

# THE EFFECT OF TRANSURETHRAL PROSTATECTOMY ON SERUM PROSTATE SPECIFIC ANTIGEN AND PROSTATIC ACID PHOSPHATASE LEVELS

Önder KAYIGİL, M.D., Nahide GÖKÇORA\*, M.D., Nuri DENİZ, M.D.,  
Haluk TOKUÇOĞLU, M.D., Üstünoğlu KARAOĞLAN, M.D., İbrahim BOZKIRLI, M.D.

Gazi University, Faculty of Medicine, Departments of Urology and Nuclear Medicine\*,  
Ankara, Turkey  
Gazi Medical Journal 3 : 129-136, 1992

*SUMMARY : The values of prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) have been determined in 37 patients with prostatism symptoms between February 1991 and July 1991 in Urological Department of Gazi University, School of Medicine.*

*Of these 37 patients, 27 (72.97 %) had benign prostatic hyperplasia (BPH) and the remaining 10 (27.03 %) had prostatic carcinoma.*

*Serum samples were taken preoperatively, peroperatively, immediately after the surgical procedure and on the first postoperative day and the values of.*

*PSA and PAP were evaluated. It was found that, these values were increased during the peroperative period and immediately after the surgical procedure, later decreasing to nearly normal levels on the first postoperative day. This difference has been found statistically significant ( $P < 0.05$ ).*

*On the other hand, the difference in these parameters were found insignificant in prostatic carcinoma group.*

*These two different reactions of PSA and PAP molecules during transurethral resection enables us to diagnose BPH or advanced prostatic carcinoma before histopathological diagnosis.*

*Key Words : Benign Prostatic Hyperplasia, Prostatic Carcinoma, Prostate Specific Antigen, Prostatic acid Phosphatase, Transurethral Prostatectomy.*

## INTRODUCTION

Searching for a valuable marker for diagnosing and staging of prostatic carcinoma has been the field of study of many researchers for the last fifty years.

Nowadays, PSA and PAP are believed to be the best and important markers for prostate malignancy.

PSA was first identified from seminal plasma by Hara et al. (1971). It is a single chain glycopro-

tein that consists of 93 % aminoacids and 7 % carbohydrates. Its half life is 2-3 days long (Wang et al. 1982).

Functionally PSA is a kallikrein-like serine protease which is produced by the epithelial cells of the prostate gland (Lilja, 1981). It has been shown that serum PSA level is increased by digital rectal examination, endoscopic manipulation and transurethral resection (Stamey, 1989).

PAP is a sialoglycoprotein which is produced by the acinar epithelium and secreted to the seminal fluid (Reid et al. 1990). The first half life of this marker is 0.5-2.5 hours and second half is 2 days (Reid et al. 1990).

Some researchers proved that digital rectal examination, urethral instrumentation and transurethral prostatic resection caused a 24-48 hour lasting increase in serum PAP levels (Pearson et al. 1985; Tokuçođlu et al. 1989).

The purpose of this study is to determine the changes of PSA and PAP levels during transurethral prostatectomy in benign prostate hyperplasia and prostatic carcinoma.

### MATERIALS AND METHODS

In this study 37 patients with prostatism symptoms who had BPH or prostate carcinoma treated with TURP were studied. Mean age was 64.02 years (Range 51-78) (Table 1). Routine blood tests, urinalysis, intravenous pyelography (IVP), ultrasonography (USG) and in necessary cases computed tomography (CT) and scintigraphy were performed prior to the operation. In 2 (5.4 %) patients epidural anaesthesia and in 35 (94.6 %) spinal anaesthesia were used. During TURP 15 (40.55 %) patients were irrigated with distilled water and 22 (59.45 %) with sorbitol mannitol solution. Preoperative, peroperative, immediate postoperative and postoperative first day serum samples were taken, and PSA and PAP levels were determined.

Age	Patient no.	%
50-60	12	32.43
60-70	19	51.35
Above 70	6	16.22
<b>Total</b>	<b>37</b>	<b>100.00</b>

Table - 1 : Age distribution of patients.

Serum PSA assays were performed using the PSA double antibody radioimmunoassay kit (Diagnostic Products Cooperation 31 Station Lane Witne, GAN United Kingdom Lot No : KPSDI 0320). The values under 4 ng/ml were accepted normal.

