



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

Radikal Prostatektomi Materyallerinde Parsiyel Örnekleme Yöntemi Ne Kadar Güvenilir?

Tuba Dilay Kökenek Ünal, Ayşe Selcen Oğuz Erdoğan*, Nesrin Gürçay**, Murat Alper**

Kayseri Training and Research Hospital, Clinic of Pathology, Kayseri, Turkey

*Ankara Children's Hematology and Oncology Hospital, Clinic of Pathology, Ankara, Turkey

**Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Pathology, Ankara, Turkey

Abstract

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

Öz

Amaç: Prostatik adenokarsinomlar dünyada erkeklerde görülen kanserler arasında en yaygın olarak görülen kanser olup radikal prostatektomi materyalleri patoloji laboratuvarlarında en çok takibe alınan materyallerin başında gelmektedir. Prostatektomi materyallerinin histopatolojik incelemesi sonucunda elde edilen prognostik parametreler hastalığın seyri ve uygulanacak tedavi yöntemi konusunda klinisyene yol göstermektedir. Radikal prostatektomi materyalleri için dünya çapında kabul görmüş tek bir örnekleme yöntemi bulunmamaktadır. Farklı merkezlerde farklı yöntemler tercih edilmektedir. Bu tercihte mali sorunlar, arşivleme kapasitesi, personel sayısı gibi faktörler rol oynamaktadır.

Metod: Bu çalışmada kliniğimize kabul edilen 50 radikal prostatektomi materyali total ve parsiyel örnekleme yöntemi ile değerlendirilerek sonuçlar karşılaştırılmıştır.

Bulgular: Parsiyel örnekleme yöntemi sonucunda elde edilen blok sayısında belirgin ve dolayısıyla iş yükünde ve mali yükte bir azalma görülürken sonuçların istatistiksel olarak korelasyon gösterdiği sonucuna varıldı.

Sonuç: Çalışmamız göstermiştir ki, parsiyel örnekleme yöntemi ile klinik için önemli olan parametrelere ulaşılabilmektedir ve klinik ve radyolojik bulgulardan da destek alınarak radikal örnekleme yerine tercih edilebilecek bir yöntemdir.

Anahtar Sözcükler: Prostat, radikal prostatektomi, örnekleme yöntemler

Address for Correspondence/Yazışma Adresi: Tuba Dilay Kökenek Ünal
Kayseri Training and Research Hospital, Clinic of Pathology, Kayseri, Turkey
E-mail: tubadilay@gmail.com

Received/Geliş Tarihi: 21 March 2016 **Accepted/Kabul Tarihi:** 23 May 2016

This study was presented in part as poster presentation at 24th European Congress of Pathology, which was held on 8-12 September 2012, in Prague and published in part in Virchows Archiv. 2012;(Suppl 1): S291.

©Copyright 2017 by The Medical Bulletin of Haseki Training and Research Hospital
The Medical Bulletin of Haseki published by Galenos Yayınevi.

©Telif Hakkı 2017 Haseki Eğitim ve Araştırma Hastanesi
Haseki Tıp Bülteni, Galenos Yayınevi tarafından basılmıştır.

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 embedded 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 tumoral 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 from 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

	Mean	Median	Standard deviation	Minimum	Maximum
Weight	45.54 gr	42.50 gr	13.964 gr	21 gr	75 gr
Number of slices	7.32	7.00	1.285	5	12
The largest diameter	5.06 cm	5.00 cm	1.018 cm	3 cm	9 cm

gr: Gram, cm: Centimeter

Table 2. The number of blocks per specimen

	Mean (n)	Median (n)	Standard deviation (n)	Number of blocks per specimen	
				Minimum	Maximum
Total sampling	37.98	35.50	7.795	27	61
Partial sampling	22.56	22.00	4.643	10	33

n: number

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

		Gleason score (total sampling) (p)			Total (n)
		2-6	7	8-10	
Gleason score (partial sampling) (p)	2-6	10	3	0	12
	7	8	21	6	35
	8-10	0	0	2	2
Total (n)		18	24	8	50

n: number of cases, p: points

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

		Pathologic stage (total sampling) (n)				Total (n)
		T2a	T2c	T3a	T3b	
Pathologic stage (partial sampling) (n)	T2a	7	3	1	0	11
	T2c	1	24	2	3	30
	T3a	0	0	2	2	4
	T3b	0	0	0	5	5
Total (n)		8	27	5	10	50

