

The 20-core prostate biopsy as an initial strategy: impact on the detection of prostatic cancer

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Abstract

Introduction: To increase the detection rate of prostate cancer in recent years, we examined the increase in the number of cores taken at initial prostate biopsy. We hypothesized that an increasing number of cores may undermine the accuracy of models predicting the presence of prostate cancer at initial biopsy in patients submitted to 20-core initial biopsy.

Methods: A total of 232 consecutive patients with prostate-specific antigen (PSA) between 4 and 20 ng/mL and/or abnormal digital rectal examination (DRE) underwent 12-core prostate biopsy protocol (group 1) or 20-core prostate biopsy protocol (group 2). The patients were divided into subgroups according to the results of their serum PSA and prostate volume. We evaluated the cancer detection rate overall and in each subgroup. Clinical data were analyzed using chi-square analysis and the unpaired t-test or 1-way ANOVA with significance considered at 0.05.

Results: The 2 groups of patients were not significantly different with regard to parameters (age, abnormal DRE and serum PSA), although median prostate volume in group 1 (57.76 ± 26.94 cc) were slightly greater than in group 2. Cancer detection rate for patients submitted to 20 prostate biopsy was higher than patients submitted to 12 prostate biopsy (35.2% vs. 25%, $p = 0.095$). Breakdown to PSA level showed a benefit to 20 prostate biopsy for PSA < 6 ng/mL (37.1% vs. 12.9%, $p = 0.005$). Stratifying results by prostate volume, we found that the improvement of cancer detection rate with 20 prostate biopsy was significant in patients with a prostate volume greater than 60 cc (55% in 20 prostate biopsy vs. 11.3% $p < 0.05$). Morbidity rates were identical in groups 1 and 2 with no statistically significant difference. There appeared to be no greater risk of infection and bleeding with 20 prostate biopsy protocol.

Conclusion: The 20-core biopsy protocol was more efficient than the 12-core biopsy protocol, especially in patients with prostate specific antigen < 6 ng/mL and prostate volume greater than 60 cc.

Résumé

Introduction : Pour augmenter le taux de détection du cancer de la prostate dans un avenir rapproché, nous avons examiné l'incidence d'une hausse du nombre de carottes prélevées lors de la biopsie prostatique initiale. Notre hypothèse était qu'en raison du nombre accru de prélèvements, la biopsie à 20 carottes pouvait réduire l'exactitude des modèles de dépistage du cancer de la prostate à la biopsie initiale.

Méthodologie : Au total, 232 patients consécutifs avec des taux d'antigène prostatique spécifique (APS) situés entre 4 et 20 ng/mL et/ou des anomalies au toucher rectal ont subi une biopsie prostatique à 12 (groupe 1) ou à 20 carottes (groupe 2). Les patients ont été répartis en sous-groupes en fonction de leurs taux sériques d'APS et de leur volume prostatique. Nous avons évalué le taux de dépistage du cancer de façon globale et par sous-groupes. Les données cliniques ont été analysées par la méthode du chi carré et du test t pour échantillons non appariés ou par analyse unilatérale de la variance (ANOVA), avec un seuil de signification de 0,05.

Résultats : On n'a noté aucune différence significative entre les deux groupes quant aux paramètres (âge, anomalie au toucher rectal et taux sériques d'APS), malgré que le volume prostatique médian ait été légèrement supérieur dans le groupe 1 ($57,76 \pm 26,94$ mL) par rapport au groupe 2. Le taux de dépistage du cancer avec la biopsie prostatique à 20 carottes était plus élevé que le taux obtenu avec la biopsie à 12 carottes (35,2 % vs 25 %, $p = 0,095$). La répartition des patients en fonction des taux d'APS a fait ressortir un avantage pour la biopsie à 20 carottes lorsque les taux d'APS étaient inférieurs à 6 ng/mL (37,1 % vs 12,9 %, $p = 0,005$). La stratification des données selon le volume de la prostate a montré que la hausse des taux de dépistage du cancer associée à la biopsie prostatique à 20 carottes était significative lorsque le volume prostatique dépassait 60 mL (55 % pour la biopsie à 20 carottes vs 11,3 %, $p < 0,05$). Les taux de morbidité étaient semblables dans les deux groupes, la différence n'étant pas significative sur le plan statistique. La biopsie prostatique à 20 carottes ne semblait pas associée à un risque plus élevé d'infection et d'hémorragie.

