TURKISH JOURNAL OF UROLOGY Turkish Journal of Urology 2015; 41(1): 32-8 • DOI: 10.5152/tud.2015.91249

UROONCOLOGY

Invited Review

When prostate cancer remains undetectable: The dilemma

Mahmoud Othman Mustafa[1], Louis Pisters[2]

ABSTRACT

Since the first report on the efficacy of sextant biopsy under transrectal ultrasound guidance, there have been many modifications related to the total number of cores and the localization of biopsies to improve the prostate cancer (PCa) detection rate. The 2010 National Comprehensive Cancer Network Early PCa Detection Guidelines noted the 12-core biopsy scheme as the standard. However, this extended biopsy scheme still fails to detect 20% of high-grade PCa that can be detected by detailed pathological evaluation of radical prostatectomy; therefore, there is need for saturation biopsies. The existence of suspicions of PCa after previous negative biopsy or biopsies represents a valid indication for saturation biopsy. There has been no significant increment in morbidity or in insignificant PCa detection rates when a saturation biopsy scheme was used with an extended biopsy scheme. Along with the improvement in the PCa detection rate, accurate oncological mapping of PCa is another important consideration of saturation biopsies. The ideal number of cores and the diagnostic value of saturation biopsy after the failure of initial therapy are some of the issues that need to be addressed. Preliminary reports have shown that magnetic resonance imaging can improve the PCa detection rate, save patients from unnecessary biopsies, and decrease the need for a high number of cores; however, multiple limitations continue to exist.

Keywords: Prostate; prostate biopsy; prostate cancer

[1]Department of Urology, An-najah National University, Nablus, Palestine

[2]Department of Urology, MD Anderson Cancer Center, University of Texas, Houston, Texas, USA

Submitted: 19.02.2014

Accepted: 01.09.2014

Correspondence: Mahmoud Othman Mustafa, Department of Urology, An-najah National University, Nablus, Palestine
Phone: 0232-2434444
E-mail: dr_mahmoud681@yahoo.com

Available online at www.turkishjournalofurology.com

History of prostate biopsy (PBx)

Watanabe et al.[1] first introduced the use of transrectal ultrasound-guided (TRUSG) biopsy into the armamentarium of prostate cancer (PCa). Hodge et al.[2] reported on the efficacy of sextant biopsy under TRUS guidance for PCa detection. Initially, only ultrasonically detected hypoechoic areas were sampled.[3,4] In 1995, Stamey et al.[5] suggested that biopsy should be obtained from a more lateral location to better sample the anterior horn of the peripheral zone. Similarly, Norberg et al.[6] noticed that the second set of sextant biopsies performed immediately after the first set increased the PCa detection rate by as much as 30%. These findings prompted investigators to seek alternative biopsy schemes with an increased number of biopsy cores and/or sampling of the lateral peripheral zones for improved PCa detection.[7-15] Mc Neal et al.[16] provided the ground for better sampling of peripheral zones with special attention to the anterior horn. These modifications related to the total number of cores and the localization of biopsies improved the PCa detection rate.

Extended biopsy scheme

Uzzo et al.[17] and Karakiewcz et al.[18] were the first to demonstrate an increase in the PCa detection rate in proportion to the number of biopsy cores obtained. Their findings provided the foundation for extended PBx where at least 10 cores are taken. Chen et al.[19] examined various biopsy schemes to define the approach associated with the highest PCa detection rate. They suggested that an 11-core biopsy strategy may present the ideal detection scheme as it resulted in the highest detection rate relative to the standard sextant biopsy scheme (29%).[20] A number of studies have supported the same findings; Noberg et al.,[6] Elabbady et al.,[7] Babian et al.,[8] Eskicorapci et al.,[9] Ravery et al.,[21] Durkan et al.,[22] and Singh et al.[23] all showed an increment in the detection rate from 15% to 31% with the number of cores ranging from 10 to 12 (Table 1).

