Contemporary Detection of Prostate Cancer

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US Too Support Group
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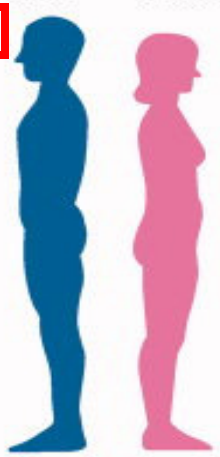
New cancer cases

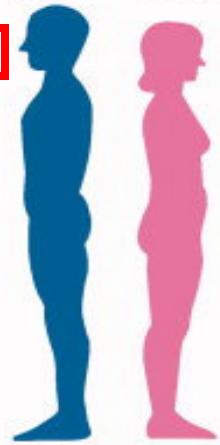
Estimated New Cases*

Males			Females		
Prostate	241,740	29%	Breast	226,870	29%
Lung & bronchus	116,470	14%	Lung & bronchus	109,690	14%
Colon & rectum	73,420	9%	Colon & rectum	70,040	9%
Urinary bladder	55,600	7%	Uterine corpus	47,130	6%
Melanoma of the skin	44,250	5%	Thyroid	43,210	5%
Kidney & renal pelvis	40,250	5%	Melanoma of the skin	32,000	4%
Non-Hodgkin lymphoma	38,160	4%	Non-Hodgkin lymphoma	31,970	4%
Oral cavity & pharynx	28,540	3%	Kidney & renal pelvis	24,520	3%
Leukemia	26,830	3%	Ovary	22,280	3%
Pancreas	22,090	3%	Pancreas	21,830	3%
All Sites	**848,170**	**100%**	**All Sites**	**790,740**	**100%**



Estimated Deaths

Males			Females		
Lung & bronchus	87,750	29%	Lung & bronchus	72,590	26%
Prostate	28,170	9%	Breast	39,510	14%
Colon & rectum	26,470	9%	Colon & rectum	25,220	9%
Pancreas	18,850	6%	Pancreas	18,540	7%
Liver & intrahepatic bile duct	13,980	5%	Ovary	15,500	6%
Leukemia	13,500	4%	Leukemia	10,040	4%
Esophagus	12,040	4%	Non-Hodgkin lymphoma	8,620	3%
Urinary bladder	10,510	3%	Uterine Corpus	8,010	3%
Non-Hodgkin lymphoma	10,320	3%	Liver & intrahepatic bile duct	6,570	2%
Kidney & renal pelvis	8,650	3%	Brain & other nervous system	5,980	2%
All Sites	**301,820**	**100%**	**All Sites**	**275,370**	**100%**