Conclusion : La biopsie à 20 carottes était plus efficace que la biopsie à 12 carottes, surtout chez les patients dont le taux d'APS était inférieur à 6 ng/mL et le volume prostatique, supérieur à 60 mL.

Introduction

During the last decade, many modifications have been made to improve the technique of prostate biopsy (PBx). While for many years the systematic sextant biopsy protocol (a fixed pattern with 6 cores taken from parasagittal region in the mid, between the urethra and lateral margin of the prostate) has been the standard procedure,¹ studies have argued that the traditional protocol misses 10% to 30% of cancers^{2,3} and that more extensive sampling of the lateral aspect of the peripheral zone is crucial to optimize the detection rate.

It is still a matter of debate which is the most efficient

number of prostate biopsies, particularly since it is more than probable that this number may vary widely according to patient age, prostate volume and the type of treatment anticipated. We assessed the rates of diagnosis yielded by 2 biopsy protocols: 12-core biopsy and 20-core biopsy, in different subgroups of patients distributed according to prostate-specific antigen (PSA) level and prostate volume.

Methods

Between January 2004 and March 2009, we recruited 232 consecutive patients with PSA between 4 and 20 ng/mL and/or abnormal digital rectal examination (DRE) to undergo a PBx procedure. All repeat biopsies were excluded from the final analysis. Before January 2007, our initial technique strategy was to perform a 12-core laterally focused biopsy. These 144 patients became part of group 1. Around that time, we reported improved cancer detection during repeat biopsy using an office-based saturation biopsy strategy. As a result of this successful endeavour we began performing 20-core biopsy as an initial biopsy technique. The remaining 88 patients became part of group 2 and are the patients of interest in this report.

Patients were administered a fluoroquinolone antibiotic on the day of the procedure and for 4 days subsequently. They were placed in the left lateral decubitus position and the ultrasound probe was inserted transrectally. Prostate volume was calculated using the formula for a prostate ellipsoid (transverse width × transverse length × longitudinal height × 0.52). All patients received local anesthesia (periprostatic block) with a total of 10 mL lidocaine 1% injected at the level of the angle between the seminal vesicle and prostate base bilaterally. All biopsies were performed on an outpatient basis, transrectally under ultrasound guidance and were

performed using a biopsy gun and an 18-gauge needle.

In the 12-biopsy protocol, 6 parasagittal and 6 laterally targeted biopsies covering the base, mid zones and apices, were obtained (Fig. 1). In the 20-biopsy protocol, 4 cores were taken from each base (1 peripherally, 2 more lateral peripherally and 1 central), 4 were taken from each mid-gland (1 peripherally, 2 more lateral peripherally and 1 central) and 2 were taken from each apex (1 peripherally, and 1 more lateral peripherally) (Fig. 2).

Each core was separately sampled and stored in one bottle before being sent for pathological assessment. Any nodule detected by DRE or echography was also biopsied, but these results were not included in the final analysis to avoid methodological bias. The morbidity rate according to the number of biopsies taken was noted. Unwanted effects included persistent hematuria, hemospermia, urinary tract infection, bacteremia and acute prostatitis.

Biopsy results were considered positive only when adenocarcinoma cells were seen on histological slides. When high-grade prostatic intraepithelial neoplasia or atypical glands suggestive of carcinoma were noted, biopsy results were considered negative. The patients were divided into subgroups according to the results serum PSA and prostate volume. We evaluated the cancer detection rate overall and in each subgroup. Clinical data were analyzed using chi-square analysis and the unpaired t-test or 1-way ANOVA with significance considered at 0.05. Statistical analysis was performed using SPSS 17.0 software (SPSS, Inc. Chicago, IL).