Some authors started moving beyond 12 cores. Eskew et al.[24] first examined 13 cores; they found that this particular scheme resulted in a 35% increase in the PCa detection rate. Similarly, Scattoni et al.[25] assessed the diagnostic yield of a scheme using 18 cores in 1776 patients and compared it with the 12-core biopsy strategy. No statistically significant difference in the PCa detection rate was observed between the 2 strategies except in patients with a prostate volume of less than 55 cc (+6.7% gain was recorded).[25] It is clear that the yield of sextant biopsy can be significantly improved when extended biopsy is performed. However, as the number of cores exceeds 10, the gain becomes more marginal. The cancer detection benefit associated with the 10-core scheme has been reported to range from 15.5% to 29.4% compared with 11.6% to 31% for the 12-core biopsy scheme. To date, no study has demonstrated a meaningful benefit when 12 cores are taken instead of 10-core biopsy. Nonetheless, the 2010 National Comprehensive Cancer Network Early PCa Detection Guidelines reported the 12-core biopsy scheme as the standard.[26]

Saturation biopsy

The need for saturation biopsies came from the fact that extended biopsy approaches still fail to detect 20% of high-grade PCa that can be detected by detailed pathological evaluation of radical prostatectomy.[27] Prostate saturation biopsy was initially introduced by Borboroglu et al.[28] and consisted of at least 20 biopsy cores. Saturation biopsy may provide increased accuracy for the predictability of PCa volume and grade. Most studies have shown that TRUSG biopsy can be a useful diagnostic tool in men with prior negative biopsies with a cancer detection rate of 14%–34%.[29-32] As for the initial saturation biopsy scheme, several investigators have tested saturation biopsy schemes where more than 20 cores were obtained. De la Taille et al.[33] showed that a 21-core initial biopsy procedure increases the PCa detection rate by as much as 37.9% relative to sextant biopsy and by as much as 10.6% relative to a 12-core biopsy scheme in patients with prostate gland volumes of ≥40 cc. However, Ravery et al.[34] showed a 20% increase in the detection rate when an initial 20-core biopsy scheme was used compared with a 10-core biopsy scheme. This benefit was observed only in patients with prostate-specific antigen (PSA) levels of <6 ng/mL.[34] Delonchamps et al.[35] found no benefit of saturation biopsy over the 18-core biopsy scheme. Pepe et al.[36] showed a virtually equivalent PCa detection rate when using an initial 12-core (39%), an 18-core (49%), or saturation biopsy (range of 24-37 cores; 46.9%). Guichard et al.[37] also found no significant increase in the PCa detection rate when a 21-core biopsy scheme (42.5%) was chosen over an 18- or 12-core biopsy scheme (41.5% and 38.7%, respectively). It is very clear that most of the studies did not support the use of an initial saturation biopsy scheme with more than 12 cores.

Table 1. Extended versus sextant core biopsy scheme.

	Patients (n)	Biopsy cores (n)	Increase in PCa detection rate (%)
Norberg et al.[6]	512	6 vs. 8-10	15
Ravery et al.[21]	303	6 vs. 10-12	17
Babian et al.[8]	362	6 vs. 11	33
Durkan et al.[22]	493	6 vs. 12	19
Eskicorapci et al.[9]	303	6 vs. 12	25
Elabbady et al.[7]	289	6 vs. 12	12
Singh et al.[23]	179	6 vs. 12	31

PCa: prostate cancer; n: number

Repeat PBx and saturation biopsy

One of the most valid indications for saturation biopsy is previous negative biopsy or biopsies with a continued suspicion of PCa. As a rule, standard repeat biopsy should consist of at least 10-12 biopsy cores. Several studies have reported an improvement in the PCa detection rate when saturation biopsy was used.[13,30,33] The detection rate with repeat saturation biopsy has been reported to range from 13%-41%.[13,28-30,32,38] The differences in PCa detection with repeat saturation biopsies are related to the number of previous negative biopsies and number of cores. Therefore, high detection rates (30%-40%) with repeat saturation biopsies have been reported when a negative sextant scheme was previously used and a detection rate of 22% was reported when saturation biopsy was used after previous negative extended biopsy.[36] Walz et al.[13] reported a detection rate of 41% when saturation biopsy of 18 cores was used after at least 2 previously negative 8-core biopsy sessions. Among those who had at least ≥2 negative biopsies, 14% were found to harbor PCa of Gleason score 8-10 at subsequent saturation biopsy.[39] Taken together, repeat saturation biopsies result in PCa detection rates comparable to those of standard extended biopsy. There have been no convincing data supporting a benefit from the use of saturation biopsy after previous negative extended initial biopsy. Use of repeat saturation biopsy may be reserved for individuals who had ≥2 extended biopsies with benign findings but the clinical context still dictated the need for additional biopsies.

