Prognostic Significance of Tumor Volume in Radical Prostatectomy and Needle Biopsy Specimens

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Abbreviations and Acronyms

EPE = extraprostatic extension
FPC = fraction of positive cores
GLC = greatest length of cancer
GPC = greatest percent of cancer
MTD = maximum tumor diameter
PSA = prostate specific antigen
RP = radical prostatectomy
TLC = total length of cancer
TPC = total percent of cancer
TV = tumor volume

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Purpose: This review addresses the controversies that persist relating to the prognosis and reporting of tumor volume in adenocarcinoma of the prostate.
Materials and Methods: A search was performed using the MEDLINE database and referenced lists of relevant studies to obtain articles addressing the quantification of cancer on radical prostatectomy and needle biopsy.
Results: In the 2010 TNM classification system T2 tumor at radical prostatectomy is subdivided into pT2a (unilateral tumor occupying less than ½ a lobe), pT2b (unilateral tumor greater than ½ a lobe) and pT2c (bilateral tumor). This pathological substaging of T2 disease fails on several accounts. In most studies pT2b disease almost does not exist. By the time a tumor is so large that it microscopically occupies more than ½ a lobe, in the majority of cases there is bilateral (pT2c) tumor. An even greater flaw of the substaging system for stage pT2 disease is the lack of prognostic significance. In reporting pathologically organ confined cancer, it should be merely noted as pT2 without further subclassification. The data are conflicting as to the independent prognostic significance of objective measurements of tumor volume in radical prostatectomy specimens. The most likely explanation for the discordant results lies in the strong correlation of tumor volume with other prognostic markers such as extraprostatic extension and positive margins. In studies where it is statistically significant on multivariate analysis, it is unlikely that knowing tumor volume improves prediction of prognosis beyond routinely reported parameters to the degree that it would be clinically useful for an individual patient. An alternative is to record tumor volume as minimal, moderate or extensive, which gives some indication to the urologist as to the extent of disease. Not only does providing an objective measurement not add useful prognostic information beyond what is otherwise routinely reported by the pathologist, but many objective measurements done in routine practice will likely not be an accurate indicator of the true tumor volume.

There is also a lack of consensus regarding the best method of measuring tumor length when there are multiple foci in a single core separated by benign intervening prostatic stroma. Some pathologists, this author included, consider discontinuous foci of cancer as if it was 1 uninterrupted focus, the rationale being that these discontinuous foci are undoubtedly the same cancer going in and out of the plane of section. Measuring the cancer from where it starts to where it ends on the core gives the minimal length of cancer in the prostate. Others measure each focus individually, and the sum of these measurements is considered the cancer length on the core. Quantifying cancer with an ocular micrometer to record the total length or percent length of cancer is time-consuming, and the data are conflicting whether this is superior to other, simpler methods and whether any potential differences in predictive accuracy would translate into changes in clinical management. It is recommended that at a minimum the number of

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positive cores be recorded, unless fragmented involved cores preclude evaluation, along with at least 1 other more detailed measurement such as the percent of core involvement or length of cancer.

Conclusions: Consensus has been reached on some of the issues relating to quantifying tumor volume in prostate cancer, such as the lack of utility of substaging pT2 disease. Other questions such as whether to include or subtract intervening benign prostate tissue on prostate needle cores will require additional studies. Finally, matters such as the need to quantify cancer at radical prostatectomy or which method of quantifying cancer on needle biopsy is superior will likely remain contentious due to the close interrelationship and redundancy of prognostic variables.

Key Words: prostatectomy; prostatic neoplasms; tumor burden; biopsy, needle

Controversies persist relating to the prognosis and reporting of tumor volume in adenocarcinoma of the prostate. In radical prostatectomy specimens these controversies include the substaging of pathologically organ confined (pT2) prostate cancer and whether tumor volume provides independent prognostic information beyond what is routinely reported in pathology reports. There is no controversy that tumor volume in needle biopsy specimens should be reported, but there is also no consensus regarding which method of tumor quantification should be adopted.

PATHOLOGICAL SUBSTAGING OF pT2 DISEASE

Stage cT2 adenocarcinoma of the prostate is tumor confined to the gland on digital rectal examination, as opposed to stage pT2, which is tumor that is organ confined on pathological examination of the RP. In the 2010 TNM classification system cT2 is subdivided into T2a (unilateral tumor less than ½ a lobe), T2b (unilateral greater than ½ a lobe) and T2c (bilateral tumor). Numerous studies have validated this clinical staging classification system which intuitively makes sense. A larger palpable tumor, although clinically organ confined, has an increased likelihood of extraprostatic extension when examined at RP. The 2010 TNM system defines pT2 and cT2 stages using the same criteria, which fails on several accounts.

Incidence of pT2b

In most studies pT2b disease almost does not exist. By the time a tumor is so large that it microscopically occupies more than ½ a lobe, in the majority of cases there is bilateral (pT2c) tumor. Except in 1 outlier study the median percentage of pT2 disease that was pT2b was 1.5% and in some cases does not exist (table 1).[1–7]

Prognosis of Subdividing pT2

An even greater flaw of substaging pT2 disease is its lack of prognostic significance. Of 10 studies 9 demonstrated no significant difference in the risk of progression after RP among substages of pT2 disease on univariate analysis.[2,4–11] The only exception showed that pT2a disease had a better prognosis than pT2b/pT2c disease, although there was no difference between pT2b and pT2c.[1] In all 10 studies pT2 substaging did not correlate with prognosis once prostatectomy Gleason score and margins were accounted for. Why is pT2c (bilateral) cancer not a worse prognostic feature than pT2a (unilateral) disease? There are several scenarios resulting in pT2c (see figure). pT2c tumor may reflect a single large bilateral tumor, which could be associated with an adverse prognosis. This is the type of tumor that typically corresponds to clinical T2c disease (part *A* of figure). However, pT2c also refers to cases where there is only a minute focus of contralateral cancer, which would not necessarily be associated with a poor prognosis (parts *B* and *C* of figure). As pathological examination of RP specimens often reveals minute foci of bilateral cancer, there is a marked preponderance of pT2c disease in most studies. Excluding 1 outlier study, on average 72.3% of pathologically organ confined cancers were pT2c. In the extreme example, one can have insignificant bilateral minute foci of cancer, which would be staged as pT2c (part *B* of figure). Given the marked variation of tumor extent in pT2c disease and the virtual absence of pT2b disease, the lack of prognostic difference among pT2 substages is not surprising. The data are clear that subdividing pT2 disease, as is currently recommended in the 2010 TNM classification system, is without merit. In reporting pathologically organ confined cancer at our institution cases are merely noted as pT2 without further subclassification.

Table 1. *Incidence of pT2a, pT2b and pT2c disease at radical prostatectomy*

References	% pT2a	% pT2b	% pT2c
Caso et al[1]	18	6	76
DeCastro et al[2]	10.8	8.4	80.8
Eichelberger and Cheng[3]	19.6	0	80.4
Hong et al[4]	23.4	0.3	76.3
Kordan et al[5]	24.8	2.6	72.6
van Oort et al[6]	22	0	78
Chun et al[7]	16.2	66.0	17.8