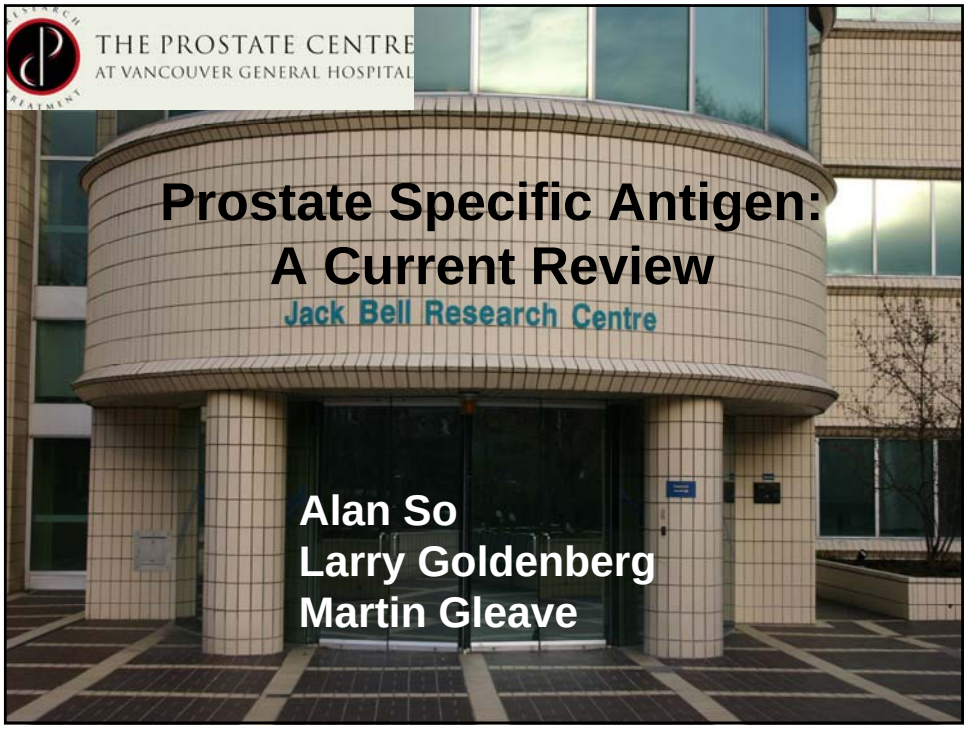
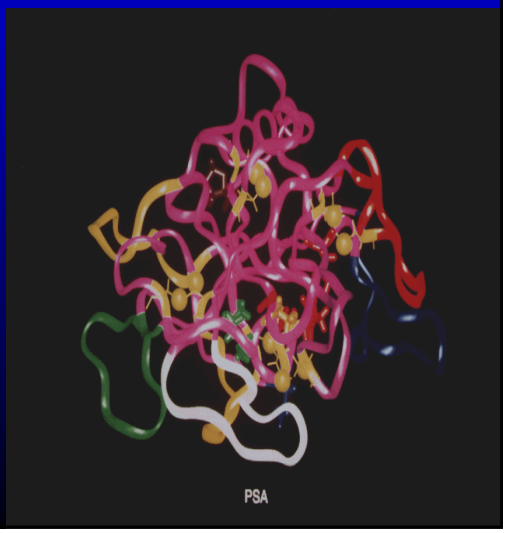


PSA

- 28 400 Da (240 a.a.) glycoprotein
  - (19q13.2-13.4)
- Kallikrein family- serine protease
- secreted into prostatic ducts at 2.0 g/L
- In serum at ug/L (ng/cc)
- liquefies seminal coagulum

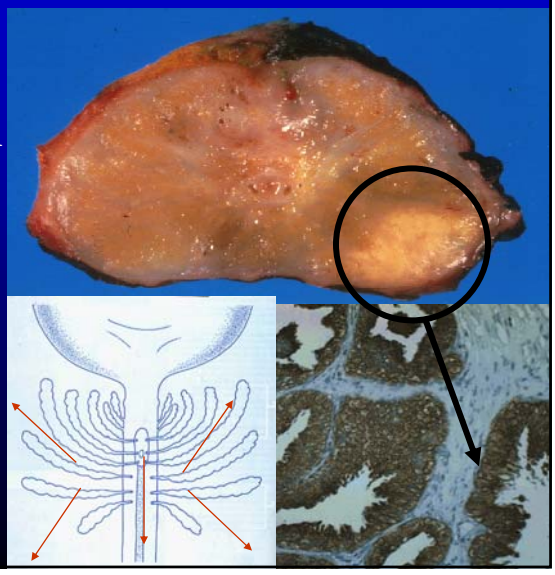


PSA - History

- Ablin (1970) – first demonstrated PSA in prostatic tissue
- Hera (1971) - seminal plasma
- Sesabaugh (1978) - semen-specific
- Wang (1979) - specific to prostatic tissue
- Papsidero (1980) - found it in serum

PSA

- All types of prostate epithelium produce PSA
  - Normal
  - Hyperplastic
  - Neoplastic
  - Infected



PSA

- detected at low concentrations (IHC) in:
  - the endometrium
  - normal breast tissue
  - breast tumors
  - adrenal neoplasms
  - renal cell carcinomas
  - Hepatic tumors
- Although tissues immunostain (+) - no evidence that these cause significant measurable serum levels

PSA - Confounders

- Increases PSA
  - Prostatitis
  - BPH
  - DRE
  - Prostate Biopsy
  - Cystoscopy
  - Physical Activity (?)
- Decreases PSA
  - Surgical / Medical Castration
  - Finasteride (50%)
  - Ejaculation (?)