Results

All patients tolerated complete biopsies and obtained the planned numbers of cores. Table 1 lists the clinical char-

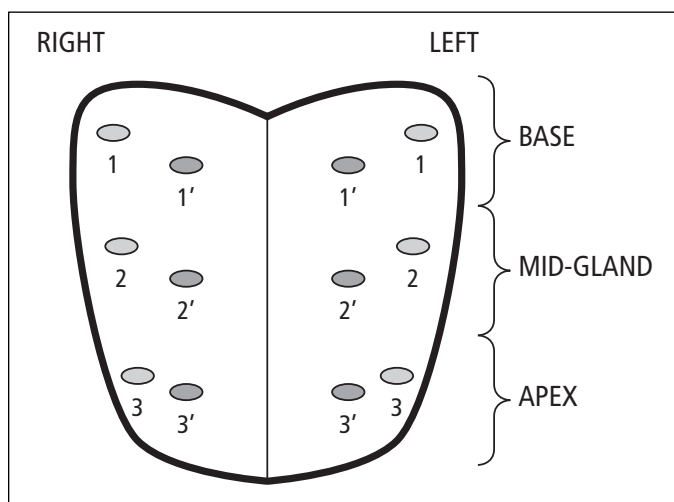


Fig. 1. The 12-core biopsy. 1 = Base periphery; 1' = Base central; 2 = Mid-gland periphery; 2' = Mid-gland central; 3 = Apex periphery; 3' = Apex central.

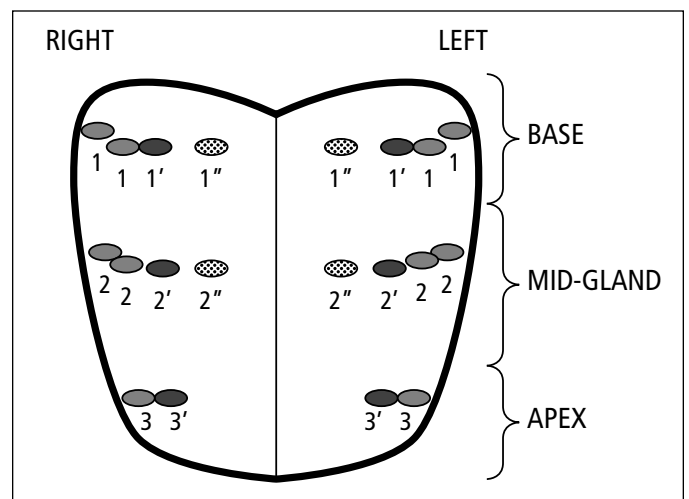


Fig. 2. The 20-core biopsy. 1 = More laterally base periphery; 1' = Base periphery, 1'' = Base central; 2 = More laterally mid-gland periphery; 2' = Mid-gland periphery; 2'' = Mid-gland central; 3 = More laterally apex periphery, 3' = apex periphery.

acteristics of 232 patients stratified according to the number of PBx. The 2 groups of patients were not significantly different with regard to parameters (age, abnormal DRE and serum PSA), although median prostate volume in group 1 (57.76 ± 26.94 cc) were slighter greater than in group 2 (51.1 ± 18 cc, $p = 0.04$).

Cancer was detected in 31 of 88 patients (35.2%) who underwent 20-PBx and in 36 of 144 patients (25%) who underwent 12-PBx ($p = 0.095$). There were no significant differences in Gleason score between the 2 groups (6.55 ± 0.93 in 20-PBx group vs. 6.97 ± 0.81 in 12-PBx group; $p = 0.05$). When we stratified the results by PSA level, we found a higher cancer detection with 20-PBx than 12-PBx in patients with a PSA less than 6 ng/mL (37.1% vs. 12.9%, $p = 0.005$) (Table 2).