Serum PAP assays were performed using Fishman and Lerner's L Tartarat Inhibition Method. The values between 0.1 - 0.8 King Armstrong Unit (KAU) were considered normal. Pathological examination of the specimens was done by Department of Pathology, Gazi University School of Medicine.

Statistical analysis was performed using the Student's t test.

### RESULTS

In this study, 27 of 37 patients (72.97 %) were diagnosed as BPH histopathologically and the rest 10 patients (27.03 %) as prostatic carcinoma (Table 2). Six (60 %) patients who had prostatic carcinoma had bone metastases, 4 patients had no metastatic lesions.

Diagnosis	Patient no.	%
BPH	27	72.97
Prostatic Carcinoma	10	27.03
<b>Total</b>	<b>37</b>	<b>100.00</b>

Table - 2 : Patient distribution according to histology.

High serum PSA levels were found in 20 (74.04 %) of 27 patients with BPH. In 7 (25.96) patients PSA levels were normal (Table 3).

Serum PSA level (ng/ml)	Patient no.	%
Belove 4	7	25.96
Above 4	20	74.04
<b>Total</b>	<b>27</b>	<b>100.00</b>

Table - 3 : Distribution of patients with BPH according to PSA level.

In BPH patients, mean preoperative PSA level was  $11.49 \pm 16.60$  ng/ml, mean peroperative PSA level was  $22.49 \pm 23.21$  ng/ml, mean postoperative PSA level was  $51.51 \pm 48.24$  ng/ml and mean postoperative first day PSA level was  $18.48 \pm 15.56$  ng/ml (Fig 1, Table 4).

All the prostatic carcinoma patients had high PSA levels (Table 5).

In prostatic carcinoma patients mean preoperative PSA level was  $63.57 \pm 40.61$  ng/ml, mean peroperative PSA level was  $74.21 \pm 40.73$  ng/ml, mean postoperative PSA level was  $72.27 \pm 44.95$  ng/ml and mean postoperative first day PSA level was  $79.53 \pm 53.08$  ng/ml (Fig 2, Table 6).

High serum PAP levels were found in 10(37.03 %) of 27 patients with BPH. In 17(63.97 %) patients PSA levels were normal (Table 7).

In BPH patients mean preoperative PAP level was  $1.2 \pm 0.79$  KAU, mean peroperative PAP level was  $2.54 \pm 2.59$ , mean postoperative PAP level was

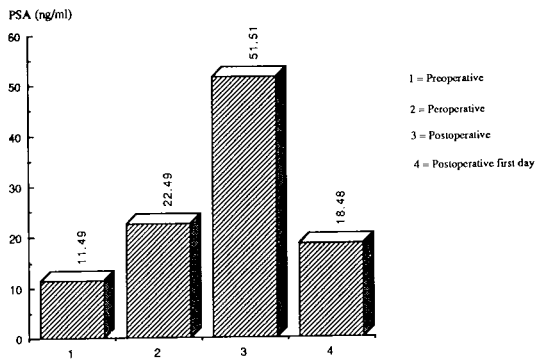


Fig. 1 : Mean PSA levels in patients with BPH.

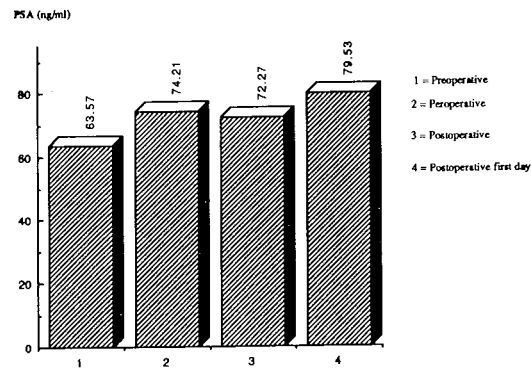


Fig. 2 : Mean PSA levels in patients with prostatic carcinoma

Variable	No. of patients (27)	PSA (ng/ml)	±SD	t value	P
		Mean (Range)			
1		11.49(1.72-87.33)	±16.60		
2		22.49(1.55-116.40)	±23.21	-2.151	P<0.05 Significant
1		11.49	±16.60		
3		51.51(1.71-151.05)	±48.24	-4.6	P<0.05 Significant
1		11.49	±16.60		
4		18.48(3.25-67.01)	±15.56	-1.84	P<0.05 Significant
2		22.49	±23.21		
3		51.51	±48.24	-3.419	P<0.05 Significant
2		22.49	±23.21		
4		18.48	±15.56	0.819	P>0.05 Not significant
3		51.51	±48.24		
4		18.48	±15.56	3.75	P<0.05 Significant
3		51.51	±48.24		
4		18.48	±15.56		

1= mean preoperative PSA level 2= mean peroperative PSA level 3= mean postoperative PSA level 4= mean postoperative first day PSA level.