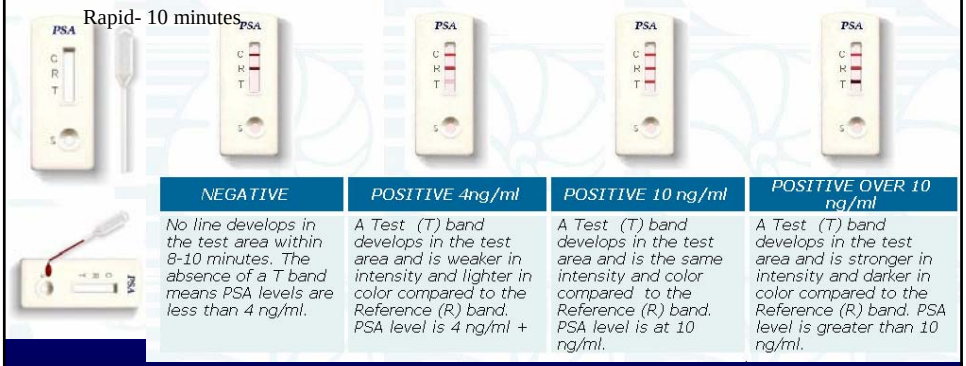
PSA

- Serum PSA T1/2= 2.2-3.2 days
- Serum free PSA T1/2= < 2 hours
- PSA molecule contains 5 immunoreactive, antibody binding sites (epitopes)
- Commercial PSA assays are available to detect:
  - total PSA (FDA approved "home" kits available)
  - free PSA – FDA approves
  - a1-antichymotrypsin (cPSA) – FDA approved
  - BPSA + ProPSA (research use only, may be purchased from Beckman Coulter)
  - Hk-2 (research use only, may be purchased)

	Capture antibody	Tracer antibody	Minimum detectable limit (µg/L)	MDA report and ref.
Total PSA				
[illegible]	[illegible]	[illegible]	[illegible]	95/86 [72]
Abbott AxSYM	m	m	0·02 *	99/20 [73]
[illegible]	[illegible]	[illegible]	[illegible]	
Bayer ACS: 180	m	sh	0·09	96/54 [74]
Bayer ACS: 180 PSA2	m	sh	0·06 *	
Bayer ADVIA Centaur	m	sh	0·06 *	
Bayer IMMUNO-1	m	g	0·07	97/07 [75]
Beckman ACCESS	m	m		
Beckman ACCESS Hybritech	m	m	0·008	00/85 [76]
Biodata MAIAclone	m	m	0·13	96/34 [77]
BioMérieux VIDAS	m	m		
BYK-Sangtec Liaison	m	m	0·03 *	99/18 [78]
BYK-Sangtec LIAmat	m	m	0·12	96/02 [79]
CanAg ELISA	m	m	0·10 *	99/38 [80]
CIS ELSA-2	m	m	0·14	96/53 [81]
CIS KRYPTOR	m	m	0·04 *	99/21 [82]
DPC Immulite Total PSA	g	m	0·05	95/82 [83]
DPC Immulite 3rd gen PSA	m	g	0·003 *	99/22 [84]
DPC Immulite 2000 Total PSA	g	m	0·05 *	
DPC Immulite 2000 3rd gen PSA	m	g	0·003 *	
DPC IRMAcount	m	m	0·10	96/68 [85]
DPC Milenia ELISA	m	m	0·02	96/67 [86]
Hybritech TANDEM-E	m	m	0·22	96/19 [87]
Hybritech TANDEM-R	m	m	0·02	95/75 [88]
NETRIA IRMA	m	sh	0·5 *	
Ortho Vitros ECi	m	g	0·02 *	
Roche COBAScore	m	m	0·11	96/11 [89]
Roche Enzymun	m	m	0·08	97/26 [90]
Roche Elecsys	m	m	0·03 *	99/19 [91]
Socolab PCx	m	m		
TOSOH	m	m		
Wallac DELFIA EQM	m	m	0·005	96/45 [92]
Wallac DELFIA Prostatus	m	m	0·07	96/46 [93]
Free PSA				
Abbott AxSYM	m	m		99/20 [73]
Abbott Architect	m	m		
Beckman ACCESS	m	m		
Beckman ACCESS Hybritech	m	m		00/85 [76]
BYK-Sangtec Liaison	m	m		99/18 [78]
CanAg ELISA	m	m		99/38 [80]
CIS KRYPTOR	m	m		99/21 [82]
DPC Immulite	m	g		99/22 [84]
DPC Immulite 2000	m	g		
Hybritech TANDEM-R	m	m		
Roche Elecsys	m	m		99/19 [91]
Wallac DELFIA Prostatus	m	m		96/46 [93]
Complexed PSA				
Bayer IMMUNO-1	m	g		**

The Home PSA Test

Rapid- 10 minutes



NEGATIVE	POSITIVE 4ng/ml	POSITIVE 10 ng/ml	POSITIVE OVER 10 ng/ml
No line develops in the test area within 8-10 minutes. The absence of a T band means PSA levels are less than 4 ng/ml.	A Test (T) band develops in the test area and is weaker in intensity and lighter in color compared to the Reference (R) band. PSA level is 4 ng/ml +	A Test (T) band develops in the test area and is the same intensity and color compared to the Reference (R) band. PSA level is at 10 ng/ml.	A Test (T) band develops in the test area and is stronger in intensity and darker in color compared to the Reference (R) band. PSA level is greater than 10 ng/ml.