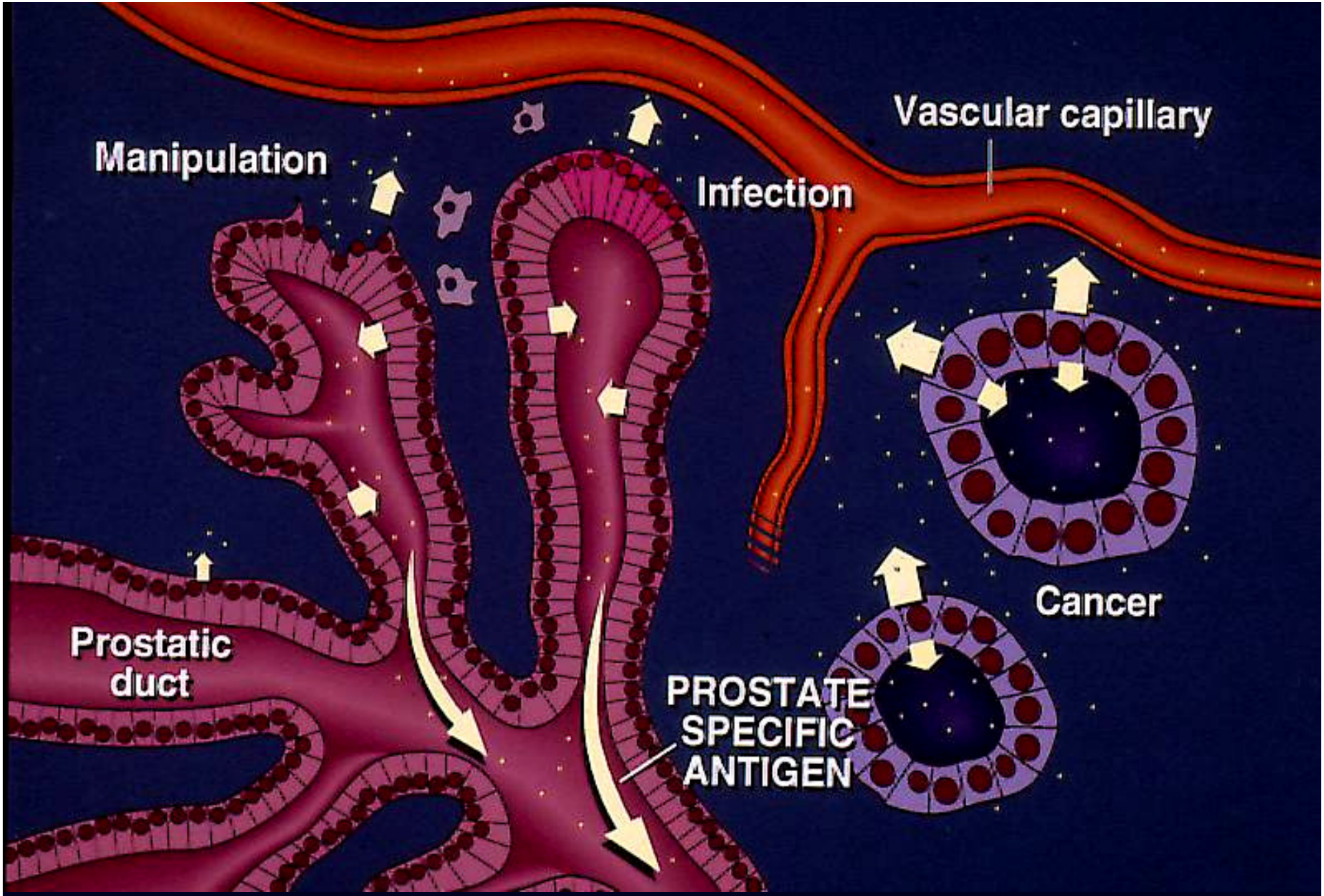


Siegel et al., CA J Clinicians 62:10-29, 2012

Prostate Cancer Detection

Biopsy to detect prostate cancer

- ✓Indication for biopsy may change type of cancer that is detected
- ✓In 1980s, abnormal exam led to most biopsies
  - Detected cancers were mostly locally advanced or extensively metastatic
- ✓In 2000s, abnormal PSA led to most biopsies
  - Many prostate cancers detected were indolent, small, slow-growing



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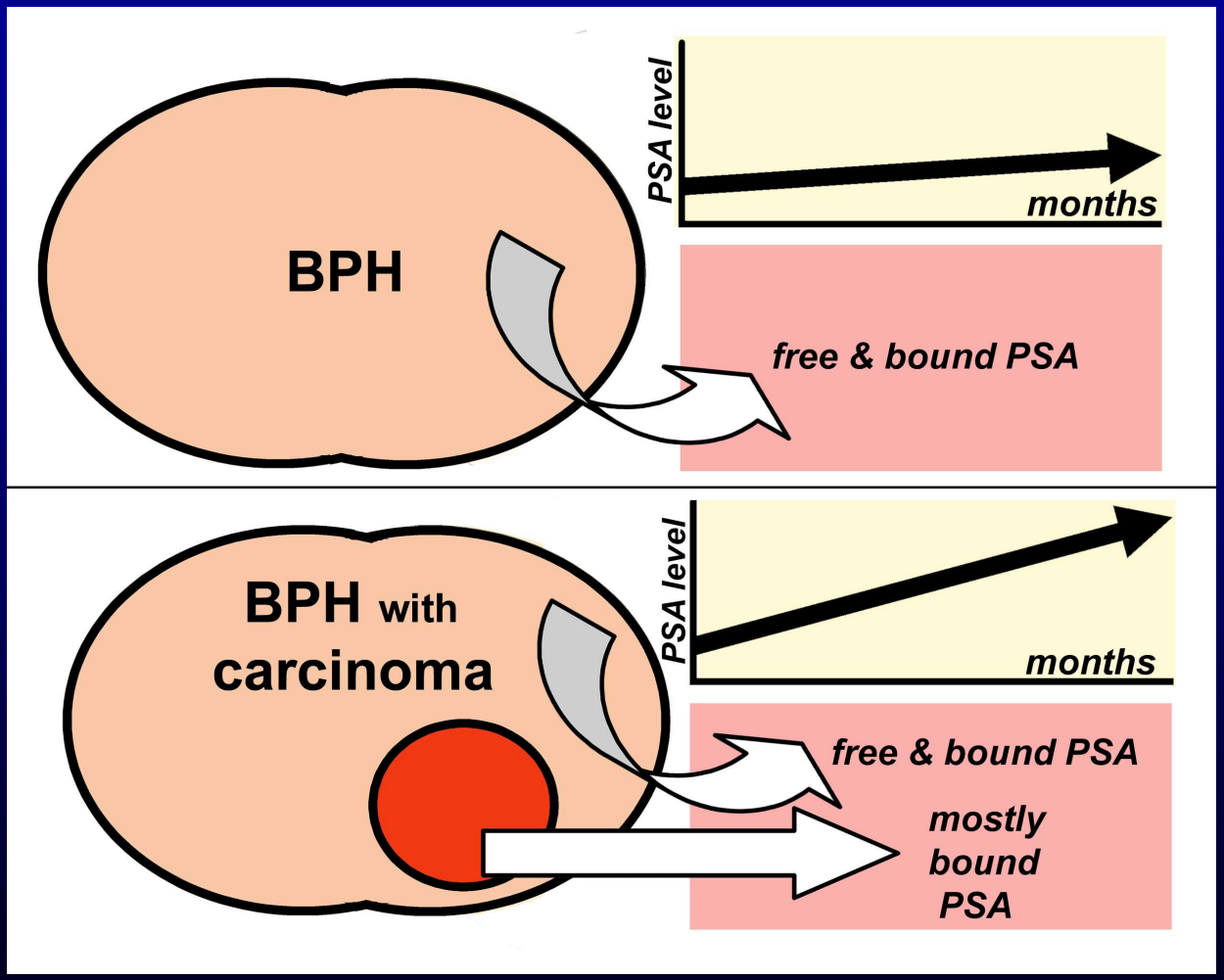
PSA relationship to cancer



