Recent advances in PSA for screening and surveillance of prostate cancer.

Essay
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ACT	Anti ChemoTrypsin.
API	α_1-protease inhibitor.
ASCO	American Society of Clinical Oncology.
ASTRO	American Society for Therapeutic Radiology an Oncology.
AUA	American Urological Association.
BCR	Biochemical Recurrence**.**
BMI	Body Mass Index.
BPH	Benign Prostatic Hyperplasia.
BPSA	Benign PSA.
CAB	complete Androgen Blockade.
cPSA	Complexed PSA.
CSAP	Cryo-Surgical Ablation of the Prostate.
CT	Computed Tomography .
CZ	Central Zone**.**
DRE	Digital Rectal Examination.
EBL	Estimated blood loss.
EDRN	EarlyDetectionResearchNetwork
ELISA	Enzyme -Linked Immuno-Sorbent Assay.
EORTC	European Organization for Research and Treatment of Cancer.
ESRPC	European Randomized Screening for Prostate Cancer.
FDA	Food and Drug Administration
F/T PSA	Free to Total PSA.

fPSA	Free PSA.
FRET	Fluorescence Resonance Energy Transfer.
HGPIN	HighGradeProstate Intraepithelial Neoplasia.
HIFU	high-intensityfocusedultrasound.
HRPC	Hormone-Refractory PCa.
IAD	IntermittentAndrogenDeprivation.
iPSA	Intact PSA.
Mab	Monoclonal Antibodies.
MG	Macroglobulin.
MRI	Magnetic Resonance Imaging.
MRIS	MRI Spectroscopy.
NCI	National Cancer Institute.
PAP	prostate acid phosphatase.
PCa	Prostate Cancer.
PCA3	PCa Antigen 3.
PET	Positron Emition Tomography.
PIA	ProliferativeInflammatoryAtrophy.
PIN	Prostate Intraepithelial Neoplasia.
PLCO	Prostate, Lung, Colorectal and Ovary.
pPSA	Pro PSA.
PSA	Prostate Specific Antigen.
PSA-ACT	PSA complexed to anti-chymotrypsin.
PSAD	PSA Density.
PSADT	PSA Doubling Time.
PSADTZ	PSAD of the transition zone.

PSAV	PSA Velocity.
PSMA	Prostate Specific Membrane Antigen.
PZ	Peripheral Zone.
RNA	Ribo Nnucleic Acid
RP	Radical Prostatectomy**.**
ROC	Receiver Operator Characteristic
SEER	Surveillance, Epidemiology, and End Results.
SWOG	South West Oncology Group.
TNM	Tumor, Node, and Metastasis.
tPSA	Total PSA.
TRUS	Trans-Rectal Ultra-Sonography.
TURP	Trans-Urethral Resection of the Prostate.
TZ	Transition Zone**.**
US	United States of America.
VS	Versus
WHO	World Health Organization.
WW	watchful waiting.

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Prostate cancer (PCa) is the most common non cutaneous cancer in men in the US and the second leading cause of male cancer mortality, accounting for an expected 28,660 deaths in 2008. There have been many efforts to detect this malignancy in an early curable stage and to reduce its mortality rate. ***(Jemal et al, 2008)***

Since its discovery more than 20 years ago, prostatic specific antigen (PSA) has been established as the most valuable tool for early detection, staging, and monitoring of PCa. ***(Partin et al, 1994)***

In the early 1990s, at least five large series of studies clearly showed that for the detection of PCa. PSA determination alone is better than DRE or other parameters, and that the combination of PSA and DRE is the most effective way to detect PCa. ***(Catalona et al, 1993)***

A large multicenter PCa screening trial of 6630 men showed that the positive predictive value of PSA increased from 10% in men with PSA concentrations 4 ng/ml to 80% when the concentrations were 20 ng/ml .***(Catalona et al, 1994)***

Most patients with a PSA value <10 ng/ml were diagnosed with early stage disease, where as 50% of patients with PSA concentrations >10 ng/ml had advanced disease. These data demonstrated the need for a low PSA cutoff point

for detecting PCa in early, curable stages. The generally accepted PSA cutoff of 4 ng/ml leads to a rather high number of 65% false-positive findings, demonstrating the inability of PSA to discriminate PCa from other benign diseases. ***(Beduschi et al, 1995)***

This is because PSA is mostly organ- but not cancer-specific. Elevated PSA concentrations are also observed in BPH, prostatic ischemia or infarction, acute and chronic prostatitis, and after clinical manipulations. ***(Catalona et al, 1991)***

Various methods were proposed for improving the sensitivity and specificity, especially in the range of a PSA 4–10 ng/ml to detect PCa. ***(Brawer et al, 2000)***

Several concepts such as PSA density, PSA Transition zone density, PSA velocity, and age- or race-specific reference ranges have been developed to reduce the false negative and false-positive rates .***(Kamoi et al, 1999)***

Moreover, it has been shown that PSA in serum exists in different molecular forms, (cPSA,proPSA, BPSA) and that the measurement of these forms offers new possibilities to improve the diagnostic discrimination between PCa and BPH. ***(Heidenreich et al, 2009)***

The most recent research suggests further PSA testing is unnecessary in men 75 years and a PSA level 3 ng/mL at their first screening visit. This is because these men have a very low risk of dying from PCa. ***(Carter et al, 2008)***

The widespread use of PSA testing has caused many men to be diagnosed with prostate cancer much earlier in their lives when compared to the pre-PSA era. ***(Gann et al, 1995)***

It had been originally estimated that the mean lead time associated with PSA testing was 50 years. *Draisma et al*, recently published a model based on data from the ERSPC suggesting that prostate cancer diagnosis was advanced by as much as 10 years among men aged 55 and by five years for men aged 75years. ***(Draisma et al, 2003)***

Aim of the work

The main purpose of this essay is to discuss the new about prostatic specific antigen (PSA) and its application in early detection, pretreatment staging and post-treatment management of prostate cancer.

