How Much Extent can We Rely on Partial Sampling of Radical Prostatectomy Specimens?

Radikal Prostatektomi Materyallerinde Parsiyel Örnekleme Yöntemi Ne Kadar Güvenilir?

Aim: Prostatic adenocarcinoma is the most common cancer among men in the world and prostatectomy specimens are one of the most commonly encountered materials in pathology laboratories. Histopathological evaluation of radical prostatectomy specimens provides very important prognostic parameters to predict patient’s prognosis and to choose an appropriate treatment. There is no globally accepted standard grossing method for radical prostatectomy materials. Different grossing protocols are preferred in different centers considering financial condition, storage spaces, number of technicians and pathological workload.

Methods: In this study, we evaluated 50 radical prostatectomy specimens using total and partial sampling methods and compared the results.

Results: As a result of the partial sampling method the number of blocks per case was reduced prominently, and depending on this workload and financial burden also reduced. The correlation between total and partial sampling methods was statistically significant.

Conclusion: Partial sampling method can be a choice of grossing of radical prostatectomy specimens with the help of macroscopic, clinical and radiological findings.

Keywords: Prostate, radical prostatectomy, sampling methods


Metod: Çalışmamız kliniğimize kabul edilen 50 radikal prostatektomi materyal toplam ve parsiyel örneklemenin yöntemleri ile değerlendirilerek sonuçlar karşılaştırılmıştır.

Bulgular: Parsiyel örneklemeye yöntemi sonucunda elde edilen blok sayılarında belirgin ve dolayısıyla iş yükü ve mali yükte bir azalma görülürken sonuçların istatistiksel olarak korelasyon sunucuna varlığı belirlenmiştir.

Sonuç: Çalışmamızı gerçekleştirme hatıra parsiyel örneklemeye yöntemi ile klinik için önemli olan parametreleri ulaşabilir maket ve klinik ve radyolojik bulgulardan da destek alılarak radikal örneklemeyi yerine tercih edilebilecek bir yöntemdir.

Anahtar Sözcükler: Prostat, radikal prostatektomi, örneklemeye yöntemler

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Abstract

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**Introduction**

Prostatic adenocarcinoma is the most common cancer and second leading cause of cancer death among men in the world (1). The incidence of prostate cancer in early stage had been sharply increased at the end of twentieth century as a result of efficiency of modern cancer scanning programs detecting asymptomatic diseases and developing awareness of the disease (1). Radical prostatectomy is an initial and the most important step in the treatment of prostatic adenocarcinoma because only accurate pathological examination of specimens provides important diagnostic, prognostic, and therapeutic clues. Therefore, there is a considerable increase in the number of radical prostatectomy specimens in pathology laboratories of university and research hospitals. Several different sampling methods are recommended by surgical pathology text books, grossing manuals, and published working group reports. Histopathological evaluation of prostatectomy materials provides important pathologic information such as Gleason score, margin status, and pathologic stage which are crucial for selecting adjuvant therapy and for determining the prognosis (2). Preferred sampling method should provide all these necessary parameters. The 2009 International Society of Urological Pathology (ISUP) Consensus Conference put emphasis on cost restraints and time consuming procedures of total embedding and left to the pathologist’s decision and recommended some strict protocols to be followed if partial embedding will be used (3). A survey conducted by the American Society of Clinical Pathologists concluded that only 12% of pathologists used entire sampling method (4). Another survey performed in our country, Turkey, revealed that 57% of our pathologists embeded entire gland (5). Total embedding is a costly and time-consuming procedure and causes increased workload in all sampling, blocking, staining, scanning and archiving stages. The aim of this study was to compare the results of total and alternative sampling methods in radical prostatectomy specimens and to investigate the reliability of alternative sectioning methods in terms of key pathologic prognostic parameters.