Mail in

PSA - Variability

- Bioassay Variability:
  - Mean variation: 4%
  - 95% of the time variability will be less than 11%
    - Stamey et al, 1987 , J Urol
- Physiologic Variability:
  - "Intrapatient" biovariability : 25%
  - 95% of the time the variability will be less than 50%
    - Carter et al., 1997
  - Coefficient of Variation: 13.4%
    - Yan et al, 2001, Cancer

Variation of PSA Levels: Evaluation of Year-to-Year Fluctuations

Eastham et al. JAMA 289:2695, 2003

- 972 men in Polyp Prevention Trial (1991-8)
  - Healthy population
  - 5 yearly samples

Criteria	Next Test Normal (1y)	Any Other Year
> 4 ug/L	30%	44%
> 2.5 ug/L	26%	40%
Abnormal age-specific	37%	55%
F/T < 25%	35%	53%

- Caveat: mean PSA at baseline - 0.8-4.4; median- 0.7-2.0
- Recommendations:
  - "PSA Confirmation" in a "few weeks"
  - Spontaneous return to "normal" range without antibiotics or NSAIDs

PSA – The Great Screening Debate

- AUA, CUA, American College of Radiology, American Cancer Society, etc
  - DRE or PSA should not be routinely used for screening purposes
  - Shared decision making
  - Evaluate the PROS and CONS
- American College of Physicians- American Society of Internal Medicine (2002) and American Academy of Family Physicians
  - "Individualized"
  - "Benefits, Harms of Treatment all need to be discussed"
- This will not be resolved until results of PLCO and ER-SPC studies (?2009-10)

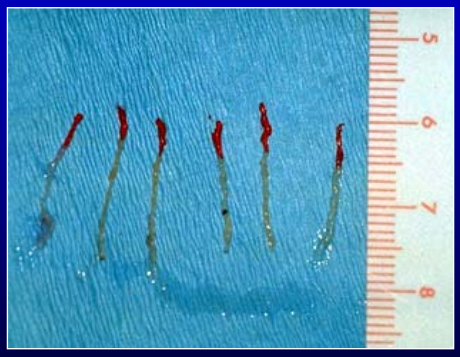
What Is Acceptable Screening?

Merenstein D. JAMA 291:15-16, 2004

- Family Practice resident treated 53 year old man for "general checkup"
- Risks and benefits of PSA and other health issues discussed – all well documented
- Did not order PSA (mutual agreement)
- Later PSA ordered by another doctor who did not discuss risks and did not perform DRE
- Pt dx with high PSA and Gleason 8 cancer
- Jury found Doctor Merenstein's residency program liable for **$1 million**

Can PSA Help us Determine Who To Biopsy?

Trans-Rectal Ultrasound Probe



Biopsy Cores

PSA 4.0 cutoff– Valuable ?

- Using 4.0 ng/cc as a cutoff:
  - Sensitivity: 67.5- 80%
  - Specificity: 60-70%
- Why was 4.0 ng/cc picked?
- Is it sensitive and specific enough?

Effect Of Verification Bias on Screening for Prostate Cancer by Measurement of PSA

Punglia, D'Amico, Catalona, Roehl, Kuntz, NEJM 349:4, 2003

- Adjusting for verification bias significantly increases diagnostic accuracy
- VB arises when disease status is not determined in all subjects who undergo screening
- "Gold Standard" that is used for comparison does not capture all of the disease that it is meant to
- Ie. Sensitivity underestimated, Specificity overestimated

Effect Of Verification Bias on PSA

Punglia, D'Amico, Catalona, Roehl, Kuntz, NEJM 349:4, 2003

- If threshold for Bx > 4.1 ng/ml
  - Missed 82% of cancers in younger men (< 60) missed
  - Missed 65% of cancers in older men
- Threshold for Bx of 2.5 ng/ml in men < 60 may be reasonable
  - Double the detection rate 18 → 36%
  - Reduce specificity only from 98 → 94%

PSA- Predictor of Cancer?

- 15% have PSA > 4.0ng/cc over 50 yo
- CaP will be Dx in 11-34% of these patients on biopsy
- What about < 4.0ng/cc ?

Author	Initial % > 4.0	CaP %
Catalona	8.34	2.2
Mettlin	14	1.5
Brawer	15	2.6
Labrie	12.4	4.1
Catalona	9.4	3.1
Catalona	15	3.3

PSA + the PCPT

- "The chance of cancer on biopsy is **1/50** for men with a **PSA < 4 ng/cc**" 2002, Alan Partin, Campbells Urology

Ian Thompson et al., The Influence of Finasteride on the Development of Prostate Cancer. NEJM, 349:3, 2003

PSA at Entry (ng/cc)	Patients	(+) Biopsy	Relative Risk of Ca
0.0-1.0	2196	357(16.3%)	0.66
1.1-2.0	3311	457(27.7%)	0.77
2.1-3.0	1506	332(39.2)	0.81
3.1-4.0	1	1(100.0)	