Table - 4 : Statistical analyses of mean serum PSA levels in patients with BPH.

Serum PSA ng/ml	Patient no.	%
Belove 4	0	0
Above 4	10	100
<b>Total</b>	<b>10</b>	<b>100</b>

Table - 5 : Distribution of patients with prostatic carcinoma according to PSA level.

Serum PAP Level (KAU)	Patient no.	%
Belove 0.8	10	37.03
Above 0.8	17	63.97
<b>Total</b>	<b>27</b>	<b>100.00</b>

Table - 6 : Distribution of patients with BPH according to PAP level.

Serum PAP Level (KAU)	Patient no.	%
Above 0.8	10	37.03
Belove 0.8	17	63.97
<b>Total</b>	<b>27</b>	<b>100.00</b>

Table - 7 : Distribution of patients with BPH according to PAP level.

4.01±3.41 KAU and mean postoperative first day PAP level was 1.88±0.68 KAU (Fig 3, Table 8).

Serum PAP Level (KAU)	Patient no.	%
Belove 0.8	0	0
Above 0.8	10	100
<b>Total</b>	<b>10</b>	<b>100</b>

Table - 9 : Distribution of patients with prostatic carcinoma according to PAP level.

All 10 patients with prostatic carcinoma had high PAP levels (Table 9).

Variable	No. of patients (27)	PSA (ng/ml)	±SD	t value	P
		Mean (Range)			
1		1.20(0.3-3.9)	0.79		
2		2.54(0.1-5.8)	2.59	-2.543	P<0.05
1		1.20	0.79		
3		4.01(0.7-8.8)	3.41	-4.340	P<0.05
1		1.20	0.79		
4		1.88(0.1-2.6)	0.68	-0.852	P>0.05
2		2.54	2.59		
3		4.01	3.41	-3.94	P<0.05
2		2.54	2.59		
4		1.88	0.68	2.92	P<0.05
3		4.01	3.41		
4		1.88	0.68	4.55	P<0.05

1= mean preoperative PAP level 2= mean peroperative PAP level 3= mean postoperative PAP level 4= mean postoperative first day PAP level.

Table - 8 : Statistical analyses of mean serum PAP levels in patients with BPH.

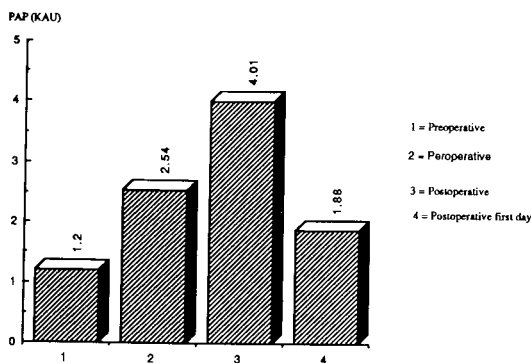


Fig. 3 : Mean PAP levels in patients with BPH.

In prostatic carcinoma patients mean preoperative PAP level was 4.93±2.65 KAU, mean peroperative PAP level was 4.35±3.10 KAU, mean postoperative PAP level was 3.72±1.49 KAU, mean postoperative first day PAP level was 5.13±3.12 KAU (Fig 4, Table 10).

In BPH patient group the difference between mean preoperative and mean peroperative PSA levels was significant (P<0.05). The difference between mean preoperative and mean postoperative PSA levels (P<0.05), between mean preoperative and mean postoperative first day PSA levels and mean peroperative and mean postoperative PSA levels were also significant (P<0.05). The difference between mean peroperative and mean postoperative first day PSA levels was found to be insignificant

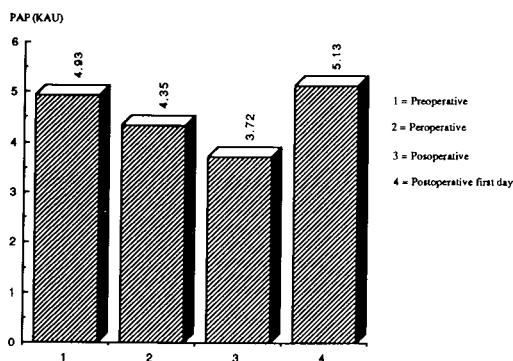


Fig. 4 : Mean PAP levels in patients with BPH.