Saturation biopsy: Questions remain to be answered

There are a number of issues and questions regarding saturation biopsies that need to be addressed; there has been no consensus on the ideal number of cores, no study has reported

Turkish Journal of Urology 2015; 41(1): 32-8
DOI:10.5152/tud.2015.91249

on the diagnostic value of saturation biopsy after the failure of initial therapy, insignificant cancer versus number of cores, and the difference between the transrectal and transperineal approaches remains unclear. Regarding the number of cores, some authors have gone beyond saturation to supersaturation or extensive PBx. Stewart et al.[30] in 2001 coined saturation biopsy or extensive prostate sampling to be repeat on prostate biopsy, including up to 22 cores with a PCa detection rate of 30%. Merick et al.[40] reported a detection rate of 42.2% when 50 cores were taken; Simon et al.[41] also reported a detection rate of 45% when 64 cores were taken. At the MD Anderson Cancer Center (MDACC), we conducted a study regarding saturation biopsies (under consideration for publication); the PCa detection rate was 47.9% when 59 cores were taken. Currently, the studies of Merick et al.[40] and Simon et al.[41] and our study represent the studies where the highest number of cores was taken. It remains to be seen if the number of cores will extend beyond these numbers in future and when saturation biopsy will be saturated.

Transrectal versus transperineal biopsy

The majority of PBxs are performed transrectally; however, a few saturation biopsies are performed using the transperineal approach. The transperineal method has the advantages of fewer complications and higher PCa detection rate.[42,43] Transperineal biopsy can detect cancer in the anterior horn of the prostate; this is due to the fact that transperineal biopsy can provide good access to the apex and upper part of the base of the prostate. Many studies have demonstrated that the apical region in general and the apex in particular have a significantly higher incidence of cancer than the rest of the prostate gland.[40,44] In our study at MDACC, we used transperineal saturation biopsy in patients who had failed primary therapy (radiation and/or brachytherapy); the detection rate in treated and untreated patients was 58.82% and 41.17%, respectively. Abdollah et al.[45] conducted a comparison between the 2 approaches using 472 patients where 70% had undergone transrectal biopsies and 30% had undergone trasperienal biopsies; the researchers found no difference in the detection rate between the approaches (31.4% versus 25.7%; p=0.3). Accordingly, the transperineal technique can be a valid approach for patients who need supersaturation biopsies, particularly for those who have received prior treatment with radiation and/or cryotherapy because the anterior part and the apex are the most common regions for recurrence.

Safety of saturation biopsy

Many studies have reported on the safety of extended and saturation biopsy and there has been no significant difference between these approaches. Djavan et al.[46] reported on the morbidity and safety of repeat transrectal PBx; the authors concluded that it was generally well-tolerated with minor morbidities that rarely require treatment. Merrick et al.[47] reported on the morbidity of transperineal template-guided prostate mapping biopsy and concluded that it was a promising procedure with comparable results in terms of urinary, bowel, and erectile function and difference in the incidence of temporary urinary retention. Simon et al.[41] reported that hematuria occurred in 40% of patients who underwent extensive saturation biopsies. Walz et al.[13] reported that urinary retention occurred in 1.24% patients and the morbidity rate was 2.48%. Moran et al.[44] stated that 10% had urinary retention after repeat transperineal PBx. Akbal et al.[48] described that saturation biopsy with a median of 22 cores had a minimal risk of temporary erectile dysfunction. It is clear that morbidity associated with saturation biopsies is not significantly greater than that associated with an extended PBx scheme.