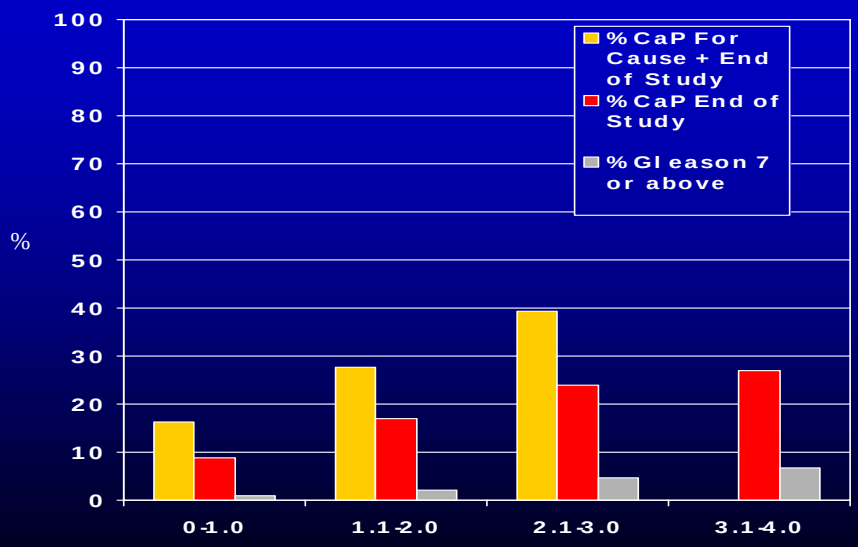
PSA + the PCPT

Ian Thompson et al., Prevalence of Prostate Cancer among Men with a PSA < 4.0 ng/ml. NEJM, 350:22, 2004

- If all cause for biopsy removed (i.e. only end of study biopsy included), can finally estimate + biopsy rates in men with PSA < 4.0 + normal DRE

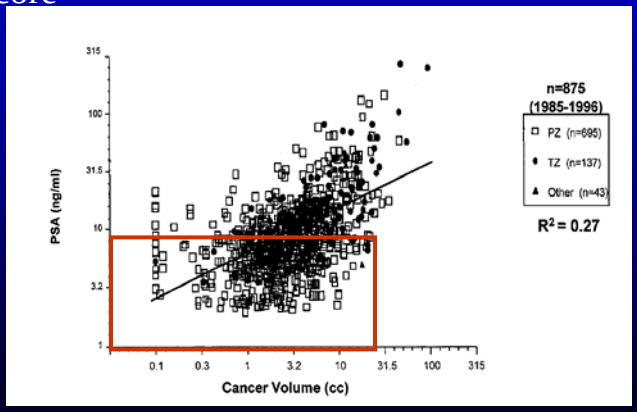
PSA at Time of Biopsy (ng/cc)	Patients	(+) Biopsy	High Grade Tumors
0.0-1.0	1277	112(8.8%)	12(0.94%)
1.1-2.0	998	170(17%)	20(2.0%)
2.1-3.0	482	115(23.9%)	22(4.6%)
3.1-4.0	193	52(26.9%)	13(6.7%)

PSA + the PCPT



tPSA - A Predictor of BPH (Not Cancer?)

- PSA does not predict tumor volume or Gleason Score



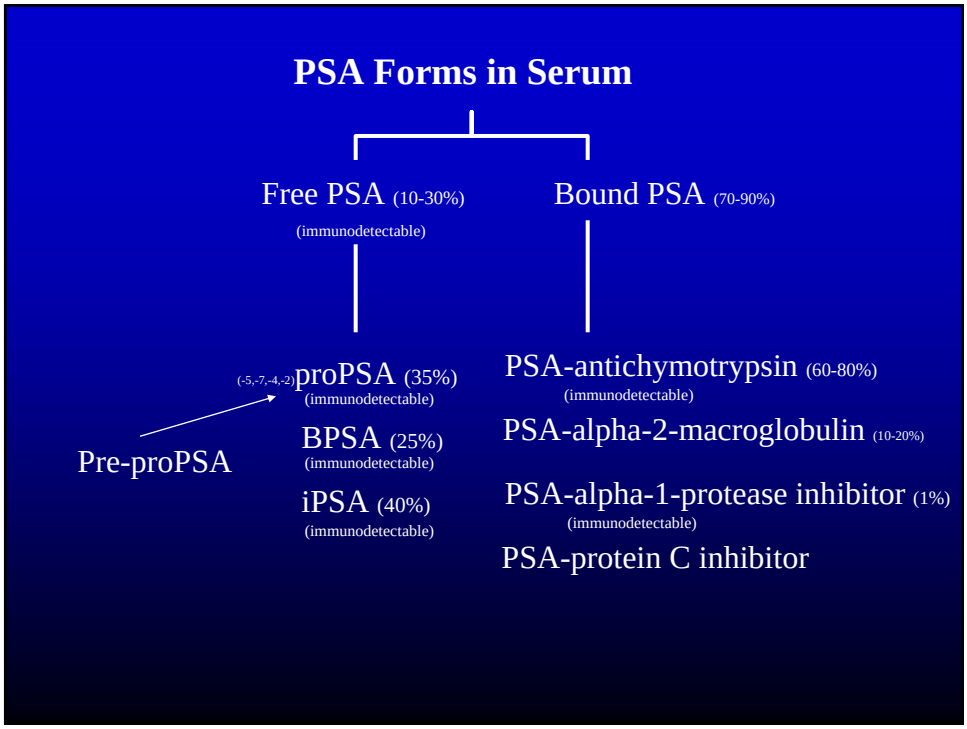
Stamey et al, J Urol, 2002, Lam et al. J Urol, 2003

tPSA Summary

- Evidence to show:
  - 1) Sub-optimal Specificity
  - 2) Poor Predictive Power
- What can we do?