**Methods**

With the approval of institutional review board of Dışkapı Yıldırım Beyazıt Training and Research Hospital (approval ID: 230515.21/17), 50 patients, who underwent radical prostatectomy with the diagnosis of acinar prostatic adenocarcinoma between 2009 and 2011, were randomly included in this study. Originally all samples were assessed according to total embedding protocol as summarized below. Formalin-fixed surgical specimens were weighed, measured and inked carefully. The apical and basal margins were sectioned parallel to the urethra in 5 mm thickness and serially resected perpendicular to the inked margin. Seminal vesicles and ducts were totally embedded. After that, serial transverse sections of 3-5 mm thickness were made. The sections were evaluated carefully for macroscopically identifiable tumor and dissected into four quadrants as right posterior, left posterior, right anterior and left anterior segments. Each segment was blocked separately and named precisely. Average block number was 38 per case.

All tumor samples were evaluated for key pathologic parameters, such as Gleason score, presence of perineural invasion, extraprostatic extension and pathologic stage. Then, all cases were reevaluated with selected slides in accordance with partial sampling method by two other pathologists. The limited sampling method was built to include haematoxylin and eosin stained slides representing the whole slice which were selected by skipping every other slice beginning from apical portion as forming an alternate slicing. Slides representing apical margins, bladder neck margins and seminal vesicles were retained. Selection of blocks according to alternate slice method resulted in an average of 22 blocks per case.

**Results**

The sampled surgical specimens weighed 45.54 g on average (range: 21-75 g). The specimens were sectioned into 7-12 slices (mean: 7.32). The macroscopic features of the surgical specimens are summarized in Table 1. 37% reduction was achieved in the number of blocks (Table 2). The sensitivity of partial sampling method for Gleason score 7 was 87.5%, but the sensitivity of partial sampling method for Gleason score ≥7 was 8% (4). However, the specificity of alternative method for Gleason score ≥7 was 44% (Table 3). For extraprostatic extension, the sensitivity and specificity rates were 61.5% and 100%, respectively. The correlation rates between two sampling methods were 70.3%, and 60%, respectively for extraprostatic extension and pathologic stages. There was complete correlation in surgical margin and perineural invasion evaluation between the two sampling methods. Alternative slicing and total sampling methods provided identical pathologic stage in 76% of cases (Table 4). All correlation rates were statistically significant (p<0.001).

**Statistical Analysis**

Statistical analysis was performed by using SPSS for Windows Version 15.0 Software Package and Cohen’s Kappa statistics was used to measure the agreement of two sampling methods.

**Discussion**

Radical prostatectomy specimens are one of the most common materials which pathologists encounter in routine
practice. For grossing radical prostatectomy specimens, many protocols and recommendations have been proposed, but general consensus has not been achieved yet (3,6-11). Although recent conference of the ISUP concluded that partial methods were also acceptable (3), there are still controversies on partial sampling of radical prostatectomy materials. In macroscopic examination, recognizing tumor areas is often difficult, especially in early stages (12-14). Therefore, some pathologists prefer total embedding as the safest method (5,13). On the other hand, many studies revealed that limited sample methods also provided key histopathologic parameters (14-17). In terms of partial sampling of radical prostatectomy materials, there are many different approaches (14,18). In the presence of grossly visible tumor, it is recommended to embed proximal and distal margins, seminal vesicles, visible tumors with relevant margins and susceptible other tumor foci (19). Some guidelines also recommend embedding of the posterior aspects of every transverse slice and single mid anterior slice form each side in addition to proximal and distal margins and seminal vesicles in the absence of grossly visible tumor (19). In this study, we preferred to perform alternate slicing method as one of the partial sampling methods. It is a simple, easy-to-use method and allows the pathologist or inexperienced residents good orientation of unsampled tissue in case of necessity. In the case of macroscopically identifiable tumor, it can be appropriate to include extra blocks representing all tumoral or suspected areas. In some centers, digital images of gross specimens are taken and saved (20). It is also a useful method to reevaluate macroscopic appearance of slices in some circumstances.