Number of cores versus insignificant PCa

The increased detection rate of insignificant PCa (defined as a tumor volume of <0.5 cc, no Gleason 4–5 pattern, and organ-confined disease) represents one of the potential drawbacks of extended initial and repeat PBxs. The rate of clinically-insignificant PCa increased by 12% when extended PBx was used instead of the sextant biopsy scheme.[23] Similarly, Hass et al.[49] showed that an extended PBx increased the detection rate of insignificant cancer by 22%. Other studies found no difference in the proportion of clinically insignificant PCa between a 12-core biopsy scheme and the sextant strategy.[50] Eskew et al.[51] also found no difference in the rate of clinically insignificant PCa between 13 cores and the sextant biopsy scheme. In recent study by Plousard et al.,[52] it was shown that a considerable number of patients that were considered for the active surveillance program according to preoperative parameters, e.g., Gleason scores of ≤6, had significant cancer according to the histopathological report. In the present study from MDACC, 82% of the patients had Gleason scores of ≥7 and all patients except one had ≥3 positive cores; the length of cancer was >5 mL for all patients except 2. Thus, individuals with clinically insignificant PCa at the time of extended biopsy should be considered for saturation biopsy before the cancer can be definitely classified as clinically insignificant and before active surveillance or focal therapy are considered. Currently, at MDACC, second extended biopsy is used to select patients for active surveillance. Confirmation of insignificant PCa may present the most valid and beneficial indication for saturation biopsy. Accordingly, saturation biopsy can be used in patients who are candidates for active surveillance in order to have an accurate oncological mapping for PCa**.** These arguments were corroborated by Delongchamps et al.[53] and Berglund et al.[54]

when they examined a cohort of 107 patients who were active surveillance candidates who underwent 14-core repeat biopsy; the researchers found a rate of upgrading/upstaging of 27%. It is expected that approximately 30% of individuals with small volume and/or low-grade disease at initial biopsy will harbor a higher-grade disease. Therefore, there has been no convincing evidence that the extended PBx scheme increased the rate of insignificant PCa detection beyond that of the sextant biopsy scheme.

Saturation biopsy to predict the pathologic specimen at radical prostatectomy

The rate of incorrect grade assignment relative to RP ranged from 25%-57% with the sextant-biopsy scheme.[55-57] Extended biopsy with more than 10 cores improved the concordance by 13% relative to sextant biopsy.[58] Further studies reported improvements that ranged from 15% to 35.2%.[7,59] Therefore, increasing the number of scores clearly improves the ability of surgeons to predict the oncological features of PCa with RP specimens. The rate of Gleason score upgrading decreased from 47.9% to 23.5% when the 12-core biopsy scheme was replaced with an 18-core biopsy scheme.[60] This also can be considered as an important consideration for an extensive initial PBx along with an improvement in the cancer detection rate.

Presence of extraprostatic disease has been one of the prognostic factors for patients with PCa. The follow-up policy and necessity for further treatment, such as radiotherapy or hormonal therapy, can be determined according to the extraprostatic involvement. Unfortunately, the negative predictive value of uninvolved cores in the extended PBx scheme has been reported to be low (24%-31%).[61] Consequently, the negative extended Bx findings cannot safely justify the use of focal therapies or define the need for further treatments.[61] As for new tests that may help in solving the dilemma of undetectable PCa, genetic testing, such as that related to prostate cancer antigen 3 (PCA3), may play a significant role in detecting PCa and decrease the number of unnecessary PBxs; however, the availability and technical issues may limit the use of these tests.[62]

Role of 3 Tesla multiparametric magnetic resonance imaging (3TMPMRI) in the detection of PCa

Reducing the number of cores and saving patients from unnecessary PBxs is an ideal target in the detection of PCa. Magnetic resonance imaging-guided PBx has demonstrated a high PCa detection rate; the tumor detection rate was 82.6%, and the targeted cores versus systematic core detection rate was 30% and 8.2%.[63] The specificity and sensitivity of 3TMPMRI were 85% and 97%, respectively, with a positive predictive value of 74.6%.[64] In a large study where 844 patients underwent 3TMPMRI, there were 438 patients with PSA levels of ≥4 ng/mL and ≥1 negative TRUSG biopsy sessions.[65] The authors concluded that the PCa detection rate was 41% and the majority of cancers were significant (87%).[65] Kuru et al.[63] compared the standard systematic TRUSG biopsy with 3TMPMRI; the authors concluded that although 3TMPMRI improved the PCa detection rate, it still had some limitations and systematic biopsies should not be omitted at present. In general, 3TMPMRI-guided PBx does improve the PCa detection rate. It is preferable for patients with negative systematic PBx(s). Cost-effectiveness, availability, systematic restrictions, and vagueness of its diagnostic value in treated patients, particularly in patients after radiation, are the most important limitations of 3TMPMRI.

