopsies, the absolute number of involved cores should be reported out of the total number of cores received. In cases with fragmented cores where one can not accurately derive the number of involved or total number of intact cores, one can merely state the overall percentage of the fragmented specimen involved by cancer. In addition one should provide one other more detailed measurement of cancer, such as the linear extent of involvement in millimeters (either per core or total) or the percentage of cancer in each involved core. There is no consensus whether one should give the linear extent or percentage of involved core by either counting gaps of uninvolved tissue in the measurement or by "collapsing" the tumor by ignoring the intervening gaps of benign tissue. As different foci of cancer along a core most likely represent the same tumor as opposed to multifocal cancer, it is preferred to record the tumor extent including the uninvolved tissue in the measurement as it more accurately represents the minimal extent of the cancer in the prostate. To distinguish small discontinuous foci from continuous cancer, one can report the following: "Small foci of cancer discontinuously involving X% of the length of the core", where "X" is measured from one end of the cancer to the other on the core regardless of intervening benign tissue.

In TURP and enucleation specimens, the percentage of tissue involved by carcinoma is reported, with 5% the cut-off between T1a and T1b disease.

There us no uniform data that tumor volume in radical prostatectomy specimens is an independent predictive parameter of prognosis once other standard parameters are recorded. Nonetheless, it is recommended that some measurement of tumor volume be

recorded even if it is a subjective quantification of “minimal, moderate, and extensive”. If more precise measurements are required by the clinician, an “eyeball” estimate of the percentage of the specimen involved by cancer is sufficient.

4. Margins of Resection - The entire surface of a radical prostatectomy specimen should be inked to evaluate the surgical margins. Usually, surgical margins should be designated as “negative” if tumor is not present at the inked margin and as “positive” if tumor cells touch the ink at the margin. When tumor is located very close to an inked surface but is not actually in contact with the ink, it is considered negative. Positive surgical margins should not be interpreted as extraprostatic extension. Intraprostatic margins are positive in the setting of capsular incision (so-called pT2+ or pT2x disease). The specific locations of the positive margins are useful to report, and there should be some indication of the extent of margin positivity (e.g. unifocal versus multifocal or focal versus extensive or number of positive sites [blocks] or linear extent in millimeters).

The apical and bladder neck surgical margins should be submitted entirely, preferably with a perpendicular sectioning technique. Microscopic involvement of bladder neck muscle fibers in radical prostatectomy specimens should not be equated with a pT4 designation. The latter generally requires gross involvement of the bladder neck.. A recent study has shown that patients with microscopic bladder neck involvement have recurrence rates similar to patients with seminal vesicle involvement (pT3b).

5. Extraprostatic Extension (EPE). This is the preferred term for the presence of tumor beyond the confines of the prostate gland. Tumor abutting on or admixed with fat constitutes EPE and in general is the only method to reliably diagnose EPE on needle biopsy. However, if one relies on the identification of tumor in fat to diagnose EPE on radical prostatectomy specimens, EPE will be underdiagnosed. One should also diagnose EPE when tumor extends beyond the condensed smooth muscle of the prostate to involve the looser connective tissue and thinner less compact smooth muscle outside of the prostate. One can also use the overall scanning magnification to assess whether tumor has extended beyond the normal contour of the gland. Reporting EPE at the apex is controversial as the boundaries of the prostate gland in this region are vague; benign prostatic acini are seen admixed with skeletal muscle in this region. One option is merely to state whether tumor is present and whether the margins are positive or negative in the apical region, while not attempting to determine if tumor is organ-confined in this area.

The other option is to assume that the urologist has gone as wide as possible and the inked margin at the apex is outside of the prostate. Tumor not extending to the ink is considered organ-confined and tumor at the inked margin is considered as showing EPE, unless benign prostatic glands are also seen at the inked margin whereby capsular incision is diagnosed. The specific location(s) of EPE are useful to report. Descriptors of EPE (unifocal versus multifocal or focal versus nonfocal or focal versus extensive or linear millimeters or number of blocks) may be used.