### Table 1. Macroscopic features of surgical specimens

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Median</th>
<th>Standard deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>45.54 gr</td>
<td>42.50 gr</td>
<td>13.964 gr</td>
<td>21 gr</td>
<td>75 gr</td>
</tr>
<tr>
<td>Number of slices</td>
<td>7.32</td>
<td>7.00</td>
<td>1.285</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>The largest diameter</td>
<td>5.06 cm</td>
<td>5.00 cm</td>
<td>1.018 cm</td>
<td>3 cm</td>
<td>9 cm</td>
</tr>
</tbody>
</table>

gr: Gram, cm: Centimeter

### Table 2. The number of blocks per specimen

<table>
<thead>
<tr>
<th></th>
<th>Mean (n)</th>
<th>Median (n)</th>
<th>Standard deviation (n)</th>
<th>Number of blocks per specimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Minimum</td>
</tr>
<tr>
<td>Total sampling</td>
<td>37.98</td>
<td>35.50</td>
<td>7.795</td>
<td>27</td>
</tr>
<tr>
<td>Partial sampling</td>
<td>22.56</td>
<td>22.00</td>
<td>4.643</td>
<td>10</td>
</tr>
</tbody>
</table>

n: number

### Table 3. Gleason scores achieved by total and partial sampling method

<table>
<thead>
<tr>
<th>Gleason score (total sampling) (p)</th>
<th>2-6</th>
<th>7</th>
<th>8-10</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-6</td>
<td>10</td>
<td>3</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>21</td>
<td>6</td>
<td>35</td>
</tr>
<tr>
<td>8-10</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total (n)</td>
<td>18</td>
<td>24</td>
<td>8</td>
<td>50</td>
</tr>
</tbody>
</table>

n: number of cases, p: points

### Table 4. Pathologic grades achieved by total and partial sampling method

<table>
<thead>
<tr>
<th>Pathologic stage (total sampling) (n)</th>
<th>T2a</th>
<th>T2c</th>
<th>T3a</th>
<th>T3b</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2a</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>T2c</td>
<td>1</td>
<td>24</td>
<td>2</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>T3a</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>T3b</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Total (n)</td>
<td>8</td>
<td>27</td>
<td>5</td>
<td>10</td>
<td>50</td>
</tr>
</tbody>
</table>

n: Number of cases
In addition, in the presence of preoperative needle biopsy reports, additional samples from positive quadrants can be taken. In comparison with total embedding method, the alternate slicing method successfully estimated all histopathologic predictive parameters and had a statistically significant correlation with total sampling in our study. We obtained identical Gleason score in 34 of the cases (68%). When we consider interobserver variability and reproducibility levels for Gleason scoring, this partial sampling method provided good correlation (21). We obtained complete correlation in perineural invasion and surgical margin evaluation between the two methods. Partial sampling method was failed to detect extraprostatic extension only in five of the cases (10%). However, we assume that it is a reasonable result, because there was no complete concordance in interpretation of extraprostatic extension among even expert pathologists (22). In addition to that, partial sampling method is a very practical and time-saving method providing an important reduction in block numbers and reducing financial costs in pathology laboratories.

Conclusion

In conclusion, although the limited sampling protocol provides statistically significant results, because of the critical role of pathological assessment in the treatment of prostatic adenocarcinoma, it can be found unsatisfactory by some pathologists. However, we think that with the help of advanced radiologic modalities, and macroscopic and clinical findings, an alternate slicing method can be preferred and it can provide key prognostic parameters.

Ethics

Ethics Committee Approval: This study was approved by Ethics Committee of Board of Dışkapı Yıldırım Beyazıt Training and Research Hospital with approval ID: 230515.21/17. Informed Consent: It was taken.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Tuba Dilay Kökenek Ünal, Ayşe Selcen Oğuz Erdoğan, Nesrin Gürçay. Concept: Tuba Dilay Kökenek Ünal, Ayşe Selcen Oğuz Erdoğan, Murat Alper. Design: Tuba Dilay Kökenek Ünal, Ayşe Selcen Oğuz Erdoğan, Murat Alper. Data Collection or Processing: Tuba Dilay Kökenek Ünal. Analysis or Interpretation: Tuba Dilay Kökenek Ünal, Ayşe Selcen Oğuz Erdoğan. Literature Search: Tuba Dilay Kökenek Ünal, Nesrin Gürçay. Writing: Tuba Dilay Kökenek Ünal. Conflict of Interest: No conflict of interest was declared by the authors. Financial Disclosure: The authors declared that this study received no financial support.

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