( $P > 0.05$ ) and the difference between mean postoperative and mean postoperative first day PSA levels were significant ( $P < 0.05$ ) (Table 4).

In prostatic carcinoma patients group the difference between mean preoperative and mean perioperative PSA levels were significant ( $P < 0.05$ ) and between mean preoperative and mean postoperative PSA levels were insignificant ( $P > 0.05$ ). The difference between mean preoperative and mean postoperative PSA levels was significant ( $P < 0.05$ ) and the difference between mean preoperative and mean postoperative PSA levels was determined to be insignificant ( $P > 0.05$ ). The difference between mean perioperative and mean postoperative first day PSA levels was insignificant ( $P > 0.05$ ) and the difference between mean postoperative and postoperative first day PSA levels were significant (Table 6).

In BPH patients the difference between mean preoperative and mean perioperative PAP levels and also mean preoperative and mean postoperative PAP levels were significant ( $P < 0.05$ ). The difference between mean preoperative and mean postoperative first day PAP levels were insignificant ( $P > 0.05$ ). The difference between mean preoperative and mean postoperative PAP levels and also mean preoperative and mean postoperative first day PAP levels were significant ( $P < 0.05$ ). The difference first day PAP levels were significant ( $P < 0.05$ ) (Table 8).

In prostatic carcinoma patients all statistical analyses except mean preoperative and mean postoperative first day PAP levels was insignificant ( $P > 0.05$ ) (Table 10).

## DISCUSSION

There has recently been a great deal of improvement in the diagnosis and treatment of BPH and prostatic carcinoma. The diagnosis and the differential diagnosis of BPH and prostatic carcinoma has become easier with the developments in the diagnostic methods. Tumor markers are being widely used for the detection of the prostatic pathology and follow-up of the treatment.

Preoperative PSA levels were found 68 % higher than normal limits by Kuriyama et al. (1980) in patients with BPH, and several authors (Hudson et al. 1984; Stamey et al. 1987; Yang et al. 1989) found PSA levels 62 %, 86 %, 28 % higher than normal limits respectively.

In our study high serum PSA levels were found 20 (74.07 %) of 37 patients with BPH.

High serum PSA levels were found 36 (40 %) of 91 patients with prostatic carcinoma by Siddall et al (1986). In this study researchers suggested that high PSA levels were in relation with prostatic weight in patients with nonmetastating prostatic carcinoma.

By morphometric evaluation of radical prostatectomy specimens Stamey et al. (1986) showed that as the tumor volume and stage got higher, serum PSA levels also increased. Myrtle et al. (1986) showed that in PSA levels were normal 43 % of patients with prostatic carcinoma. In patients with organ limited prostatic carcinoma the authors suggested that if PSA levels was above 4 ng/ml, it had a diagnostic value and if it was above 10 ng/ml, the diagnostic accuracy was 70 %.

In our study serum PSA levels has been found above 10 ng/ml in all patients with prostatic carcinoma.

The advanced stage of illness and the difficulty in diagnosing the subcapsular metastasis are the reasons for this high PSA level.

When PAP levels are considered, Fleischman et al. (1983) showed high PAP levels in 6 % of patients with BPH preoperatively. This ratio was 27 % in the study of Salo et al. (1990).

In our study high serum PAP levels were found in 10 (37.03 %) of 27 patients with BPH.

We think that high PAP levels in our study are due to early elevation of this marker after digital rectal examination and transrectal ultrasonog-

Variable	No. of patients (27)	PSA (ng/ml)	±SD	t value	P
		Mean (Range)			
1		4.93(1.3-11.2)	±2.65	1.973	P>0.05 Not significant
2		4.35(0.7-1.2)	±3.10		
1		4.93	±2.65	1.5973	P>0.05 Not significant
3		3.72(1.2-3.6)	±1.49		
1		4.93	±2.65	0.236	P>0.05 Not significant
4		5.13(1.2-12.8)	±3.12		
2		4.35	±3.10	0.718	P>0.05 Not significant
3		3.72	±1.49		
2		4.35	±3.10	-2.2807	P<0.05 Significant
4		5.13	±3.12		
3		3.72	±1.49	-1.549	P>0.05 Not significant
4		5.13	±3.12		

1= mean preoperative PAP level 2= mean properative PAP level 3= mean postoperative PAP level 4= mean postoperative first day PAP level.

