# The Impact of Repeat Prostate Biopsies on Oncologic, Pathological and Perioperative Outcomes after Radical Prostatectomy

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**Purpose:** The impact of repeat biopsy sessions on radical prostatectomy remains controversial regarding perioperative, pathological and oncologic outcome.

**Materials and Methods:** We analyzed the records of 12,624 patients who underwent radical prostatectomy from 2007 to 2013. The association of the number of biopsy sessions (range 1 to 3 or more) with pathological outcomes and perioperative complications was analyzed using the Wilcoxon matched pair test. To test the association between biopsy sessions and biochemical recurrence-free survival we used Kaplan-Meier curves and multivariable Cox regression analysis.

**Results:** Of the patients 89.2% had 1 biopsy session, 7.4% had 2 sessions and 3.4% had 3 or more sessions. Median followup was 36.6 months. In patients with 1, 2 and 3 or more biopsy sessions prostate volume (38, 44 and 45 ml) and prostate specific antigen (6.7, 7.6 and 10.1 ng/ml, respectively) were greater (each $p < 0.001$). The perioperative outcome was more favorable. Patients with 1, 2 and 3 or more biopsy sessions more often had organ confined tumors (67.6%, 72.1% and 72.9%, $p = 0.003$) and higher tumor volume (3.1, 3.0 and 3.6 ml, $p < 0.001$) but a lower tumor percent (7.5%, 3.7% and 2.4%, respectively, $p < 0.001$). More biopsy sessions were associated with fewer lymph node metastases (1, 2 and 3 sessions 0.23, 0.13 and 0.17, respectively, $p < 0.001$). Gleason score and surgical margin status did not differ. The overall biochemical recurrence rate was 18.9% and it was comparable among the biopsy groups. No association was found between the number of biopsies and biochemical recurrence.

**Conclusions:** Patients with multiple biopsy sessions experience a slightly more favorable pathological outcome without an impact on the oncologic outcome. The perioperative outcome was more favorable in patients with multiple biopsies.

**Key Words:** prostatic neoplasms, prostatectomy, biopsy, outcome and process assessment (health care), prostate specific antigen

**Abbreviations and Acronyms**

AS = active surveillance
BCR = biochemical recurrence
Bx = biopsy
DRE = digital rectal examination
LN = lymph node
PCa = prostate cancer
PSA = prostate specific antigen
RP = radical prostatectomy

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PROSTATE Bx is the gold standard to diagnose PCa. In the current era initial prostate Bx is triggered by abnormal serum PSA or abnormal DRE.[1] In many men the initial Bx is negative.[2] Indications for repeat Bx are consecutively rising and/or persistently high PSA, and suspicious DRE. In some cases of atypical small acinar proliferation or prostatic intraepithelial neoplasia at multiple biopsy sites a repeat Bx is indicated

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as well.[1] Furthermore, repeat biopsies are included in deferred treatment strategies such as AS.[3]

These factors lead to an increasing number of men presenting with multiple Bx sessions at RP. Especially many men considering AS fear the potential risk of cancer spreading and, therefore, a worse outcome caused by multiple biopsies.[4] Further concerns are the common complications of Bx such as hemospermia, hematuria and prostatitis.[5] Patients fear that inflammation might cause tissue reactions that could lead to a higher perioperative rate of complications.

Previous studies demonstrate only different PCa locations and sizes in patients after repeat biopsies while grade and stage did not seem to be influenced.[6,7] In contrast, other previous data revealed that patients who undergo RP after repeat Bx harbor PCa that is related to better pathological outcomes.[8,9]

Therefore, at a large European cohort we determined whether repeat prostate Bx sessions before RP were associated with different perioperative, pathological and oncologic outcomes. Specifically, we hypothesized that multiple Bx sessions would be associated with better pathological and oncologic outcomes but a worse perioperative outcome.