Table 3 lists the detection rates in the subgroups defined by prostate volume. The data demonstrated a benefit to the saturation technique especially for prostate volume greater than 60 cc (55% in 20-PBx protocol vs. 11.3% in 12-PBx protocol). The differences were statistically significant ($p < 0.05$). Morbidity rates were identical in groups 1 and 2 with no statistically significant difference (14% and 16%, respectively, $p = 0.8$). There appeared to be no greater risk of infection and bleeding with 20-PBx protocol.

Discussion

The traditional sextant technique has been clearly demonstrated to have an unacceptably high false-negative rate.⁴ Studies have shown quite convincingly that increasing the number of biopsy cores and directing biopsies laterally increase prostate cancer detection rates.⁵ Extended biopsy techniques have resulted in the identification of prostate cancer in about a third of patients who have previously undergone a negative (no evidence of cancer) sextant biopsy.^{6,7} Moreover, authors have found that these extended/saturation biopsies

can be performed safely with little discomfort for the patient using a periprostatic block.⁸ Given that these saturation biopsy strategies appear to be safe and offer a more extensive sampling of the prostate, why not offer them to all patients with an indication for biopsy?

In this study, we analyzed the performance of a 20-core PBx as initial strategy. Several studies confirmed that it is unnecessary to sample the transitional zone of the prostate on initial biopsy since the detection rate was only 0% to 3%.^{9,10} These findings support our decision to biopsy only the peripheral and central zones.

The overall prostate cancer detection rate was improved by 20-PBx protocol compared with that of 12-PBx (35.2% and 25%, respectively, $p = 0.095$). In particular, patients with PSA <6 ng/mL who underwent 20-PBx had a significant higher prostate cancer detection rate (37.1%) than patients who underwent 12-PBx (12.9%, $p = 0.005$).

Our findings concur with those reported by Ravery and colleagues,¹¹ who noted that the 20-core biopsy protocol was more efficient than the 10-core biopsy protocol, especially in patients with PSA between 3 and 6 ng/mL.

On the other hand, Jones and colleagues¹² demonstrated that the saturation technique (24 cores) as an initial PBx strategy does not improve prostate cancer detection. The cancer detection rate was 44.6% for those patients undergoing a saturation biopsy and 51.7% in those undergoing a 10-core biopsy ($p = 0.9$). Additionally, the breakdown by PSA failed to show benefit with the saturation technique. Jones and colleagues also suggested that biopsies involving greater than 10 to 12 cores are not appropriate as an initial biopsy strategy. In a recent systematic review, Eichler and colleagues have shown that there is no significant benefit in taking more than 12 cores and those methods requiring 18 or more cores have a poor side-effect profile.¹³

With regard to prostate volume, it is known that greater volume increases the risk of missing prostate cancer.¹⁴ Remzi¹⁵ and Ung and colleagues¹⁶ stressed the importance of prostate volume for prostate cancer detection and noted that detection rates depend on gland volume, especially in patients with low PSA. Rietbergen and colleagues also found

Table 1: Patient characteristics

| Parameter | Group 1 (12 PBx) | Group 2 (20 PBx) | p value |
|--|-------------------|------------------|---------|
| No. patients | 144 | 88 | |
| Mean \pm SD age (range) | 65.62 \pm 6 | 64.91 \pm 5.6 | 0.373 |
| Mean \pm SD (ng/mL) PSA (range) | 7.76 \pm 4.13 | 8.31 \pm 4.7 | 0.351 |
| Mean \pm SD (cc) prostate volume (range) | 57.76 \pm 26.94 | 51.1 \pm 18 | 0.041 |
| % abnormal DRE | 25% | 15% | 0.083 |
| No. malignancy pathology (%) | 25% | 35.2% | 0.095 |

PBx = prostate biopsy; PSA = prostate-specific antigen; SD = standard deviation; DRE = digital rectal examination.