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.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin* 2015;65:5-29.
2. Kench JG, Clouston DR, Delprado W, et al. Prognostic factors in prostate cancer. Key elements in structured histopathology reporting of radical prostatectomy specimens. *Pathology* 2011;43:410-9.
3. Samaratunga H, Montironi R, True L, et al. International society of urological pathology (ISUP) consensus conference on handling and staging of radical prostatectomy specimens. working group 1: specimen handling. *Mod Pathol* 2011;24:6-15.
4. True LD. Surgical pathology examination of the prostate gland. Practice survey by American society of clinical pathologists. *Am J Clin Pathol* 1994;102:572-9.
5. Doganavsargil B, Nalbantoglu I, Hekimgil M. Handling and reporting of radical prostatectomy specimens: A practice survey among pathologists. *Turkish Journal of Pathology* 2007;23:74-81.
6. Egevad L. Handling of radical prostatectomy specimens. *Histopathology* 2012;60:118-24.
7. Gill PS, Roberts IS, Browning L, et al. The handling and sampling of radical prostatectomy specimens for reporting and research: the Oxford approach. *J Clin Pathol* 2012;65:1057-61.
8. Ohori M, Kattan M, Scardino PT, Wheeler TM. Radical prostatectomy for carcinoma of the prostate. *Mod Pathol* 2004;17:349-59.
9. Sung MT, Davidson DD, Montironi R, Beltran AL, Cheng L. Radical prostatectomy specimen processing: A critical appraisal of sampling methods. *Diagn Histopatol* 2007;13:490-8.
10. Sringley JR. Key issues in handling and reporting radical prostatectomy specimens. *Arch Pathol Lab Med* 2006;130:303-17.
11. Montironi R, Van der Kwast T, Boccon-Gibod L, Bono AV, Boccon-Gibod L. Handling and pathology reporting of radical prostatectomy specimens. *Eur Urol* 2003;44:626-36.
12. Renshaw AA. Correlation of gross morphologic features with histologic features in radical prostatectomy specimens. *Am J Clin Pathol* 1998;110:38-42.
13. Bell KB, Kida M, Cooper K. Histopathology sampling of radical prostatectomy specimens: representative or entire submission? *Histopathology* 2011;59:1013-4.
14. Sehdev AE, Pan CC, Epstein JI. Comparative analysis of sampling methods for grossing radical prostatectomy specimens performed for nonpalpable (stage T1c) prostatic adenocarcinoma. *Hum Pathol* 2001;32:494-9.
15. Kim K, Pak PJ, Ro JY, Shin D, Huh SJ, Cho YM. Limited sampling of radical prostatectomy specimens with excellent preservation of prognostic parameters of prostate cancer. *Arch Pathol Lab Med* 2009;133:1278-84.
16. Llanos CA, Blieden C, Vernon SE. Processing radical prostatectomies: an alternate-slice method is comparable with total embedding. *Ann Diagn Pathol* 2012;16:284-7.

17. Vainer B, Toft BG, Olsen KE, Jacobsen GK, Marcussen N. Handling of radical prostatectomy specimens: total or partial embedding? *Histopathology* 2011;58:211-6.
18. Doganavsargil B, Hekimgil M, Simsir A, Cal C, Soydan S. A study on histological prognostic factors and partial sampling methods in radical prostatectomy. *Ege J Med* 2002;41:133-41.
19. Association of Clinical Pathologists. Guidelines for the macroscopic processing of radical prostatectomy and pelvic lymphadenectomy specimens. *J Clin Path* 2008;61:713-21.
20. Trpkov K, Warman L. Use of digital maps and sampling of radical prostatectomy specimens. *Arc Pathol Lab Med* 2006;130:1751-2.
21. Kuroiwa K, Shiraishi T, Ogawa O, et al. Discrepancy between local and central pathological review of radical prostatectomy specimens. *J Urol* 2010;183:952-7.
22. Evans AJ, Henry PC, Van der Kwast TH, et al. Interobserver variability between expert urologic pathologists for extraprostatic extension and surgical margin status in radical prostatectomy specimens. *Am J Surg Path* 2008;32:1503-12.