In conclusion, the urologic literature suggests that an extended biopsy scheme should consist of 12 cores. Use of a saturation biopsy scheme for repeat biopsy results in an increase in the PCa detection rate from 30%–40% without a significant increase in morbidity compared with sextant biopsy. Introduction of 3TMPMRI in PBx can be promising; it improves the PCa detection rate and saves patients from high number of cores and unnecessary biopsies. However, a number of limitations are still present. Patients who are expected to undergo active surveillance can consider saturation biopsy for accurate oncological mapping of PCa.

Peer-review: This manuscript was prepared by the invitation of the Editorial Board and its scientific evaluation was carried out by the Editorial Board.

Author Contributions: Concept - M.O.M.; Supervision - L.P.; Materials - M.O.M.; Analysis and/or Interpretation - M.O.M.; Literature Review - M.O.M.; Writer - M.O.M.; Critical Review - L.P.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Watanabe H, Kato H, Kato T, Morita M, Tanaka M. Diagnostic application of ultrasonotomography to the prostate. Nihon Hinyokika Gakkai Zasshi 1968;59:273-9.
2. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. J Urol 1989;142:71-4.

Turkish Journal of Urology 2015; 41(1): 32-8
DOI:10.5152/tud.2015.91249

3. Cooner WH, Mosley BR, Rutherford CL Jr, Beard JH, Pond HS, Bass RB Jr, et al. Clinical application of transrectal ultrasonography and prostate specific antigen in the search for prostate cancer. J Urol 1988;139:758-61.
4. Shinohara K, Wheeler TM, Scardino PT. The appearance of prostate cancer on transrectal ultrasonography: correlation of imaging and pathological examinations. J Urol 1989;142: 76-82.
5. Stamey TA. Making the most out of six systematic sextant biopsies. Urology 1995;45:2-12. [CrossRef]
6. Norberg M, Egevad L, Holmberg L, Sparén P, Norlén BJ, Busch C. The sextant protocol for ultrasound-guided core biopsies of the prostate underestimates the presence of cancer. Urology 1997;50:562-6. [CrossRef]
7. Elabbady AA, Khedr MM. Extended 12-core prostate biopsy increases both the detection of prostate cancer and the accuracy of Gleason score. Eur Urol 2006;49:49-53. [CrossRef]
8. Babaian RJ, Toi A, Kamoi K, Troncoso P, Sweet J, Evans R, et al. Comparative analysis of sextant and an extended 11-core multisite directed biopsy strategy. J Urol 2000;163:152-7. [CrossRef]
9. Eskicorapci SY, Baydar DE, Akbal C, Sofikerim M, Günay M, Ekici S, et al. An extended 10-core transrectal ultrasonography guided prostate biopsy protocol improves the detection of prostate cancer. Eur Urol 2004;45:444-8. [CrossRef]
10. Matlaga B, Eskew L, McCullough D. Prostate biopsy: indications and techniques. J Urol 2003;169:12-9. [CrossRef]
11. Philip J, Hanchanale V, Foster C, Javle P . Importance of peripheral biopsies in maximizing the detection of early prostate cancer prostate cancer in repeat 12-core biopsy protocol. BJU 2006;98:559-62. [CrossRef]
12. Bostwick DG, Meiers I. Prostate biopsy and optimization of cancer yield. Eur Urol 2006;49:415-7. [CrossRef]
13. Walz J, Graefen M, Chun FK, Erbersdobler A, Haese A, Steuber T, et al. High incidence of prostate cancer detected by saturation biopsy after previous negative biopsy series. Eur Urol 2006;50:498-505. [CrossRef]
14. Ficarra V, Martignoni G, Novella G, Cerruto MA, Galfano A, Novara G, et al. Needle core length is a quality indicator of systematic transperineal prostate biopsy. Eur Urol 2006;50:266-71. [CrossRef]