## PATIENTS AND METHODS

We analyzed the records of 15,840 patients who underwent RP between January 2007 and December 2013 at a high volume tertiary center of care. Excluded from study were 306 patients who underwent RP as a palliative treatment, 75 with a history of prior radiotherapy and 3 who received initial focal therapy. Another 2,832 patients had to be excluded because of incomplete data. Overall 12,624 patients were left for final analysis.

Data were collected prospectively in an institutional review board approved database. RP was performed by 1 of 10 high volume surgeons. Patients were stratified by the number of Bx sessions before RP.

RP was performed using an open retropubic approach or a robot-assisted laparoscopic approach as previously described.[10] The pathological outcome was assessed with the 2002 AJCC (American Joint Committee on Cancer) staging system and tumors were graded according to the Gleason grading system.[11,12] Insignificant cancer was defined as pT2, Gleason score 3 + 3, pNx or pN0 and tumor volume 0.5 ml or less.[13]

Patient followup after RP included periodic PSA testing and DRE. Postoperative imaging was performed to detect local or systemic recurrence according to PSA level, patient preference and patient symptoms. BCR was defined as PSA greater than 0.2 ng/ml and rising.

The number of Bx sessions (range 1 to 3 or more) was examined as a categorical variable (1, 2 and 3 or greater). The association between the number of prior Bx sessions and pathological outcome as well as perioperative complications was analyzed using the Wilcoxon matched pairs test. To evaluate the association between the number of Bx sessions at RP and BCR-free survival we used Kaplan-Meier curves and multivariable Cox proportional hazards regression. All statistical analyses were performed with RStudio®, version 0.99.467, an integrated development environment for R, version 3.2.2 (https://www.R-project.org). Statistical significance was considered at $p < 0.05$.

## RESULTS

### Preoperative Characteristics

Of the 12,624 men 1, 2 and 3 or more Bx sessions were performed in 11,257 (89.2%), 936 (7.4%) and 431 (3.4%), respectively. Of the 431 men with 3 or more biopsies 273, 157 and 1 underwent 3, 4 and 6 sessions, respectively. Table 1 lists patient demographics stratified by the number of Bx sessions. Median prostate volume was 39 ml (IQR 30–51). Prostate volume was statistically significantly higher in patients with more Bx sessions (1, 2 and 3 or more 38, 44 and 45 ml, respectively, $p < 0.001$). More Bx sessions were also associated with greater age at surgery (1, 2 and 3 or more 65, 66 and 67 years, $p < 0.001$), significantly higher preoperative PSA (6.7, 7.6 and 10.1 ng/ml, $p < 0.001$) and a statistically significantly greater number of cores per Bx (10, IQR 8–12; 10, 8–12; and 10, 10–12, respectively, $p < 0.001$). However, the number of positive cores per Bx was statistically significantly lower for repeat Bx sessions (1, 2 and 3 or more 3, IQR 2–5; 3, IQR 2–5; and 3, IQR 2–4, respectively, $p < 0.001$). According to the D'Amico risk classification patients with 3 or more Bx sessions were significantly more often at high risk ($p < 0.001$). Of the 12,624 patients 25 were on AS before RP, including 4, 11 and 10 with 1, 2 and 3 or more sessions, respectively.

### Outcomes

***Perioperative.*** Table 2 lists perioperative characteristics stratified by the number of Bx sessions. RP was performed via an open retropubic approach in 10,737 patients (85.1%) and a robot-assisted laparoscopic approach was used in 1,887 (14.9%).

Patients with multiple Bx sessions had severe complications (Clavien-Dindo grade III or greater) less often than patients with only a single Bx ($p < 0.001$). No association was noted for operative time, blood loss or time to catheter removal with the number of Bx sessions. Additionally, no difference was noted in rectal injuries. Mean hospital stay was significantly longer in patients with repeat Bx sessions (1, 2 and 3 or more $7.9 \pm 12.4$, $7.9 \pm 3.7$ and $8.0 \pm 3.7$ days, $p < 0.001$) and patients with more Bx sessions were more likely to undergo bilateral nerve