6. Lymph Node Status. Indicate the number of nodes involved and the total number of nodes evaluated.

7. Angiolymphatic Invasion. This finding is independently predictive of prognosis in radical prostatectomy specimens and should be recorded. The Association does not recommend the routine use of immunohistochemical stains to detect intravascular invasion.

8. Perineural Invasion. Perineural invasion in needle biopsy cores has been associated with EPE in most correlative radical prostatectomy studies, although its value as an independent prognostic factor has been questioned. Perineural invasion has been found to be an independent risk factor for predicting an adverse outcome in patients treated with external beam radiation. As it is easily measured and appears to have prognostic significance on biopsy, regardless of whether it is an independently prognostic parameter, its presence should be recorded on needle biopsy specimens. Perineural invasion has no prognostic significance in radical prostatectomy specimens and should not be mentioned in the pathology report.

9. Prostatic Intraepithelial Neoplasia (PIN) - Generally, low-grade PIN is not reported. The presence of isolated high grade PIN (HGPIN) should be reported in all biopsy specimens. The risk of cancer on repeat biopsy within 1 year of a needle biopsy diagnosis of HGPIN is not sufficiently different from the risk of cancer on repeat biopsy following a benign diagnosis on needle biopsy. Consequently, immediate repeat biopsy following a needle biopsy diagnosis of HGPIN is not necessary. Whether and when a repeat biopsy should be performed remains to be studied. The reporting of HGPIN in prostatectomy specimens is optional.

10. Staging - It is necessary to provide the TNM staging for radical prostatectomy specimens. The subdividing of pathologically organ confined disease whether the tumor involves <1/2 of one lobe (pT2a), involves >1/2 of one lobe (pT2b), or involves both lobes (pT2c) has been criticized. This aspect of the staging system will be changed in future revisions, and many urological pathologists do not subdivide pT2 tumor using the current system. Adenocarcinoma of the prostate is multifocal in more than 85% of cases. In many of these cases of bilateral and/or multifocal tumor, the other tumors are small, low-grade, and clinically insignificant. Consequently, the distinction between pathologic stages T2a and T2c may reflect several very different conditions: 1) a large single tumor nodule involving both sides; 2) separate large tumor nodules on each side; 3) dominant nodule on one side with multifocal minute tumor on the other side; or 4) bilateral minute multifocal tumor. Prognostically there are no differences between the subdivisions of pT2 (May et al, 2001; Freedland et al, 2004). Stage pT2b tumor almost never exists, as it is almost impossible for a tumor to involve greater than one-half of the lobe without involving the other lobe (Eichelberger et al, 2004). However, using the current staging system for subdividing pT2 tumor remains an option. It is now recommended by the American College of Surgeons, and will be updated in the new TNM Staging System such that pathologists do not fill in a “pM” (metastasis) category, as that is the domain of the clinician.

11. Submission of Tissue for Microscopic Evaluation in TURP and Radical Prostatectomy Specimens. TURP specimens should be sampled with 8 cassettes. In a younger man (e.g. <65 years old), consideration should be given to more extensive

sampling. Some experts suggest submitting additional cassettes based on the weight of the TURP. In general, random chips are submitted. If an unsuspected carcinoma is found in tissue submitted and it involves 5% or less of the tissue examined, the remaining tissue is generally submitted for microscopic examination, especially in younger patients.

Radical prostatectomy specimens may be totally submitted or partially sampled in a systematic fashion. For partial sampling in the setting of a grossly visible tumor, the sections with visible tumor along with the entire apical and bladder neck margins and samples from the base of each seminal vesicle should be submitted. If there is no grossly visible tumor, a number of systematic sampling strategies may be used. One that yields excellent prognostic information involves submitting the posterior aspect of each transverse slice along with a mid anterior block from each side. The anterior sampling detects tumors which predominantly involve the transition zone. The entire apical and bladder neck margins and base of each seminal vesicle should also be submitted.

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