# Value of Transition Zone Biopsy in Active Surveillance of Prostate Cancer

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**Purpose:** For patients on active surveillance there are limited data on transition zone sampling upon followup biopsy. We verified the value of transition zone biopsy in the active surveillance setting.

**Materials and Methods:** Our study included 1,059 sets of prostate biopsies from a total of 534 patients on active surveillance at the Johns Hopkins Hospital. Each set comprised at least 14 cores with 2 or more from the transition zone. Of these men 53 underwent radical prostatectomy.

**Results:** Patients with tumors in the peripheral zone as well as the transition zone had a higher maximum Gleason score and an increased maximum percent of cancer per core than men with tumor in the peripheral or transition zone only. In 12 of the 534 patients (2.2%) the tumor on active surveillance biopsy was limited to transition zone core(s). Of the 534 patients 11 (2.1%) had tumor with a high Gleason score (greater than 6) or extensive involvement (greater than 50%) of any core exclusively on transition zone biopsy. However, in 10 of 15 radical prostatectomy cases (66.7%) with prior positive transition zone biopsies the tumors had little or no transition zone component. In addition, transition zone status on biopsy had no significant relationship with Gleason score, extraprostatic extension or seminal vesicle involvement at radical prostatectomy.

**Conclusions:** Our data suggest that the additional yield is sufficiently low to argue against routine transition zone sampling in men undergoing followup biopsy on active surveillance. However, further study is needed to make definitive recommendations.

**Key Words:** prostate, prostatic neoplasms, biopsy, prostatectomy, diagnosis

**Abbreviations and Acronyms**

AS = active surveillance
EPE = extraprostatic extension
MP = multiparametric
MRI = magnetic resonance imaging
PSA = prostate specific antibody
PZ = peripheral zone
RP = radical prostatectomy
TZ = transition zone

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In the era of PSA screening and systematic ultrasound guided transrectal prostate biopsies prostate cancer has become a disease that is detectable early. To avoid complications after curative treatment AS is an increasingly common option in patients older than 65 years who have low risk cancer. Patients on AS receive regular followup. After there is evidence of disease reclassification, as typically documented by biopsies, patients undergo definitive treatment. The protocols of AS followup vary significantly among institutions in terms of rebiopsy frequency, number of cores and sampling location.

At our institution we use the Epstein criteria to define very low risk prostate cancer, including clinical stage T1c, PSA density less than 0.15 ng/ml, Gleason score 6 or less (no Gleason pattern 4 or 5), fewer than 3 positive cores and 50% or less

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cancer involvement of any positive core.[1] Patients with low risk cancer who are on AS undergo followup biopsies at 1-year intervals. In an earlier study we noted that patients initially on AS with biopsy reclassification to worse disease had large tumor nodules located predominantly anterior.[2] Because such tumors may not be detected by regular peripheral zone 12-core biopsy, we modified our AS biopsy protocol to include anterior/TZ sampling.

In this study our aim was to determine the results of yearly followup biopsies, including TZ sampling, in a cohort of men followed on AS. In particular, we determined whether TZ biopsies contained adverse findings, such as the highest Gleason score, number of positive cores or maximum percent tumor involvement. We also determined whether there would have been adverse consequences to patients had these biopsies not been performed.

## MATERIALS AND METHODS

We identified biopsies from 534 patients on AS at the Johns Hopkins Hospital that included TZ sampling in followup biopsies. A total of 1,059 sets of prostate biopsies were included, spanning from January 2009 to January 2013. All cases had at least a 14-core biopsy (median 14, range 14 to 32) with 2 or more TZ cores. Of 1,059 AS biopsy sets in our study 1,037 (97.9%) comprised 14 cores, including 12 regular PZ cores and 2 TZ cores. Extended biopsies with greater than 16 cores were done in only 3 cases (0.3%). Most initial biopsies were performed elsewhere with the requirement of a minimum of 12 sampled cores. The mean number of cores at initial biopsy was 13.2 (median 12). No patient in the current study underwent TZ sampling as part of the initial biopsy and 53 patients underwent RP with pathological specimens available.