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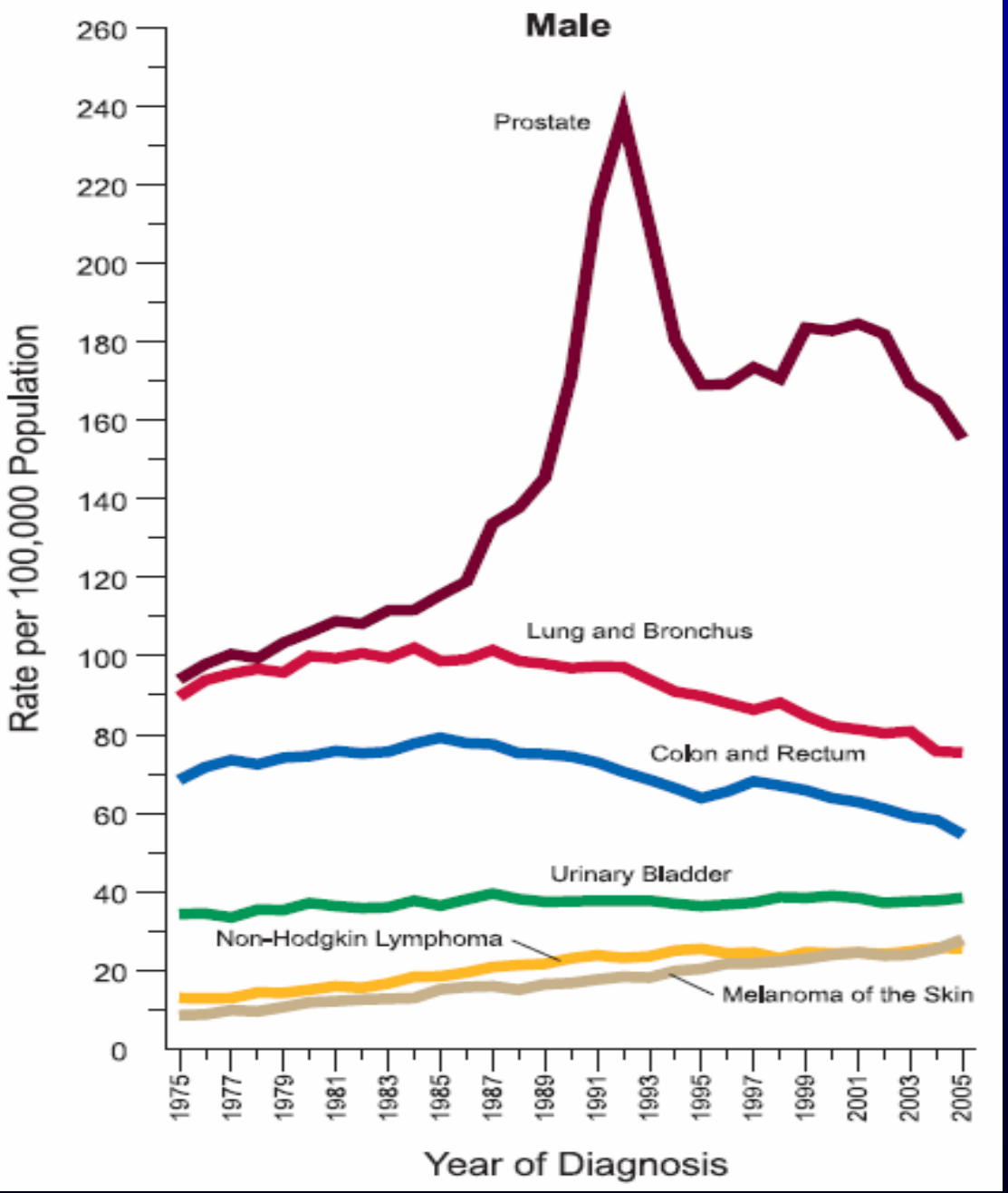

