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# Retrospective Study Comparing Six- and Twelve-Core Prostate Biopsy in Detection of Prostate Cancer

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**ABSTRACT**

*Objective:* We compared the safety and efficacy of the 12-core biopsy with those of the conventional systematic 6-core biopsy with PSA levels between 4.1 and 20.0 ng/mL.
*Materials and Methods:* This study included 428 patients who underwent a 6-core biopsy and 128 patients who underwent a 12-core biopsy. Biopsies were performed transrectally under ultrasound guidance. The 12-core biopsy scheme involved obtaining 6 far lateral cores.
*Results:* For patients with PSA level between 4.1 and 10.1 ng/mL, 47 of the 265 patients who underwent 6-core biopsy and 32 of the 91 patients who underwent a12-core biopsy were diagnosed with prostate cancer ($p = 0.0006$). Among the patients with a PSA level between 10.1 and 20.0 ng/mL, 48 of 163 patients who underwent the 6-core biopsy and 16 of 37 patients who underwent the 12-core biopsy were diagnosed with prostate cancer ($p = 0.0606$). Three of the 95 patients who were diagnosed with prostate cancer through the 6-core biopsy and 12 of the 48 patients who were diagnosed through the 12-core biopsy had cancer located in the anterior apex. The 12-core biopsy increased the diagnostic rate in the apex ($p = 0.001$). No statistically significant differences were found in incidence of complications.
*Conclusion:* We concluded that the 12-core biopsy is a safe and more effective procedure for increasing the diagnostic rate of prostate cancer than the 6-core biopsy in patients with PSA level between 4.1 and 10.0 ng/mL, and the most useful anatomical area to be added was found to be cores from the anterior apex.

***Key words**: prostate neoplasms; diagnosis; prostatic specific antigen*
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## INTRODUCTION

In Japan, prostate cancer is the most important disease in the field of urology, with a recent increase in the morbidity and mortality associated with the disease. Currently, systematic 6-core prostate biopsy is widely used in the diagnosis of prostate cancer and has improved the diagnostic rate. However, it has been reported that repeated biopsies increase the diagnostic rate of prostate cancer (1, 2), suggesting that a single set of 6-core biopsies may miss many prostate cancer lesions. In addition, the diagnostic rate of 6-core biopsy at the Department of Urology of Aichi Medical University School of Medicine was 16.5% (18/109) in patients with PSA level (Tandem-R) between 4.1 and 10.0 ng/mL, and 27.5% (22/80) in patients with PSA level between 10.1 and 20.0 ng/mL. These rates were lower than those at other institutions (3).

Therefore, since March 2003, we have been using systematic the 12-core biopsy to improve the diagnostic rate of prostate cancer in patients with PSA level between 4.1 and 20.0 ng/mL. In this retrospective study, we evaluated the efficacy and safety of the 12-core biopsy in the diagnosis of prostate cancer compared with the conventional 6-core biopsy.

## MATERIALS AND METHODS

This study included 428 patients with a PSA level between 4.1 and 20.0 ng/mL who underwent a 6-core biopsy from January 1998 to February 2003 (PSA levels: 4.1 - 10.0 ng/mL in 265 patients, 10.1 - 20.0 ng/mL in 163 patients) and 128 patients with PSA level between 4.1 and 20.0 ng/mL who underwent a 12-core biopsy from March 2003 to May 2005 (PSA levels: 4.1 - 10.0 ng/mL in 91 patients, 10.1 - 20.0 ng/mL in 37 patients). Patient characteristics are shown in Table-1.

PSA levels were determined with a Tandem-R Kit (Hybritech, San Diego, CA, USA). Transrectal ultrasound-guided systematic 6-core or 12-core prostate biopsies were performed using the Aloka SSB-650CL ultrasound system (ALOKA, Ltd., Mitaka, Tokyo, Japan) with an 18-gauge biopsy needle (Biopty, C. R. Bard, Covington, GA, USA).