How to improve the Accuracy of PSA

- 4.0 ug/cc cut-off
- Age-specific references
- PSA-velocity and doubling time
- PSA-Density
  - Total volume
  - Transition zone volume
- %fPSA
- cPSA
- proPSA
- BPSA
- proPSA / BPSA ratio
- Hk-2
- Hk-2 / fPSA ratio
- iPSA and iPSA/fPSA ratio



Free - PSA

- Stenman (1991) - first to demonstrate relationship between complexed PSA and CaP
- Suggested using PSA-ACT - ratio to to total PSA could decrease the number of unnecessary biopsies while preserving the sensitivity of PSA assay
- The lower the %fPSA , the higher the risk of CaP

Free - PSA

- Serum Sample Handling is Important in preserving the immunoreactivity of free PSA
- 1) Frozen within 24 hours (Catalona, JAMA, 1995)
  - 30% fPSA immunoreactivity lost if stored at 2-8 ^{o}C
  - 15% tPSA immunoreactivity lost if stored at 2-8 ^{o}C
- 2) Keep long term storage at – 70 ^{o}C (Woodrum, J urol, 1998)
- 3) Repeat Freeze/ Thaw cycles does not decrease immunoreactivity (Woodrum, J Urol, 1998)

Free – PSA Confounders

- **Warning:**
  - **fPSA assays all are NOT EQUAL**
  - **Hybritech Tandem R, Dianon Systems, Chiron ACS 180 – variability**
- **Free PSA levels are increased with:**
  - **needle biopsy**
  - **DRE**
  - **ejaculation**
  - **exercise (Ornstein, 1998)**

Free – PSA and PIN

- PIN does not affect % free PSA
  - (Ramos et al., J Urol.1999:162:1587-1590)
- 48 with high-grade PIN
- 50 with prostate cancer
- 50 with BPH
- % f PSA :
  - 15% with cancer, 21% with PIN, 20% with BPH or normal prostate
  - No differences in patients with PIN or BPH

Year	Reference	Number of Men (Cancer / Benign)	PSA Assay*	Total PSA (ng / ml)	f/t PSA Cutpoint (%)	Population	Sensitivity (%)	Specificity (%)
1993	45	Not applicable		2-20	18		71	95
1995	46	63/50	B	4-10	25		100	31
					20		88	50
1995	47	63/50	B	4-10	20		90	38
		26/48			23	**	90	31
1995	53	47/47		4-10	23		91	19
1996	69	28/53		2-20	23		95	26
					23		90	32
1996	51	20/28	D	4-10	23		95	64
					14		95	56
1996	52	28/53	E	3-15	15	T1c	95	40
					18	T2	78	40
1996	55	154/266	D	2-30	25		90	38
		30/205		4-10	35		90	38
1998	49	22/71	C	4-10	20		95	29
					20	Prostatism referral	91	48
1998	54	1234/2539	F	4-20	25		95	23
					22		89	34
1998	50	25/94	D	4-10	25	**	95	20
					22		90	29
1998	74	25/98	D	2-20	22		95	38
			G		34		95	19
			H		34		95	33
1999	66	22/40	D	0-4	20		86	30
					25		91	10
		96/187		4-10	15		85	32
					20		97	12
		111/157		>10	15		95	30
1999	81	106/100	D	2.5-10	27		95	17
1999	75	112/34	I	0-50	24		90	47
					15		54	67
2000	58	24/116	B	4-10	18		92	35
2000	59	38/41	B	4-10	25	**, Black only	95	17
		319/328			25	**, White only	95	20
2000	56	100/197	J	4-10	26	**	96	27
2000	57	201/237	B	4-10	23		95	17
2000	60	104/118	B	2.5-10	35	Black only	95	9
		97/201			29	White only	95	29

-Excellent Sensitivity:
Most studies between 90-95%
-Still Poor Specificity:
Most < 40%

Free – PSA – Reducing Biopsy Rate ?

- PSA 4.0-10.0 ng/cc
  - fPSA > 25% = 8% risk of CaP
  - fPSA < 10% = 56% risk of Ca
  - fPSA < 25% dx 95% of cancers
  - Avoid 20% neg bx
  - Catalona 2001, JAMA
- PSA 2.6- 4.0 ng/cc
  - fPSA < 25% dx 85% of cancers
  - Avoid 19% neg bx
  - Gann 2003, J Urol

Free – PSA

- Catalona (2001)
  - Prospective trial of 773 men with normal DRE with PSA 4-10 ng/cc
  - 25% free-PSA to total PSA ratio
    - sensitivity of 95%
    - specificity of 20%
  - fPSA 25% was optimal for all age groups

Free – PSA (When Total PSA < 4.0 ng/cc)

Year	Reference	Number of Men (Cancer / Benign)	PSA Assay* (Free / Total)	Total PSA (ng / ml)	f/t PSA Cutpoint (%)	Population	Sensitivity (%)	Specificity (%)
1997	62	73/259	A	2.6-4	27	Nonsuspicious DRE** only	90	18
1999	66	22/40	A	0-4	20		86	30
				25			91	10
1999	65	66/207	B	2.5-4	20		56	81
				30			71	65
				41			95	29
1999	63	54/314	A	2.5-4	10	Nonsuspicious DRE** only	30	94
				15			54	67

*: Manufacturers of PSA assays
A: Hybritech Tandem free and total PSA assays
B: Abbott AxSYM free and total PSA assays

**: digital rectal examination

Free-PSA Improves Prostate Cancer Detection in a High-Risk Population of Men With a Normal Total PSA and DRE

Uzzo et al, Urology 61:754-759, 2003

- 310 High Risk Men: African American or FHx but normal DRE, PSA 2-4 ng/cc
- Biopsied- if %fPSA is < 27% or any other abnormal parameter
- 52% of those biopsied CaP (6.85% overall detection)
- % Free PSA- is effective in :
  - detecting CaP in high-risk men
  - with a PSA in the range of 2-4 ng/ml

Free – PSA Predicts Prognosis Post RP

Southwick et al J Urol. 1999;162:1346-1351

- Prospective multi-centre clinical trial
- 379 – CaP
- T1c, PSA 4-10 ng/ml
- Higher % free PSA associated with favorable pathology (15% cutoff provided greatest discrimination)