Epidemic of detection of prostate cancer never previously seen

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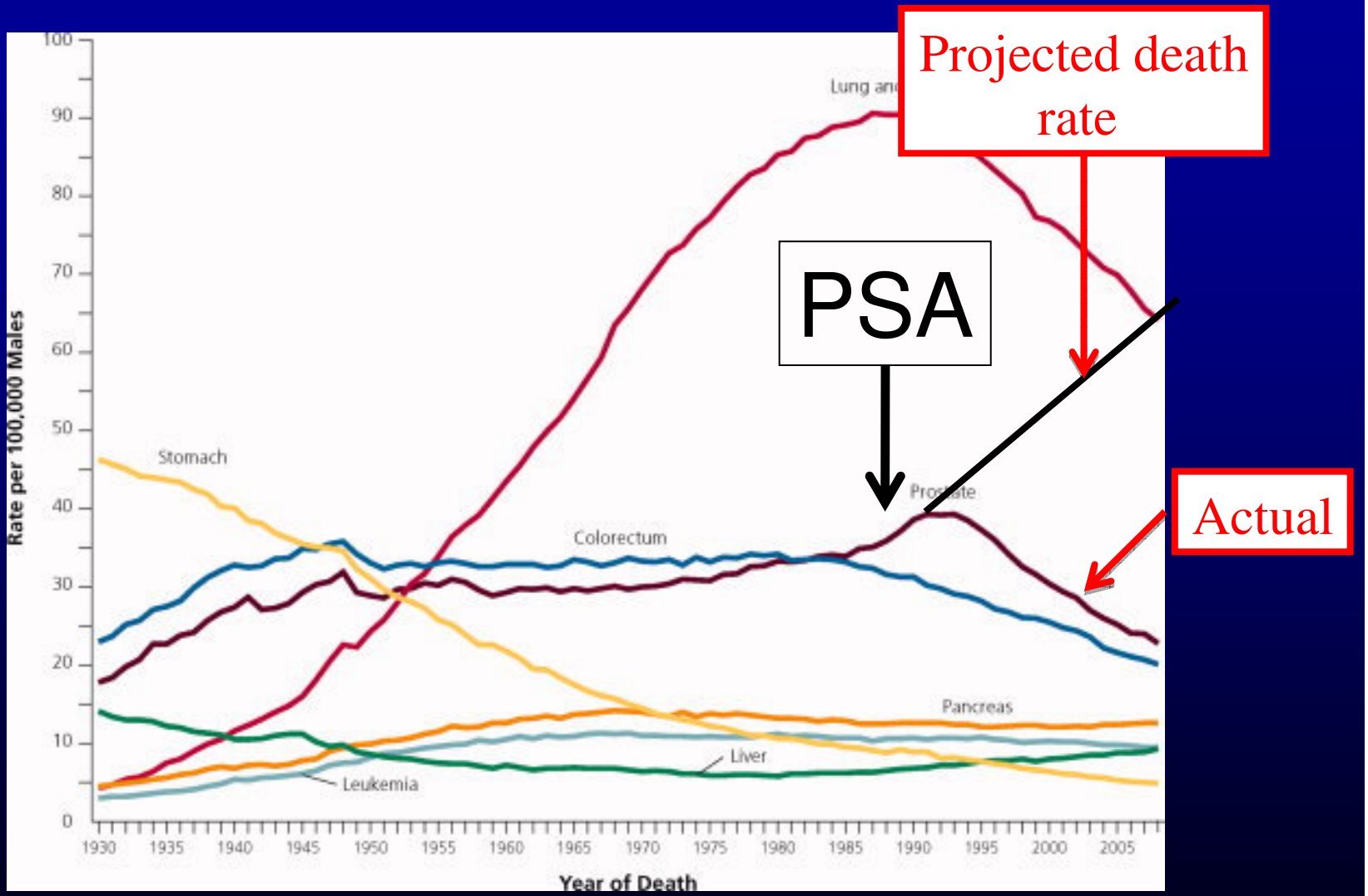
Prostate cancer deaths