The highest Gleason scores and the maximum percent of tumor involvement in TZ vs PZ cores were recorded separately for each biopsy specimen of each patient. The number of positive cores per biopsy was also recorded. If there were more than 1 biopsy specimen with time in a given patient with cancer, the maximum percent and number of cores with tumor involvement were defined as the average of all tumor positive biopsies.

Criteria to classify a patient as having exceeded the criteria to stay on AS was based only on biopsy pathology since our prior study showed that PSA kinetics are not accurate for identifying disease reclassification during AS.[3] Biopsy reclassification was defined as 1) Gleason score greater than 6, 2) more than 2 PZ cores involved by cancer or 3) tumor involvement of more than 50% of any core.

The study was approved by the Johns Hopkins institutional review board. Statistical tests were performed using Excel®. The chi-square test and Student t-test were used to compare categorical and continuous variants, respectively. Statistical significance was considered at $p < 0.05$.

## RESULTS

Of the 534 study patients 371 had prostatic adenocarcinoma on at least 1 AS followup biopsy. Mean age of the 371 patients was 67.8 years and mean followup was 25.1 months. In 12 of the 534 patients (2.2%) the only tumor on followup biopsy was exclusively present in TZ biopsies. Another 74 patients had prostate cancer in PZ as well as TZ biopsies. The age distribution in each zonal group (PZ only, TZ only, and mixed PZ and TZ) did not differ significantly. The TZ only group also did not statistically differ from the PZ only group in maximum biopsy Gleason score, maximum percent of cancer per core or proportion of biopsy reclassification. Patients with tumors in PZ as well as TZ biopsies had a higher maximum Gleason score, an increased maximum percent of cancer per core and a higher percent of biopsy reclassification than men in the PZ only group (table 1).

Three of the 12 patients with cancer limited to TZ biopsies had a Gleason score of greater than 6 or a maximum tumor percent of greater than 50% in the positive core. Also, 8 of the 74 patients with cancer in the TZ as well as the PZ had a Gleason score of greater than 6 and/or a maximum tumor percent of greater than 50% exclusively in the TZ biopsy. Taken together evidence of biopsy reclassification would have been missed in 11 of the 534 study patients (2.1%) without TZ sampling (table 2). Biopsy

**Table 1.** *Patients by tumor zonal distribution on prostate biopsy*

| | PZ Only | TZ Only | p Value | Mixed PZ + TZ | p Value vs PZ Only |
|---|---|---|---|---|---|
| No. pts | 285 | 12 | | 74 | — |
| Mean age (range) | 67.8 (48–87) | 66.8 (59–78) | 0.579 | 67.6 (55–78) | 0.810 |
| No. Gleason score (%): | | | | | |
| 6 or Less | 235 (82.5) | 10 (83.3) | 0.938* | 48 (64.9) | <0.001* |
| 3 + 4 = 7 | 32 (11.2) | 1 (8.3) | | 19 (25.7) | — |
| 4 + 3 = 7 | 12 (4.2) | 0 | | 4 (5.4) | — |
| 8 | 3 (1.1) | 1 (8.3) | | 3 (4.1) | — |
| 9 or 10 | 3 (1.1) | 0 | | 0 | — |
| Mean pos core(s) max % Ca (range) | 18.4 (5–90) | 22.9 (5–90) | 0.200 | 27.7 (5–95) | <0.001 |
| Mean No. pos cores (range) | 1.7 (1.0–7.0) | 1.0 (1.0–1.0) | 0.011 | 3.1 (1.0–8.5) | <0.001 |
| No. biopsy reclassification (%) | 98 (34.4) | 3 (25.0) | 0.501 | 75.7 (56) | <0.001 |

* Compared to greater than 6.