Table - 10 : Statistical analyses of mean serum PAP levels in patients with prostatic carcinoma.

raphy.

Vihko et al. (1985) have diagnosed prostatic carcinoma in 10 % of patients with high levels of PAP. According to Pontes et al. (1981), when PAP levels were measured high, in cases with localized protatic carcinoma then occult lymph node, bone and other organ metastases could be seen. Stamey et al. (1987) found normal PAP levels in patients with stage A<sub>1</sub>, A<sub>2</sub>, B<sub>1</sub>, B<sub>2</sub> prostatic carcinoma.

We found that all the prostatic carcinoma patients had high PAP levels. The advanced stage of the illness and the difficulty in diagnosing the subcapsular metastasis are the reasons for this high PAP level.

In our study we also investigated the effect of transurethral surgery on serum PSA, PAP levels during TURP.

In addition to preoperative and postoperative PSA and PAP levels, we included pre and postoperative first day PSA and PAP levels in order to examine serum changes of these two molecules in a wider range during TURP. Serum PSA in BPH patients reaches its peak level during postoperative period and when preoperative, peroperative, postoperative and postoperative first day PSA levels are

compared the difference is statistically significant. This can also be shown graphically as it displays the characteristic figure (Fig 1).

When the same statistical comparisons are made with patients with prostatic carcinoma, the results are found mostly insignificant and a different figure is graphically obtained (Fig 2). Therefore transurethral prostatectomy increases serum PSA levels in patients with BPH but it is noneffective in patients with prostatic carcinoma.

The effect of different manipulations on serum PSA levels has been investigated by many researchers. Brawer et al. (1988) showed that serum PSA levels was not effected by digital rectal examination. Stamey (1989) demonstrated that serum PSA level was increased 1.92 fold after digital rectal examination. In their study serum PSA level was increased 4 folds after sistoscopic manipulation and 57 folds after needle biopsy. Stamey examined serum PSA levels in 75 patients who had undergone TURP and he found serum PSA increased 53 folds.

The increase of PSA levels was statistically significant in 58 patients with BPH and no significant difference was found in patients with prostatic carcinoma. They suggest that because prostatic cancer tissue is incapable to release PSA, high serum PSA

levels in prostatic carcinoma patients result from metastatic lesions.

In our study we found that PAP levels were increased peroperative and postoperatively right after the surgical procedure, later decreasing to almost normal levels on the first postoperative day. The peak level of PAP in patients with BPH was reached during the postoperative period. Most of the statistical analyses have exhibited significant differences in these four group levels (Tablo 8).

When the graphical analysis is done it shows characteristic figure (Fig 3) which is similar to PSA pattern (Fig 1).

In patients with prostatic carcinoma these statistical analyses have been found insignificant. The graphical analysis showed a similar pattern to PSA pattern in patients with prostatic carcinoma which is different from BPH pattern (Fig 4).

Some researchers showed that 24-48 hours lasting elevations of serum PAP levels could be caused by rectal digital examination, urethral instrumentation and resection of the prostate gland (Pearson et al. 1983; Tokuçoğlu et al. 1989).

In 1957 Marberger et al measured serum PAP levels in patients with BPH and prostatic carcinoma before and after TURP and suprapubic transvesical prostatectomy. Suprapubic transvesical prostatectomy had no effect on serum PAP though it was increased dramatically in patients with BPH following TURP. They observed minimal increase in patients with prostatic carcinoma. We also found similar findings in our study.

Marberger et al (1957) revealed that prostate secretions containing enzymes were released directly to circulation via irrigation fluid, causing venous influx and elevation of serum PAP level at the same time in BPH. They informed that minimal increase in serum PAP levels following open surgery was because of the irrigation fluid and resection were not performed.