15. Kawakami S, Okuno T, Yonese J, Geri G, Fujii Y, Kageyama Y, et al. Optimal sampling sites for repeat prostate biopsy: a recursive partitioning analysis of three-dimensional 26-core systematic biopsy. Eur Urol 2007;51:675-83. [CrossRef]
16. McNeal JE. The prostate and prostatic urethra: a morphologic synthesis. J Urol 1972;107:1008-16.
17. Uzzo RG, Wei JT, Waldbaum RS, Perlmutter AP, Byrne JC, Vaughan ED Jr. The influence of prostate size on cancer detection. Urology 1995;46:831-6. [CrossRef]
18. Karakiewicz PI, Bazinet M, Aprikian AG, Trudel C, Aronson S, Nachabé M, et al. Outcome of sextant biopsy according to gland volume. Urology 1997;49:55-9. [CrossRef]
19. Chen ME, Troncoso P, Johnston DA, Tang K, Babaian RJ. Optimization of prostate biopsy strategy using computer based analysis. J Urol 1997;158:2168-75. [CrossRef]
20. Chen ME, Troncoso P, Tang K, Babian RJ, Johnston D. Comparison of prostate biopsy schemes by computer simulation. Urology 1999;53:951-60. [CrossRef]
21. Ravery V, Goldblatt L, Royer B, Blanc E, Toublanc M, Boccon-Gibod L. Extensive biopsy protocol improves the detection rate of prostate cancer. J Urol 2000;164:393-6. [CrossRef]
22. Durkan GC, Sheikh N, Johnson P, Hildreth AJ, Greene DR. Improving prostate cancer detection with an extended-core transrectal ultrasonography-guided prostate biopsy protocol. BJU Int 2002;89:33-9. [CrossRef]
23. Singh H, Canto EI, Shariat SF, Kadmon D, Miles BJ, Wheeler TM, et al. Improved detection of clinically significant, curable prostate cancer with systematic 12-core biopsy. J Urol 2004;171: 1089-92. [CrossRef]
24. Eskew LA, Bare RL, McCullough DL. Systematic 5 region prostate biopsy is superior to sextant method for diagnosing carcinoma of the prostate. J Urol 1997;157:199-202. [CrossRef]
25. Scattoni V, Roscigno M, Raber M, Dehò F, Maga T, Zanoni M, et al. Initial extended transrectal prostate biopsy--are more prostate cancers detected with 18 cores than with 12 cores? J Urol 2008;179:1327-31. [CrossRef]
26. Kawachi MH, Bahnson RR, Barry M, Busby JE, Carroll PR, Carter HB, et al. National comprehensive network cancer clinical practice guidelines in oncology: prostate cancer early detection. J Natl Compr Canc Netw 2010; 8: 240-62.
27. King C, McNeal JE, Gill H, Presti JC JR. Extended prostate biopsy scheme improves reliability of Gleason grading: implications for radiotherapy patients. Int J Rad Oncol Biol Phys 2004;59:386-91. [CrossRef]
28. Borboroglu PG, Comer SW, Riffenburgh RH, Amling CI. Extensive repeat transrectal ultrasound guided prostate biopsy in patients with previous benign sextant biopsies. J Urol 2000;163: 158-62. [CrossRef]
29. Fleshner N, Klotz L. Role of ''saturation biopsy'' in detection of prostate cancer among difficult diagnostic cases. Urology 2002;60:93-7. [CrossRef]
30. Stewart CS, Leibovich BC, Weaver AL, Lieber MM. Prostate cancer diagnosis using a saturation needle biopsy technique after previous negative sextant biopsies. J Urol 2001;166:86-91. [CrossRef]
31. Jones JS, Oder M, Zippe CD. Saturation prostate biopsy with periprostatic block can be performed in the office. J Urol 2002;168:2108-10. [CrossRef]
32. Rabets JC, Jones SJ, Patel A, Zippe CD. Prostate cancer detection with office based saturation biopsy in a repeat biopsy population. J Urol 2004;172:94-7. [CrossRef]
33. de la Taille A, Antiphon P, Salomon L, Cherfan M, Porcher R, Hoznek A, et al. Prospective evaluation of a 21-sample needle biopsy procedure designed to improve the prostate cancer detection rate. Urology 2003;61:1181-6. [CrossRef]
34. Ravery V, Dominique S, Panhard X, Toublanc M, Boccon-Gibod L, Boccon-Gibod L. The 20-core prostate biopsy protocol--a new gold standard? J Urol 2008;179:504-7. [CrossRef]