Table 2. Detection rates according to protocol type and prostate-specific antigen

| PSA (ng/mL) | % prostate cancer detection | | |
|-------------|------------------------------|------------------------------|---------|
| | Group 1 (12-biopsy protocol) | Group 2 (20-biopsy protocol) | p value |
| <6 | 8/62 (12.9%) | 13/35 (37.1%) | 0.005 |
| 6-9.9 | 15/49 (30.6%) | 9/29 (31%) | 0.969 |
| 10-20 | 13/33 (39.4%) | 9/24 (37.5%) | 0.885 |
| Overall | 36/144 (25%) | 31/88 (35.2%) | 0.095 |

PSA = prostate-specific antigen.

Table 3. Detection rates according to protocol type and prostate volume

| Prostate volume (cc) | % prostate cancer detection | | p value |
|----------------------|------------------------------|------------------------------|---------|
| | Group 1 (12-biopsy protocol) | Group 2 (20-biopsy protocol) | |
| <40 | 18/42 (42.9%) | 8/21 (38.1%) | 0.717 |
| 40-60 | 12/49 (24.5%) | 12/47 (25.5%) | 0.906 |
| >60 | 6/53 (11.3%) | 11/20 (55%) | 0.000 |
| Overall | 36/144 (25%) | 31/88 (35.2%) | 0.095 |

PSA = prostate-specific antigen.

that the most important factor for failure to diagnose prostate cancer at the primary screening was a large prostate volume.¹⁷ Evaluating the variation of prostate cancer detection in relation to prostate size through random systematic sextant biopsies, Uzzo and colleagues found that 23% of the patients had cancer in a large prostate (greater than 50 mL) compared with a 38% rate in patients with smaller prostates ($p = 0.01$).¹⁸ They concluded that significant sampling errors may occur in men with large glands.¹⁸ A study out of Vienna revealed an improved prostate cancer detection rate with choosing the optimal number of prostate biopsy cores based on patient age and prostate volume.¹⁹ Remzi and colleagues noted that an extended biopsy protocol was needed in patients with larger prostates.¹⁹ In fact, the optimal number of cores suggested by the authors was 16 to 18 in patients initially presenting with PSA between 2 and 10 ng/mL, who were younger than 50 and had a prostate volume greater than 50 mL.¹⁹ A similar breakdown of prostate volumes would be useful in the article by Jones and colleagues to support or refute their conclusions.¹² Similarly, we noted an improvement in the prostate cancer detection rate of about 34% for prostate volume greater than 60 cc when 20- and 12-core protocols were compared.

A possible disadvantage of the initial extended protocol in large prostates is that increasing the number of cores could escalate the risk of detecting small, possibly low-grade and clinically insignificant cancers; this detection could lead to unnecessary treatment and increased morbidity in patients as well as increased costs. The concern of overdiagnosis must be weighed against the risk of clinically significant malignancy being missed by inadequate biopsy strategies that have considerable false-negative rates.

Recently, Master and colleagues demonstrated that a greater number of biopsies were associated with smaller tumour volumes at radical prostatectomy.²⁰ Boccon-Gibod and colleagues have reported that 30% of patients with microfocal prostate cancer on extended PBx are at risk of having insignificant tumour and of being over-treated.²¹

Nevertheless, Siu and colleagues have demonstrated that it is possible not only to enhance tumour detection but also to ultimately lead to the finding of clinically significant disease.²² Similarly, Singh and colleagues have shown no apparent significant association between the increased number of cores and the finding of smaller and clinically insignificant cancer.²³ Meng and colleagues have recently demonstrated that performing more extensive biopsies does not significantly increase the number of lower-risk tumours identified.²⁴ They have reported that there are no differences in disease characteristics and biochemical-free survival among men with a biopsy number between 6 and 17.

Conclusion

In our experience, a 20-biopsy scheme improved significantly the diagnostic yield compared with the 12-biopsy scheme especially in patients with low PSA less than 6 ng/mL and large prostate volume greater than 60 cc. Due to the retrospective aspect of this study, no strong conclusion may be drawn before a randomized prospective trial is performed.

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Competing interests: None declared.

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