Prostate Cancer (PCa) is now recognized as one of the most important medical problems facing the male population. In Europe PCa is the most common solid neoplasm, with an incidence rate of 214 cases per 1000 men, out numbering lung and colorectal cancer. ***(Ann Oncol, 2005)***

Furthermore PCa is currently the second most common cause of cancer death in men after lung cancer**.** ***(Jemal et al, 2008)***

Zonal anatomy of the prostate:

The prostate is composed of approximately 70% glandular elements and 30% fibromuscular stroma. The stroma is continuous with capsule and is composed of collagen and abundant smooth muscle. It encircles and invests the glands of the prostate and contracts during ejaculation to express prostatic secretions into the urethra**.** ***(McNeal, 1988)***

The glandular elements of the prostate have been divided into discrete zones distinguished by the location of their ducts in the urethra, These zones can be demonstrated clearly with transrectal ultrasonography. ***(McNeal, 1988)***

Three distinct zones have been identified. The peripheral zone accounts for 70% of the volume of the young adult prostate, the central zone accounts for 25%, and the transition zone accounts for 5%.

A) The central zone (CZ):

The CZ is cone shaped with its base at the base of the prostate and apex extending down to the verumontanum. It surrounds the ejaculatory ducts along their entire course through the prostate, so there is no CZ tissue distal to the verumontanum**.** ***(Kaye, 1991)***

B) The peripheral zone (PZ):

The PZ forms the posterior, lateral and apical portions of the gland in the shape of a horseshoe. It extends from the base of the prostate to its apex along the rectal surface. It contacts the urethra at and inferior to the verumontanum **.** ***(Griswold, 1995)***

c) The Transition zone (TZ):

The TZ is presented into two small lobules on either side of the proximal urethra segment just lateral to the periprostatic sphincter. ***(McNeal et al, 1988)***

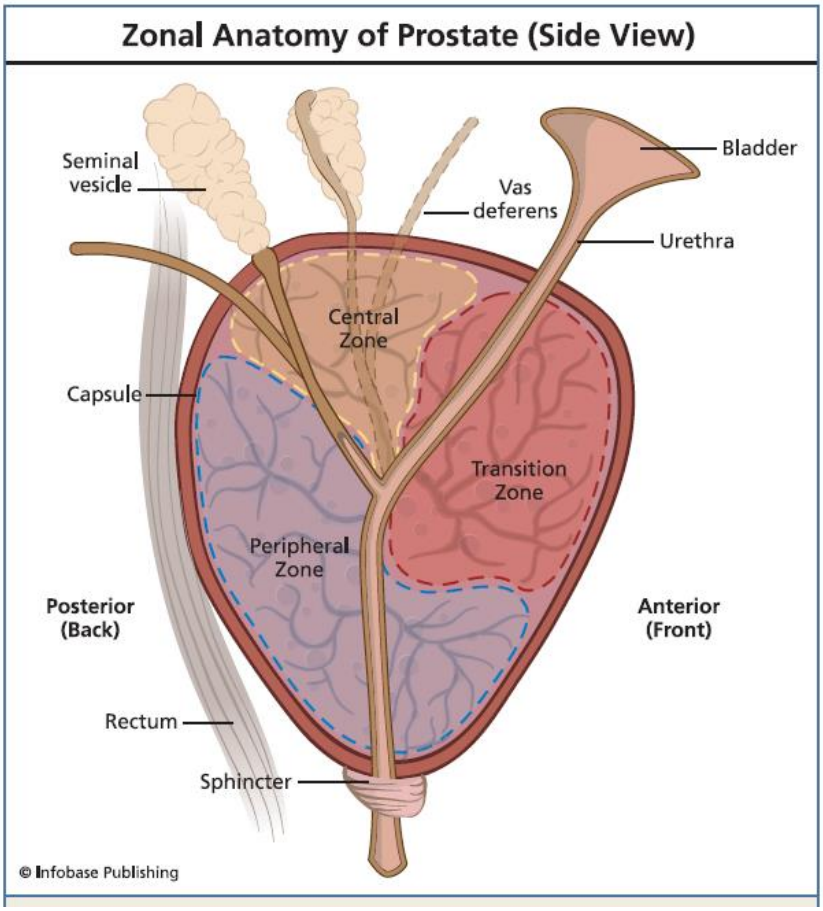

Fig1: side view of zonal anatomy of prostate gland. (Quoted from carmer, 2007)

These anatomic zones have distinct ductal systems but, more important, are differentially afflicted with neoplastic processes. Sixty to seventy percent of PCa originate in the peripheral zone, 10–20% in the transition zone, and 5–10% in the central zone. ***(McNeal, 1989)***