With the patient in the lithotomy position, prostate biopsies were performed after intrarectal injection of 10 mL of 2% lidocaine jelly. The patients were hospitalized overnight following the procedure. The 6-core biopsy scheme involved systematically obtaining 6 laterally directed cores. The 12-core biopsy scheme involved obtaining 6 far lateral cores in addition to the 6-core technique. All patients were given an enema before biopsy, and 2 g ceftazidime was administered by intravenous infusion on the day of biopsy. For the following 3 days, 300 mg levofloxacin was administered orally.

Differences between the groups were tested for significance using the Mann-Whitney U test and Fisher's exact test, and a difference of $p < 0.05$ was defined as statistically significant. Statistical analyses were performed with Stat View software (Abacus Concept, Berkeley, CA, USA).

## RESULTS

Of a total of 556 patients, 143 (25.7%) were diagnosed with prostate cancer. Ninety-five (22.2%) of the 428 patients who underwent 6-core biopsy and 48 (37.5%) of the 128 patients who underwent 12-core biopsy were diagnosed with prostate cancer; the difference between the two groups being statistically significant ($p = 0.001$). Among the patients with a PSA level between 4.1 and 10.0 ng/mL, 47 (17.7%) of the 265 patients who underwent a 6-core biopsy and 32 (35.2%) of the 91 patients who underwent a 12-core biopsy were diagnosed with prostate cancer, the difference being statistically significant ($p = 0.01$). Among the patients with PSA level between 10.1 and 20.0 ng/mL, 48 (29.4%) of the 163 patients who underwent a 6-core biopsy and 16 (43.2%) of the 37 patients who underwent a 12-core biopsy were diagnosed with prostate cancer, showing no statistically significant difference between the two groups (Table-2).

***Table 1 –*** *Patient characteristics.*

| | Sextant | 12-Cores | p Value |
|---|---|---|---|
| Number of patients | n = 428 | n = 128 | NS |
| Age (year) | 69.6 ± 8.2 (70.0) | 69.1 ± 7.3 (69.0) | NS |
| PSA (ng/mL) | 9.73 ± 4.1 (8.3) | 8.99 ± 4.03 (7.5) | NS |
| Prostate volume (mL) | 38.11 ± 24.9 (32.0) | 33.59 ± 21.17 (27.0) | NS |

*NS = not significant.*

***Table 2 –*** *Diagnostic rates of prostate cancer in sextant and 12-core biopsy groups.*

| Diagnosis of PCa | Sextant | 12-Cores | p Value |
|---|---|---|---|
| PSA 4.1-10.0 (ng/mL) | 47/265 (17.7%) | 32/91 (35.2%) | P = 0.01 |
| PSA 10.1-20.0 (ng/mL) | 48/163 (29.4%) | 16/37 (43.2%) | NS |
| Total | 95/428 (22.2%) | 48/128 (37.5%) | P = 0.001 |

*NS = not significant.*

The intraprostatic cancer distribution was determined in 48 patients who were diagnosed with prostate cancer by the 12-core biopsy, Forty of these patients (83.3%) had cancer detected in both traditional 6-core biopsy cores and laterally directed additional cores. In 6 (6.6%) of the 91 patients with a PSA level between 4.1 and 10.0 ng/mL and 2 (5.5%) of the 37 patients with a PSA level between 10.1 and 20.0 ng/mL, cancer was detected only in laterally directed additional cores and all of them were located in the anterior apex (Table-3).

In patients who were diagnosed with prostate cancer by laterally directed additional cores, cancer was located only in the anterior apex; therefore, the diagnostic rates of 6-core biopsy and 12-core biopsy in the anterior apex were investigated. Three (3.2%) of the 95 patients who were diagnosed with prostate cancer by the 6-core biopsy and 12 (25.0%) of the 48 patients who were diagnosed by the 12-core biopsy had cancer located in the apex; the 12-core biopsy significantly (p = 0.001) increased the diagnostic rate of prostate cancer in the apex (Table-4).