In our study, in BPH and prostatic carcinoma patients, the release of PSA and PAP to circulation was found to be exhibiting the same pattern during TURP. The results of PAP expressed in Marberger et al (1957)'s study for BPH and prostatic carcinoma patients were also found to be correlating with PSA levels found in our study.

In conclusion, we suggest that PSA and PAP molecules can be used as diagnostic criteria regarding their changes in serum during transurethral prostatectomy.

**Correspondence to :**

Dr.Önder KAYIGİL  
Gazi Üniversitesi Tıp Fakültesi  
Üroloji Anabilim Dalı  
Beşevler  
06510 ANKARA - TÜRKİYE  
Phone : 4 - 212 65 65 / 408

**REFERENCES**

1. Brawer MK, Schifman RB, Ahmann FR : The effect of digital rectal examination on serum levels of prostate specific antigen. *Arch Path Lab Med* 112 : 1110-1114, 1988
2. Fleischmann J, Catalona WJ, Fair WE : Lack of value of radioimmunoassay for prostatic acid phosphatase as a screening test for prostatic cancer in patients with obstructive prostatic hyperplasia. *J Urol* 129 : 312-315, 1983
3. Hara M, Inorre T, Fukuyama T : Some physico-chemical characteristics of gamma semino-protein, on antigenic component specific for human seminal plasma. *Jap J Legal Med* 25 : 322-324, 1971
4. Hudson WJ : Clinical use of prostate specific antigen in patients with prostate cancer. *J Urol* 142 : 1011-1013, 1989
5. Kuriyama M, Wang MC, Papsidero LD : Quantation of prostate specific antigen in serum by a sensitive enzyme immunoassay. *Cancer Res* 40 : 4658-4661, 1980
6. Lilja H : A kallikrein-like serine protease in prostatic fluid leaves the predominant seminal vesicle protein. *J Clin Invest* 76 : 1899-1991, 1985
7. Marberger H, Segal SJ, Flocks RH : Changes in serum acid phosphatase levels consequents to prostatic manipulation or surgery. *J Urol* 78 : 287-293, 1957
8. Myrtle JF, Klimley PG : Clinical utility of prostate - specific antigen (PSA) in the management of prostate cancer. *Adv Cancer Diag, Hybritech Inc* 2 : 38-41, 1986
9. Pearson JC, Dombrowskis S, Reyer J : Radioimmunoassay of serum acid phosphatase after prostatic massage. *Urology* 21 : 37-40, 1983
10. Pontes JE, Choc BK, Rose NR : Clinical evaluation of immunological methods for detection of serum prostatic acid phosphatase. *J Urol* 126 : 363-366, 1981
11. Reid M Morse, Martin T Resnick : Detection of clinically occult prostate cancer. *Urol Clin North Am* 17, 3 : 567-574, 1990

12. Salo JO, Rannikko S, Haapiainen R : Serum acid phosphatase in patients with localised prostatic cancer, benign prostatic hyperplasia or normal prostates. *Brit J Urol* 66 : 188-192, 1990
13. Stamey TA : Prostate specific antigen in the diagnosis and treatment of adenocarcinoma of the prostate. *Monogr Urol* 10 : 49-51, 1989
14. Stamey TA, Yang N, Hay AR : Prostate specific antigen as a serum marker for adenocarcinoma of the prostate. *New Engl J Med* 317 : 900-911, 1987
15. Li TS, Beling CG : Isolation and characterization of two specific antigens of human seminal plasma. *Fertil Steril* 24 : 134-138, 1973
16. Tokuçođlu eH, Karaođlan Ő, Demirel F : Rektal prostat muayenesinin serum prostatik asit fosfataz düzeyine olan etkisi. *T.C.D.D Hastaneleri Tıp Bülteni* 1 : 95-101, 1989
17. Vihko P, Konttur M, Lukkarinen O : Screening for carcinoma of the prostate. Rectal examination and enzymatic and radioimmunologic measurement of serum acid phosphatase compared. *Cancer* 56 : 173-176, 1985
18. Wang MC, Valenzuela LA, Murphy GP et al : A simplified purification procedure for human prostate antigen. *Oncology* 39 : 1-4, 1982
19. Yang N : Pross-Check PSA a double antibody radioimmunoassay for prostate specific antigen. In : *Clinical aspects of prostate cancer*. New York. Elsevier Science Publishing Co 3 : 172-178, 1989