Siegel et al., CA J Clinicians 62:10-29, 2012

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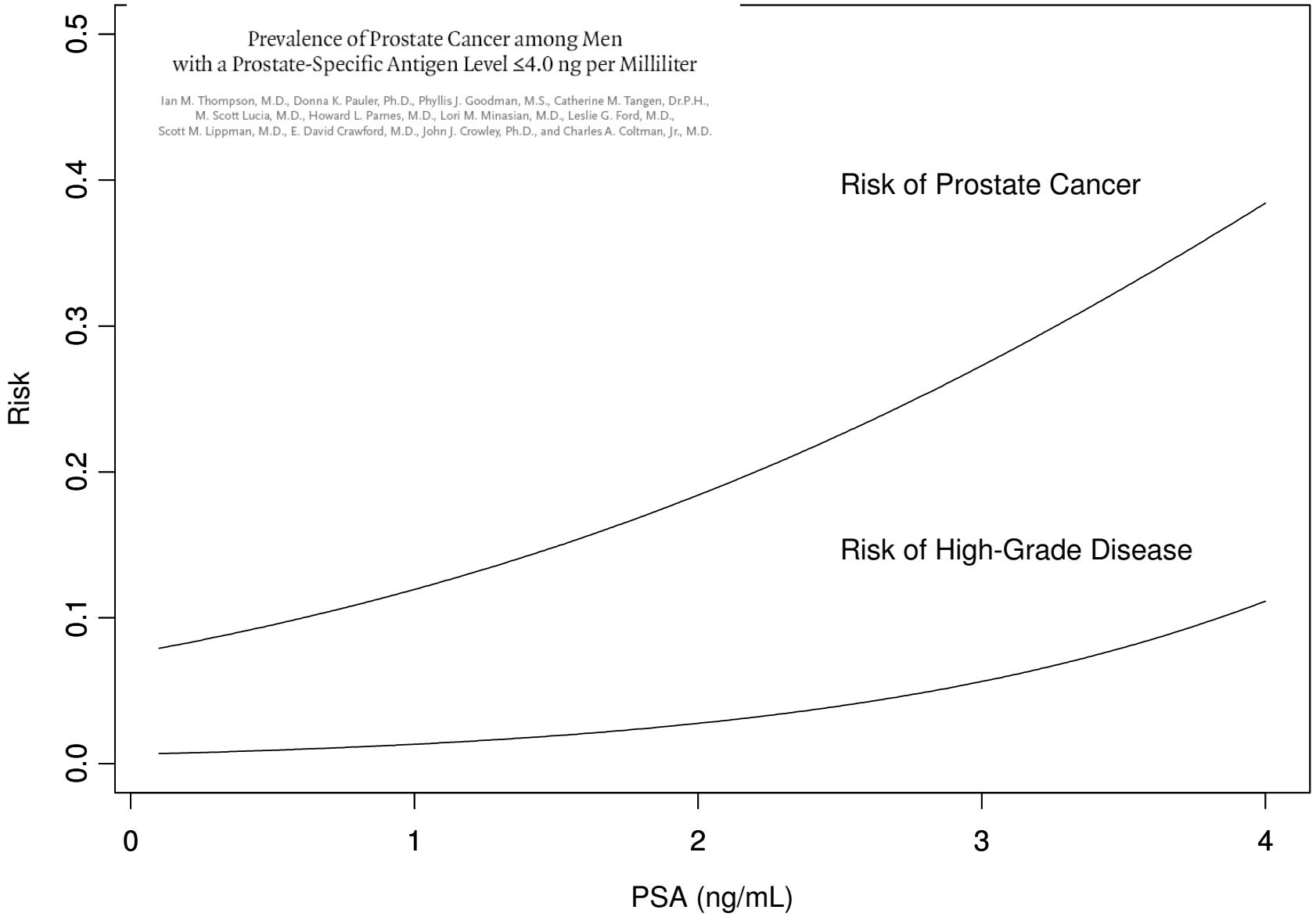
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 27, 2004 VOL. 350 NO. 22

Prevalence of Prostate Cancer among Men with a Prostate-Specific Antigen Level ≤4.0 ng per Milliliter

Ian M. Thompson, M.D., Donna K. Pauler, Ph.D., Phyllis J. Goodman, M.S., Catherine M. Tangen, Dr.P.H., M. Scott Lucia, M.D., Howard L. Parnes, M.D., Lori M. Minasian, M.D., Leslie G. Ford, M.D., Scott M. Lippman, M.D., E. David Crawford, M.D., John J. Crowley, Ph.D., and Charles A. Coltman, Jr., M.D.



Prostate Cancer

- Detection of prostate cancer led to treatment
  - Surgery
  - Radiation
- Treatment can cause side effects

- Prostate cancer treatment has risks
- Many prostate cancers do not require (initial) treatment

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No (initial) Rx of Prostate Ca