Free – PSA Predicts Px Post RP

- Favorable pathology (organ confined, Gleason <7, < 10% tumor volume)
  - 75% with >15% fPSA
  - 34% with <15%fPSA
- Multivariate analysis:
  - % free PSA strongest predictor of path stage

Free-PSA Summary

- Helpful too to improve sensitivity and of tPSA between 2 – 10 ng/cc
- Specificity lacking to be used alone
- Still an adjuvant test to PSA
- Ideal use: tool to determine who needs biopsy in 2-10 ng/cc range

Complexed PSA

- An assay to measure cPSA could potentially:
  - **Obviate** the need for 2 assays to calculate a percentage (tPSA = cPSA + fPSA)
  - **Reduce the potential error** in analyzing 2 assays
  - **Reduce costs – One test compared to two**

Complexed PSA

- Immuno - 1 cPSA assay (Bayer)
  - Measures alpha-1-antichymotrypsin bound PSA
  - Uses the "unique binding properties" of a monoclonal antibody that fails to bind fPSA in the presence of antibodies specific for fPSA
- Markit – M ACT-PSA assay
- Brawer (2000, J Urol)
  - Compared tPSA, %fPSA, and cPSA

Complexed PSA - ALL

Sens %	Total PSA		Complexed PSA		% fPSA	
	Cutoff ng/cc	Spec %	Cutoff ng/cc	Spec %	Cutoff ng/cc	Spec %
80	4.11	35.6	3.98	51.6	19	46.2
85	3.86	31.1	3.34	38.7	22	32.4
90	3.4	25.3	2.94	33.8	24	26.2
95	3.06	21.8	2.52	26.7	28	15.6
97.5	2.28	12.9	1.667	14.7	32	8.9
100	1.0	3.1	0.89	6.2	67	0

cPSA Improves Specificity for CaP Detection

Partin et al. J Urol, 2003

- 831 men (313 with CaP) , multi-centre
- tPSA range from 2-10 ng/cc
- ROC analysis showed that cPSA was significantly better than tPSA at all PSA ranges ($p < 0.001$)
- "cPSA is single best test to improve specificity over tPSA"
- Is this accurate?

Complexed PSA

- Largest Prospective Trial:
- Miller et al, Urology, 2001
  - N = 3006
  - tPSA = 2-10 – cPSA Increases detection from 35-40%
  - tPSA = 10-20 – cPSA Increases detection rate from 40-42%
  - Sensitivity of cPSA = 90% vs. % fPSA= 95%
  - Specificity same between f/t PSA and cPSA

Complexed PSA

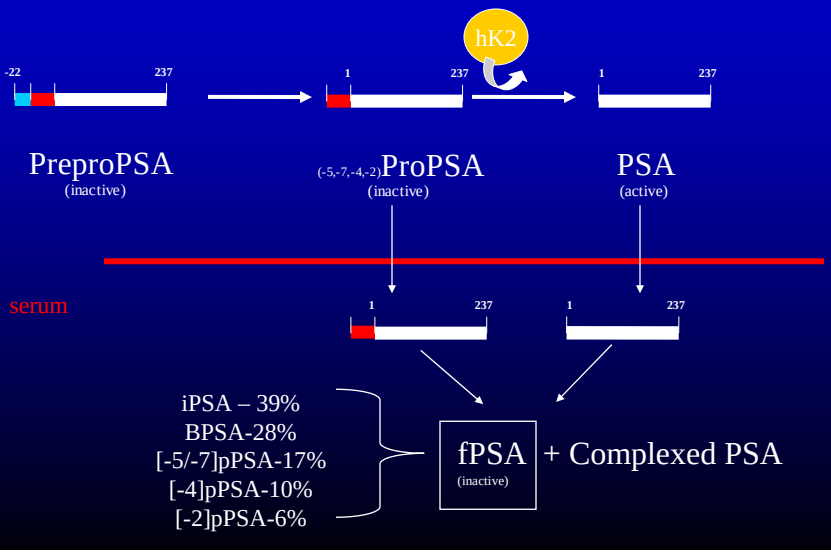
- Lein et al, (Prostate, 2001)
  - 267 men with CaP
  - 290 with BPH
  - cPSA values would not have aided in detection CaP assuming fPSA/tPSA values were known
  - Does not add sensitivity or specificity compared to free-PSA ratios

A Multicentre Clinical Trial on The Use of Complexed PSA in Low PSA Concentrations

Lein et al, J Urol 170:1175-9, 2003

- 283 men with CaP, 417 without
- tPSA range from 0-6 ng/cc
- All men had a biopsy
- For total PSA < 4 ng/ml, no difference in diagnostic accuracy was shown between complexed PSA and free/total PSA