35. Delongchamps NB, de la Roza G, Jones R, Jumbelic M, Haas GP. Saturation biopsies on autopsied prostates for detecting and characterizing prostate cancer. BJU Int 2009;103:49-54. [CrossRef]
36. Pepe P, Aragona F. Saturation prostate needle biopsy and prostate cancer detection at initial and repeat evaluation. Urology 2007;70:1131-5. [CrossRef]
37. Guichard G, Larré S, Gallina A, Lazar A, Faucon H, Chemama S, et al. Extended 21-sample needle biopsy protocol for diagnosis of prostate cancer in 1000 consecutive patients. Eur Urol 2007;52:430-5. [CrossRef]
38. Patel AR, Jones JS, Rabets J, DeOreo G, Zippe CD. Parasagittal biopsies add minimal information in repeat saturation prostate biopsy. Urology 2004;63:87-9. [CrossRef]
39. Tan N, Lane BR, Li J, Moussa AS, Soriano M, Jones JS. Prostate cancers diagnosed at repeat biopsy are smaller and less likely to be high grade. J Urol 2008;180:1325-9. [CrossRef]
40. Merrick GS, Gutman S, Andreini H, Taubenslag W, Lindert DL, Curtis R, et al. Prostate cancer distribution in patients diagnosed by transperineal templateguided saturation biopsy. Eur Urol 2007;52:715-23. [CrossRef]
41. Simon J, Kuefer R, Bartsch G Jr, Volkmer BG, Hautmann RE, Gottfried HW. Intensifying the saturation biopsy technique for detecting prostate cancer after previous negative biopsies: a step in the wrong direction. BJU Int 2009;102:459-62. [CrossRef]
42. Emiliozzi P, Corsetti A, Tassi B, Faderico G, Martini M, Pansadora V. Best approach for prostate cancer detection: a prospective study on transperineal versus transrectal six-core prostate biopsy. Urology 2003;61:961-6. [CrossRef]
43. Vis AN, Boerma MO, Ciatto S, Hoedemaker RF, Schroder FH, Vander Kwast TH. Detection of prostate cancer: a comparative study of the diagnostic efficacy of sextant transrectal versus sextant transperineal biopsy. Urology 2000;56:617-21. [CrossRef]
44. Moran BJ, Braccioforte MH, Conterato DJ. Re-biopsy of the prostate using a stereotactic transperineal technique. J Urol 2006;176:1376-81. [CrossRef]
45. Abdollah F, Novara G, Briganti A, Scattoni V, Raber M, Roscigno M, et al. Trans-rectal versus trans-perineal saturation rebiopsy of the prostate: is there a difference in cancer detection rate? Urology 2011;77:921-5. [CrossRef]
46. Djavan B, Waldert M, Zlotta A, Dobronski P, Seitz C, Remzi M, et al. Safety and morbidity of first and repeat transrectal ultrasound guided prostate needle biopsies: results of a prospective European prostate cancer detection study. J Urol 2001;166: 856-60. [CrossRef]
47. Merrick GS, Taubenslag W, Andreini H, Brammer S, Butler WM, Adamovich E, et al. The morbidity of transperineal template-guided prostate mapping biopsy. BJU Int 2008;101: 1524-9. [CrossRef]
48. Akbal C, Türker P, Tavukçu HH, Simşek F, Türkeri L. Erectile function in prostate cancer-free patients who underwent prostate saturation biopsy. Eur Urol 2008;53:540-4. [CrossRef]
49. Haas GP, Delongchamps NB, Jones RF, Chandan V, Serio AM, Vickers AJ, et al. Needle biopsies on autopsy prostates: sensitivity of cancer detection based on true prevalence. J Natl Cancer Inst 2007;99:1484-9. [CrossRef]
50. Chan TY, Chan DY, Stutzman KL, Epstein JI. Does increased needle biopsy sampling of the prostate detect a higher number of potentially insignificant tumors? J Urol 2001;166:2181-4. [CrossRef]
51. Eskew LA, Woodruff RD, Bare RL, McCullough DL. Prostate cancer diagnosed by the 5 region biopsy method is significant disease. J Urol 1998;160:794-6. [CrossRef]