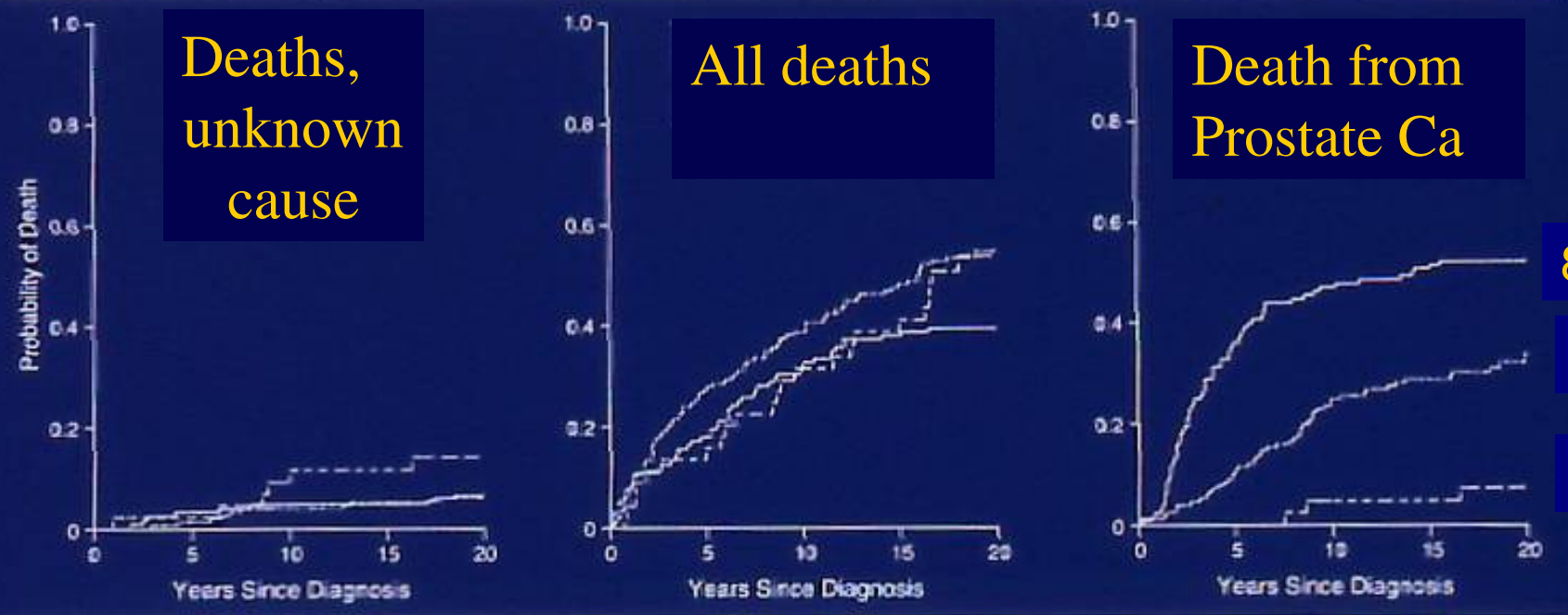

Figure 1.—Cumulative mortality since diagnosis of prostate cancer given tumor grade, displayed by cause of death (left, unknown cause [n=35]; center, cause other than prostate cancer [n=221]; and right, prostate cancer [n=154]). Cumulative mortality curves differ significantly by tumor grade for men dying of prostate cancer. Cumulative mortality curves for deaths due to causes other than prostate cancer are not statistically significantly different.

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"PSA screening for prostate cancer gets thumbs-down from federal panel"

D Klotz, Boston Globe, May 21, 2012

United States Preventative Services Task Force recommends against PSA testing (Grade D)

- Harms of testing outweigh benefits
- Prior recommendation against PSA testing for men over age 75

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How could this be true?

- Treatment of prostate cancers that don't need to be treated
  - Detection of small/insignificant cancers
  - Expansion of radiation centers (?profit motive)
  - Improvement/promotion of surgical treatment
- Studies to evaluate PSA screening were not properly designed

Re-Consideration of Prostate Cancer

- Clinically important/high risk
  - Larger volume prostate cancer (growing)
  - Gleason ≥ 7 cancers
- "Insignificant" prostate cancer
  - Low grade (Gleason 6)
  - Low volume (<3 cores, <50%)

  Classification may be wrong about 10% of the time
- Lead to wide application of active surveillance

PSA Screening: Where are we?

- Discussion needed before PSA testing
  - What we do with results
  - Not all “cancers” need treatment

- Additional testing/evaluation to select patients for treatment who are most likely to benefit

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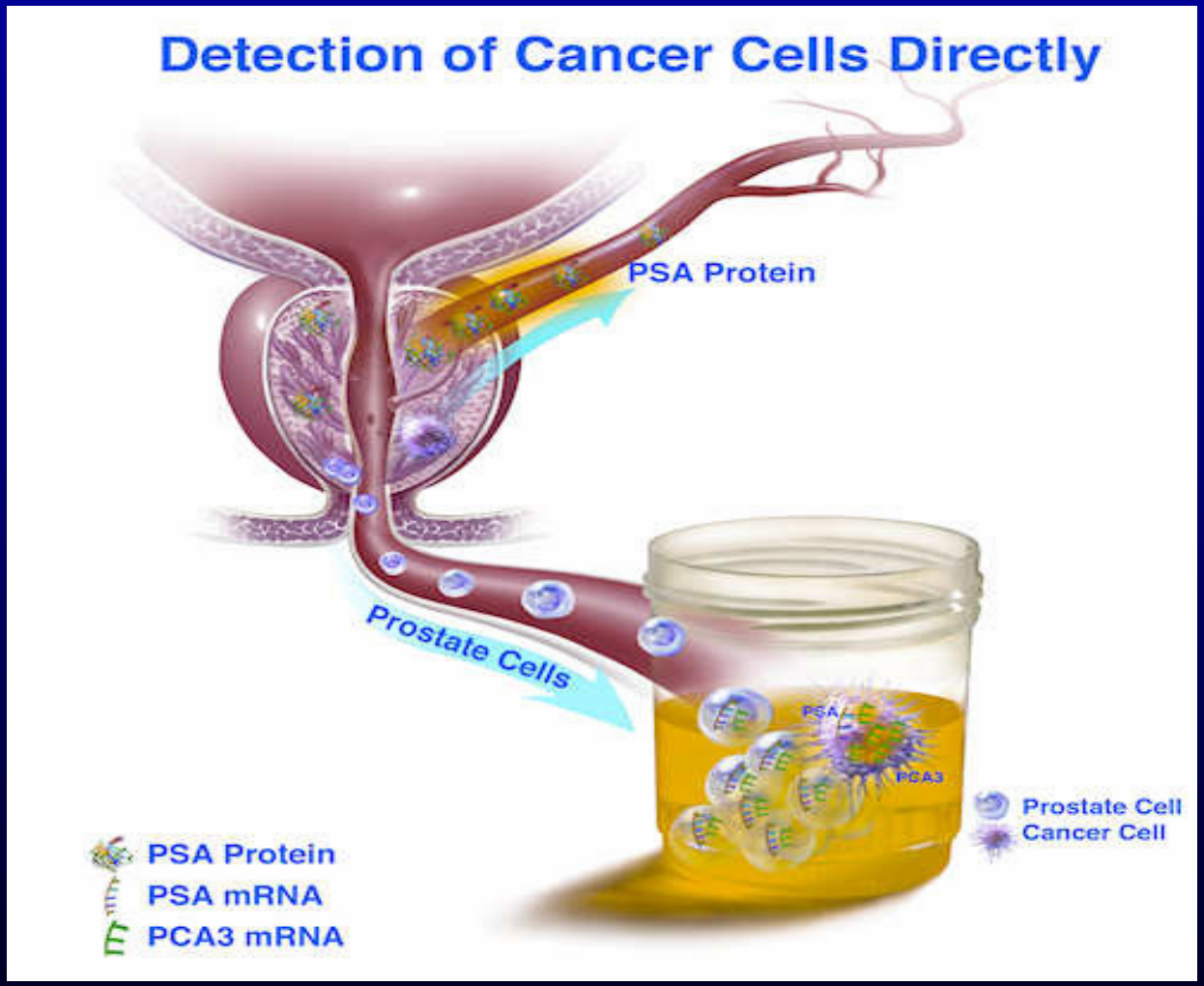
Significance of cancer:
Determining need for treatment