Complications, including fever of 38.5ºC or higher, macroscopic hematuria, rectal bleeding, the need for anesthesia, and prolongation of hospitalization, were evaluated. Macroscopic hematuria was

***Table 3 –*** *Diagnostic rate of prostate cancer by location in 12-core biopsy group.*

| | **PSA = 4.1-10.0** (ng/mL) | **PSA = 10.1-20.0** (ng/mL) | **Total** |
|---|---|---|---|
| Systematic sextant biopsy cores + 6 laterally directed additional cores | 26/91 (28.6%) | 14/37 (37.8%) | 40/128 (31.0%) |
| 6 laterally directed additional cores only | 6/91 (6.6%) | 2/37 (5.5%) | 8/128 (6.3%) |
| Total | 32/91 (35.2%) | 16/37 (43.2%) | 48/128 (37.5) |

***Table 4 –*** *Diagnostic rates prostate cancer located in the anterior apex only and in other locations detected by sextant and 12-core biopsies.*

| | Sextant | 12-Cores | p Value |
|---|---|---|---|
| Apex only | 3/95 (3.2%) | 12/48 (25%) | p = 0.001 |
| Others | 92/95 (96.7%) | 36/48 (75.0%) | NS |

*NS = not significant*

***Table 5*** *- Complications.*

| | Sextant | 12-Cores |
|---|---|---|
| Fever 38.5ºC or higher | 0 | 3 |
| Rectal bleeding | 0 | 0 |
| Macroscopic hematuria | 75/428 (17.5%) | 32/128 (25%) |
| Patients required anesthesia | 0 | 0 |
| Patients required prolongation of hospitalization | 0 | 0 |

observed in 75 patients (17.5%) who underwent a 6-core biopsy and 32 patients (25.0%) who underwent a 12-core biopsy. Fever of 38.5ºC or higher was seen in 3 patients who underwent a 12-core biopsy, showing no statistically significant difference between the two groups (Table-5).

## COMMENTS

The systematic 6-core biopsy protocol, in which 3 cores are taken from certain parts of the prostate bilaterally under transrectal ultrasound guidance regardless of the ultrasound findings, was proposed and introduced into clinical practice by Hodge et al. (4) in 1989. However, some patients with an elevated PSA level and/or abnormal findings in digital rectal examination are not diagnosed with prostate cancer by the 6-core biopsy, and sampling errors occur in about 10 -30% of 6-core biopsies (5,6).

Various biopsy schemes have been proposed to increase the diagnostic rate of prostate cancer. The 5-region biopsy protocol, which involves obtaining 2 cores from the lateral peripheral zone (1 from each side) and 3 cores from the mid peripheral zone in addition to the standard 6-core technique (11-core biopsy), proposed by Eskew et al. (7), increased the diagnostic rate up to 40.3%. Moreover, Chang et al. (8) reported that of 22 patients who underwent a 10-core biopsy, which involves obtaining 4 cores from the lateral peripheral zone in addition to the standard 6-core technique, 17 (77.3%) patients had cancer detected only in the additional biopsy cores, which would have otherwise been undetected by 6-core biopsy. In this study, the diagnostic rates of standard 6-core and 12-core biopsies were 22.2% (95/428) and 37.5% (48/128), respectively; 6 laterally directed additional cores to 6-core biopsy significantly ($p = 0.0005$) increased the rate. Among the patients with a PSA level between 4.1 and 10.0 ng/mL, a statistically significant difference in diagnostic rates was found between the 6-core and 12-core biopsy groups ($p = 0.0006$), whereas no statistically significant difference was found among the patients with PSA level between 10.1 and 20.0 ng/mL. Furthermore, Kojima et al. (9) and Matsumoto et al. (10) have reported that 6 laterally directed additional cores to 6-core biopsy increased the diagnostic rate of prostate cancer by 13.8% (18/130) and 7.7% (3/39), respectively. Terris et al. (11) reported that 68% of their patients were diagnosed by 12-core biopsy; 46% had cancer detected in both the systematic biopsy cores and additional biopsy cores, and 15% had cancer detected only in the additional biopsy cores. In our study, additional cores increased the diagnostic rate by 6.3%. However, because patients with a PSA level of 20.0 ng/mL or greater were included in their study, it may not be justified to compare their results with ours. On the other hand, it is interesting that the randomized trial reported by Naughton et al. (12), in which 244 patients were assigned to 6-core biopsy or 12-core biopsy, showed no significant difference in diagnostic rate between the groups (26% in the 6-core biopsy group and 27% in the 12-core biopsy group).