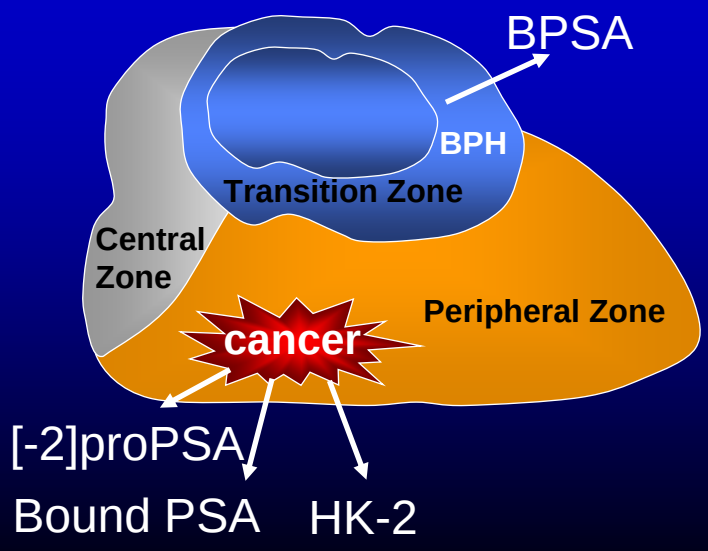
PSA Formation Pathway



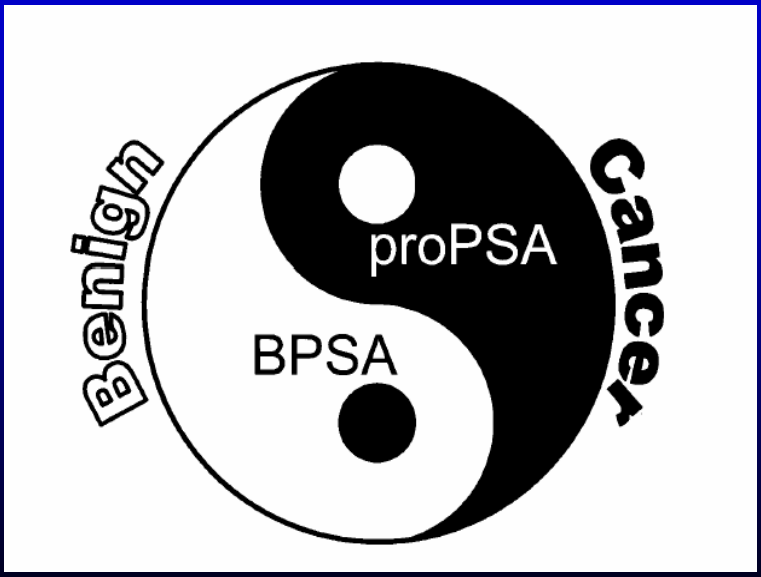
ProPSA

- [-7]pPSA – native, untruncated form
- [-5][-2][-4]pPSA
  - Truncated form
  - More stable
  - Not converted to PSA
- [-7] + [-5]pPSA are indistinguishable with current Ig-based assays
- [-2]pPSA is most associated with aggressive cancers
- Most published papers assay for pPSA refer to the detection of all isoforms

Disease-associated PSA Forms in Prostate Tissues



The Ying Yang of PSA



From Mikolajczyk + Rittenhouse, 2004

Pro-PSA is Specific For CaP + HGPIN

- [-2]proPSA shows:
  - more intense staining of HGPIN and CaP
  - weakly stains normal epithelium
  - does not stain:
    - atrophic glands
    - prostatic stroma
    - colonic epithelium
- ***No change of intensity*** with tumor grade

Pro PSA Improves Cancer Detection (vs Free and Complexed PSA) in 2-4 ng/cc PSA Range

Catalona WJ et al J Urol 170:181-5, 2003

- %Pro-PSA improves specificity
- decreased unnecessary biopsies (better compared to %fPSA or cPSA)
  - 2-4 ng/ml PSA range
  - 2-10 ng/ml PSA range
- 2-6 ng/cc PSA range
  - 90% sensitivity
  - Pro-PSA/Free-PSA spared 31% of unnecessary biopsies (20% for % Free PSA and 19% for Complexed PSA)

Proenzyme PSA for the early detection of prostate cancer in the 2.5-4.0 ng/cc total PSA range: Preliminary Analysis

sokoll et al. Urol , 2003

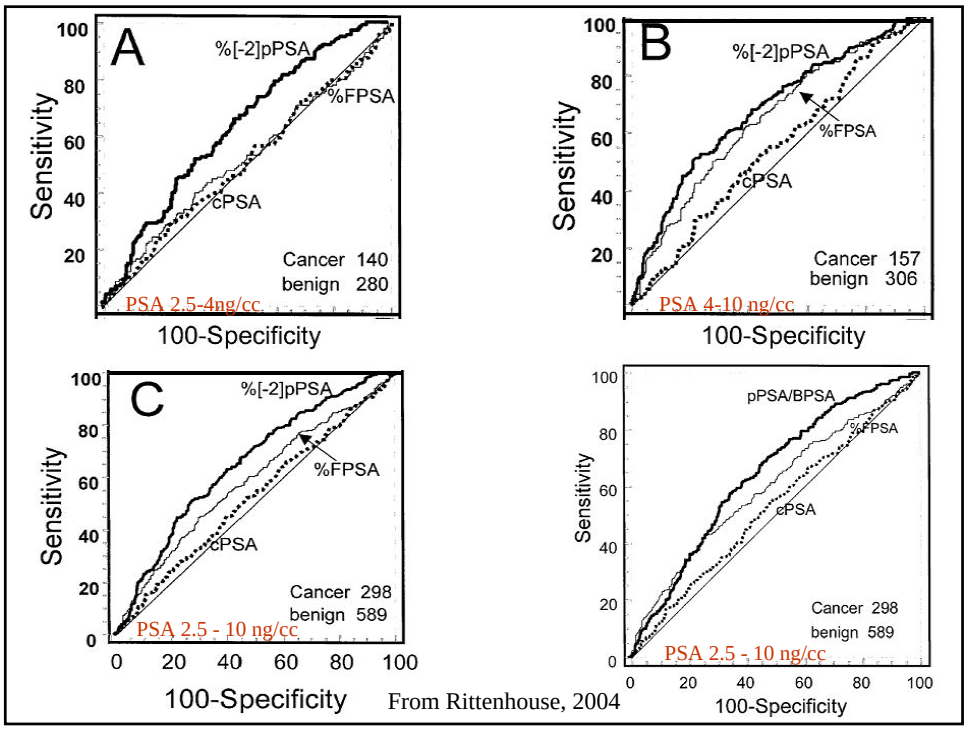
- decreased unnecessary biopsies in 2-4 ng/ml PSA range by 59%
- Able to detect 59% of cancers
- Using ROC curves and a fixed sensitivity of 75%, specificity for proPSA was 59% compared to 33% for %fPSA