- Patient (age, comorbidities)
- Gleason score
- Amount of tumor

Prostate Cancer: What's New?

- PCA3 gene test
  - Urine test done after examination
  - Quantifies (with PCR) PCA3 gene/PSA gene
  - First test to help identify "clinically relevant" cancers
  - Helps identify which cancers are more aggressive
  - Especially helpful when PSA abnormal and/or prior biopsies done & negative but PSA increases

PCA3: Urine test



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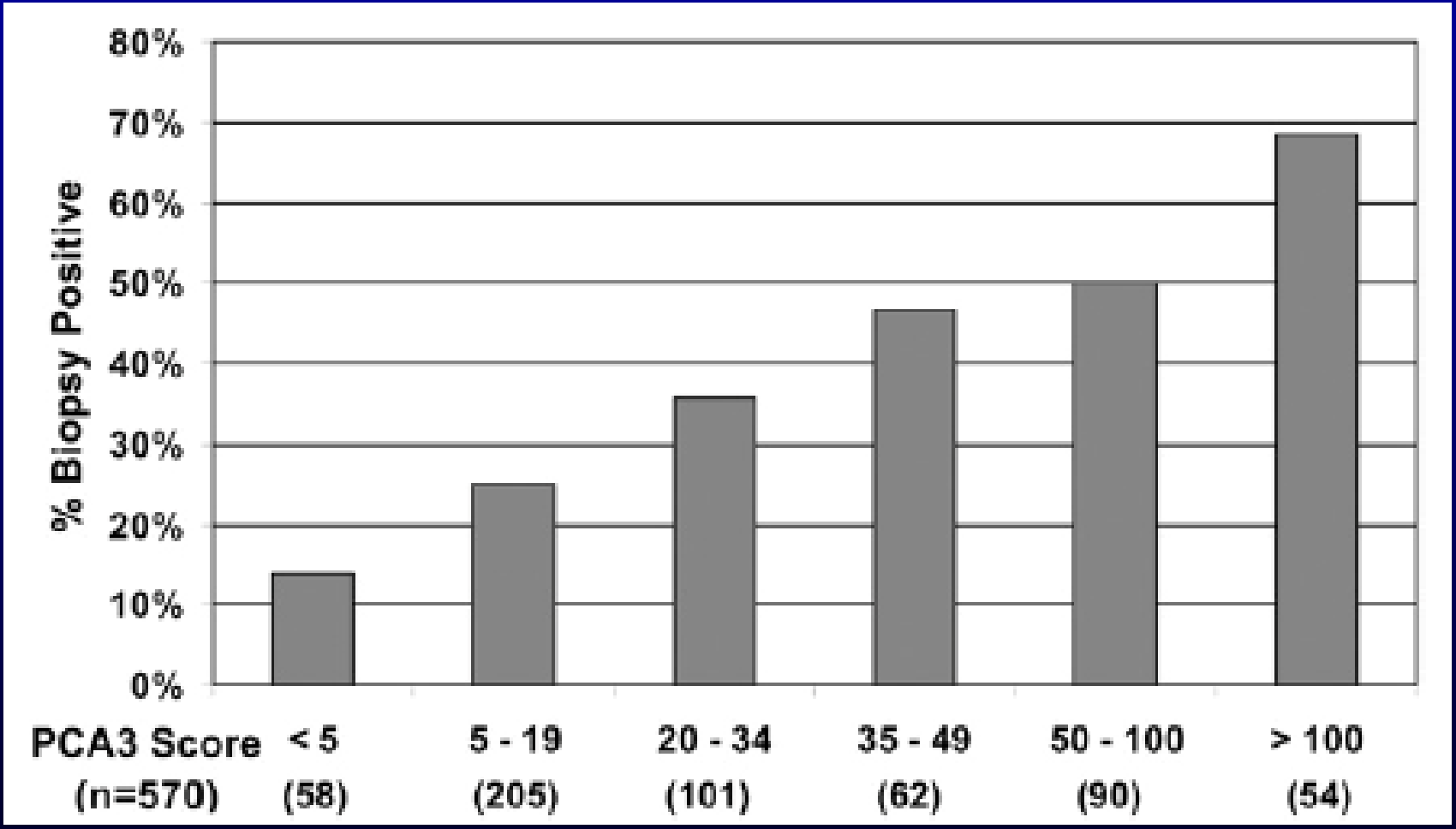
PCA3 – PCa risk