Nonpalpable prostate cancer has been reported to occur predominantly in the anterior apex (10,13). Takashima et al. (13) analyzed the distribution of prostate cancer using computer prostate models constructed from pathologic slides of radical prostatectomy specimens, and found that the distribution rates of prostate cancer in the mid-prostate level and anterior apex were 85.5% and 82.3%,

respectively, and most nonpalpable prostate cancer was located in the mid-prostate level and anterior apex. In this study, prostate cancer was located only in the anterior apex in 3 (3.2%) of the 95 patients who were diagnosed with prostate cancer by 6-core biopsy and 12 (25%) of the 48 patients who were diagnosed by 12-core biopsy; 12-core biopsy significantly increased the cancer detection rate. Therefore, obtaining additional biopsy cores from the anterior apex may increase the diagnostic rate of prostate cancer.

Berger et al. (14) studied pain control during biopsy in 100 patients assigned to receive a periprostatic injection of either 10 mL norepinephrine + 2% lidocaine (n = 50) or 10 mL physiologic saline (n = 50) before biopsy, and pain during biopsy was assessed on an analog scale. The analog scale score was 0.76 in the norepinephrine + 2% lidocaine combination group and 3.62 in the physiologic saline group, showing that periprostatic injection of 10 mL norepinephrine + 2% lidocaine was simple and safe, and significantly relieved discomfort. Moreover, Pendleton et al. (15) have reported that a combination of 30 or 75 mg oral tramadol, 650 mg oral acetaminophen, and periprostatic injection of 10 mL of 1% lidocaine was safe and effective in controlling pain. In our study, the prostate biopsy was performed after intrarectal injection of 10 mL of 2% lidocaine jelly, without pain in all patients. Given the complications of anesthesia such as vascular injury and hypotension, intrarectal injection of lidocaine is considered to be a safe and effective procedure.

The incidence of complications is not increased by increasing the number of biopsy cores (16, 17). In our study as well, none of the patients in either the 6-core or 12-core biopsy groups showed rectal bleeding, need for anesthesia, or prolongation of hospitalization. Berger et al. (17) and Raaijmakers et al. (18) reported that fever of 38.5ºC or higher was seen in 0.8% and 3.5% of biopsies, respectively. In our study, fever of 38.5ºC or higher was seen in 2.3% (n = 3) of 12-core biopsies. Fever has been reported in 6.6% of biopsies when an enema was not given before biopsy (19,20). In our study, enemas and antibiotics given before biopsy may have reduced the rate of fever. Macroscopic hematuria was seen in 75 (17.5%) of the 428 patients who underwent 6-core biopsy, and in 32 (25.0%) of 128 patients who underwent the 12-core biopsy, showing no statistically significant difference between the groups. Berger et al. (14) reported macroscopic hematuria in 14.5, 14.2, and 14.5% of the cases after 6-core, 10-core, and 15-core biopsies, respectively, and hematospermia was seen after 6-core, 10-core, and 15-core biopsies, at the rates of 31.8, 37.4, and 38.4%, respectively, showing no statistically significant difference among the groups. Their findings, in which increasing the number of biopsy cores was not a risk factor for increased incidence of complications such as macroscopic hematuria and hematospermia, are in agreement with our results.

## CONCLUSION

For patients with a PSA level between 4.1 and 10.0 ng/mL, 12-core biopsy is a safe and effective procedure that can significantly increase the diagnostic rate of prostate cancer compared to 6-core biopsy. Increasing the number of biopsy cores from the anterior apex may also increase the diagnostic rate.

## CONFLICT OF INTEREST

None declared.

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