BPSA

- Initially termed benign-PSA
- Identical to mature native PSA, except for 2 internal cleavages at Lys^{145} and Lys^{182}
- Inactive form, function unknown
- ug/cc concentration range- easily measurable with Ig based assay

BPSA

- Strongly correlates with age and transition zone volume
  - Canto et al, Baylor, Urology 2004
- Tool to assess BPH?
- May be better denominator than total PSA in any type of PSA ratio (eg proPSA / BPSA)
- Not many trials published to date (one clinical trial)
- Relationship between BPSA(benign) and pPSA(cancer) might provide more insight pPSA/bPSA is very exciting



From Rittenhouse, 2004

Human Kallikrein-2 (HK-2)

- 80% homology to PSA
- in serum -pg/cc range
- Function: cleaves PSA from proPSA to active PSA form + autoactivation
- Proteolysis involved in metastasis ?
- Levels correlate with pathological stage
- Poorly differentiated tumors continue to produce hk-2
- ROLE:
  - Screening
  - Help define clinical stage

HK-2

- Total and Gleason 4/5 cancers seem to contribute most of serum HK-2
  - Haese and Lilja, J Urol, Dec, 2003
- HK-2 and HK-2 Density may predict clinically localized tumors (pT2a/b)
  - Multivariate analysis of 148 men
  - This advantage still correlated less to prediction of localized disease when compared with clinical stage + Gleason score
    - Haese + Lilja, Prostate, Feb 2003

Human Kallikrein-2 (HK-2)

$$\frac{\text{Hk-2}}{\text{fPSA}}$$

Hk-2 → Higher in Cancer

fPSA → Lower in Cancer

} Magnify discrimination between CaP and BPH

- May be more specific and sensitive than % fPSA alone
  - When total PSA 2-4
    - HK-2 not sensitive
    - When combined with fPSA, sensitivity better than tPSA
      - Partin, Urology, 1999 + Magkara, Clin Chem, 1999
  - Similar results when total PSA 4-10 + LUTS
    - Kwaiatkowski, Urology, 1998

RT-PCR HK-2

- Reverse transcriptase polymerase chain reaction
- mRNA Assay
- Slawin et al showed that RT-PCR HK-2 of LN tissue was the most important predictor of clinical outcome, when compared to RT-PCR PSA, IHC HK-2, IHC PSA
  - – Slawin et al. Cancer Res, Aug 2003
- ? Role in metastasis

RT – PCR - PSA

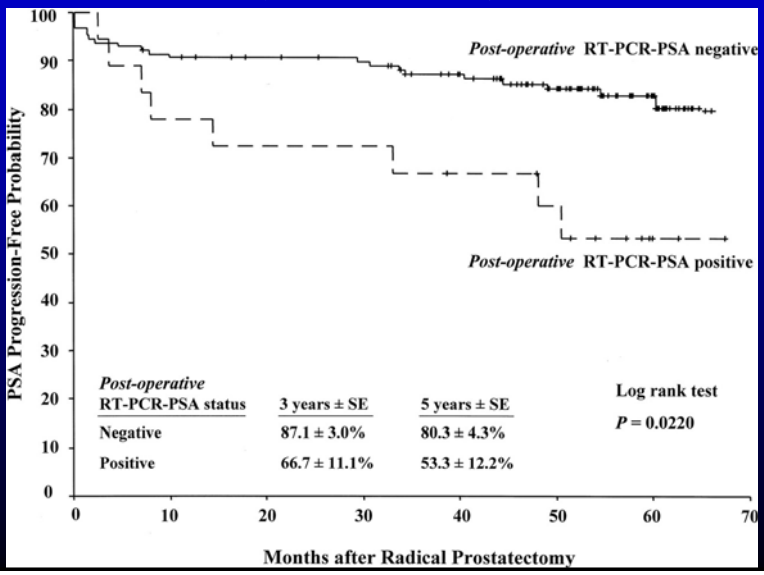
- Detection of circulating Cancer Cells (can detect one cell in 5 cc specimen = 1 lymph node positive)
- Ghossein (Urol, 1997) showed in a retrospective analysis that in hormone refractory CaP, RT-PCR can predict survival
- Kantoff (J Clin Urol, 2001) confirmed this in a prospective multi institution study
  - Positive RT-PCR was an independent prognostic factor using multivariate analysis
  - N = 390
  - Positive in 156

RT – PCR - PSA

- McIntyre (Urology, 2001) showed that RT-PCR + in:
  - 18 /24 with advanced CaP
  - 2/34 with "controlled" disease- on medical castration
  - able to detect CaP when 20 LNCaP cells inserted into 5 cc of human blood
- Important questions- is prostate cancer cells in serum equivalent to true metastatic disease?

Early RT-PCR PSA is associated with CaP progression in patients undergoing RP

- Slawin et al (Cancer Research, 2003)



PSA - Summary

- In just 25 years, over 13 000 Medline articles published
- tPSA may not be an ideal screening test or predict clinical significance
- We will need to await results of RCTs to prove whether tPSA screening improves overall survival
- Promising, more specific PSA forms will become available