52. Ploussard G, Salomon L, Xylinas E, Allory Y, Vordos D, Hoznek A, et al. Pathological findings and prostate specific antigen outcomes after radical prostatectomy in men eligible for active surveillance--does the risk of misclassification vary according to biopsy criteria? J Urol 2010;183:539-44. [CrossRef]
53. Delongchamps NB, de la Roza G, Chandan V, Jones R, Threatte G, Jumbelic M, et al. Diagnostic accuracy of extended biopsies for the staging of microfocal prostate cancers in autopsy specimen. Prostate Cancer Prostatic Dis 2009;12:137-42. [CrossRef]
54. Berglund RK, Masterson TA, Vora KC, Eggener SE, Eastham JA, Guillonneau BD. Pathological upgrading and up staging with immediate repeat biopsy in patients eligible for active surveillance. J Urol 2008;180:1964-7. [CrossRef]
55. Bostwick DG.Gleason grading of prostatic needle biopsies. Correlation with grade in 316 matched prostatectomies. Am J Surg Pathol 1994;18:796-803. [CrossRef]
56. Steinberg DM, Sauvageot J, Piantadosi S, Epstein JI. Correlation of prostate needle biopsy and radical prostatectomy Gleason grade in academic and community settings. Am J Surg Pathol 1997;21:566-76. [CrossRef]
57. King CR. Patterns of prostate cancer biopsy grading: trends and clinical implications. Int J Cancer 2000;90:305-11. [CrossRef]
58. San Francisco IF, DeWolf WC, Rosen S, Upton M, Olumi AF. Extended prostate needle biopsy improves concordance of Gleason grading between prostate needle biopsy and radical prostatectomy. J Urol 2003;169:136-40. [CrossRef]
59. Divrik RT, Eroglu A, Sahin A, Zorlu F, Ozen H. Increasing the number of biopsies increases the concordance of Gleason scores of needle biopsies and prostatectomy specimens. Urol Oncol 2007;25:376-82. [CrossRef]
60. Capitanio U, Karakiewicz PI, Valiquette L, Perrotte P, Jeldres C, Briganti A, et al. Biopsy core number represents one of foremost predictors of clinically significant gleason sum upgrading in patients with low-risk prostate cancer. Urology 2009;73: 1087-91. [CrossRef]
61. Schulte RT, Wood DP, Daignault S, Shah RB, Wei JT. Utility of extended pattern prostate biopsies for tumor localization: pathologic correlations after radical prostatectomy. Cancer 2008;113:1559-65. [CrossRef]
62. Rubio-Briones J, Casanova J, Dumont R, Rubio L, Fernandez-Serra A, Casanova-Salas I, et al. Optimizing prostate cancer screening; prospective randomized controlled study of the role of PSA and PCA3 testing in a sequential manner in an opportunistic screening program. Actas Urol Esp 2014;38: 217-23. [CrossRef]
63. Kuru TH, Roethke MC, Seidenader J, Simpfendörfer T, Boxler S, Alammar K, et al. Critical evaluation of magnetic resonance imaging targeted, transrectal ultrasound guided transperineal fusion

Turkish Journal of Urology 2015; 41(1): 32-8
DOI:10.5152/tud.2015.91249

biopsy for detection of prostate cancer. J Urol 2013;190:1380-6. [CrossRef]

64. Ferda J, Kastner J, Hora M, Hes O, Fínek J, Topolčan O, et al. A role of multifactorial evaluation of prostatic 3T MRI in patients with elevated prostatic-specific antigen levels: prospective comparison with ultrasound-guided transrectal biopsy. Anticancer Res 2013;33:2791-5.

65. Hoeks CM, Schouten MG, Bomers JG, Hoogendoorn SP, Hulsbergen-van de Kaa CA, Hambrock T, et al. Three-Tesla magnetic resonance-guided prostate biopsy in men with increased prostate-specific antigen and repeated, negative, random, systematic, transrectal ultrasound biopsies: detection of clinically significant prostate cancers. Eur Urol 2012;62: 902-9. [CrossRef]