Deras et al., J Urol 179:1587, 2008

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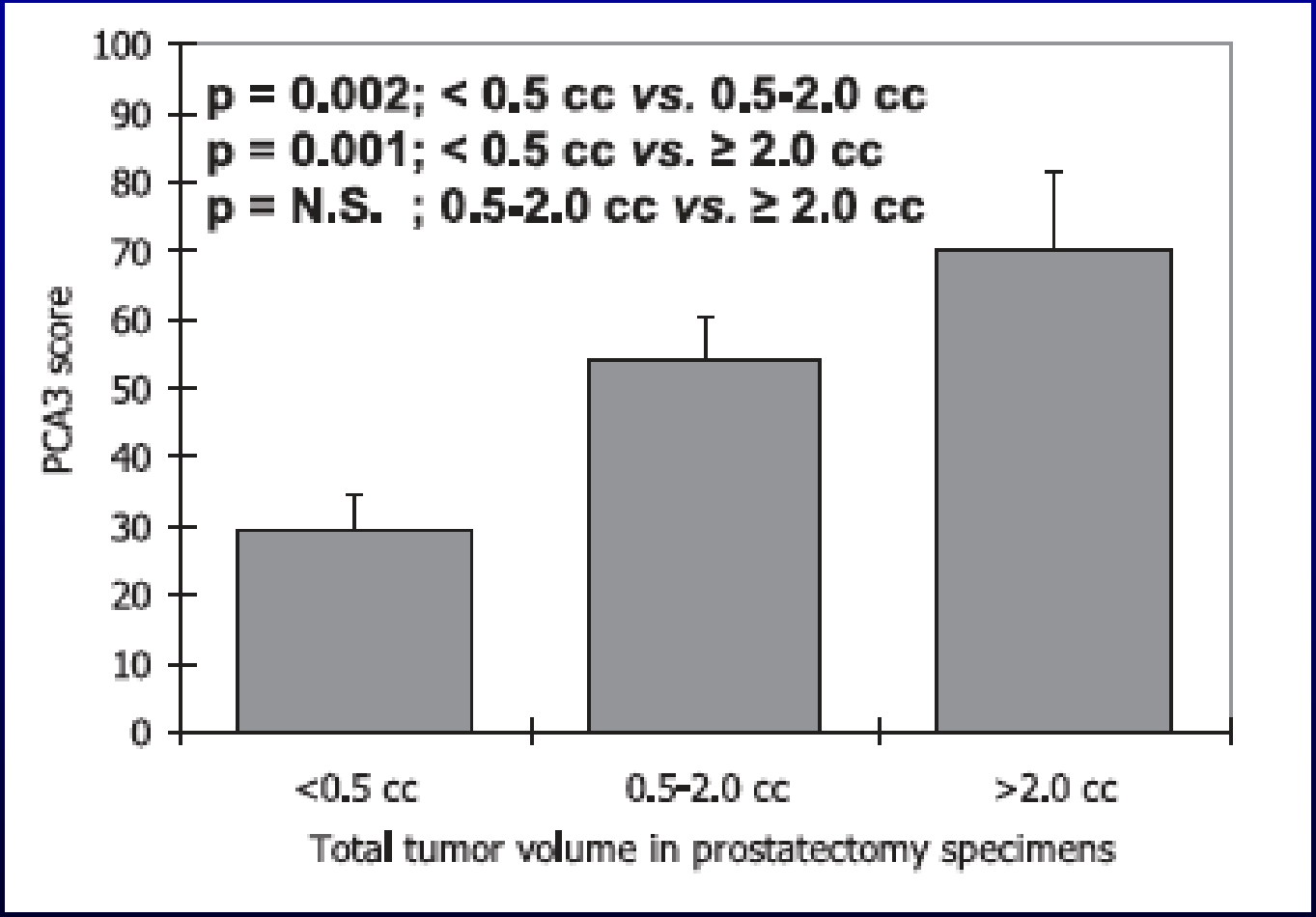
PCA3 – PCa Volume



Nakanishi et al., J Urol 179:1804, 2008

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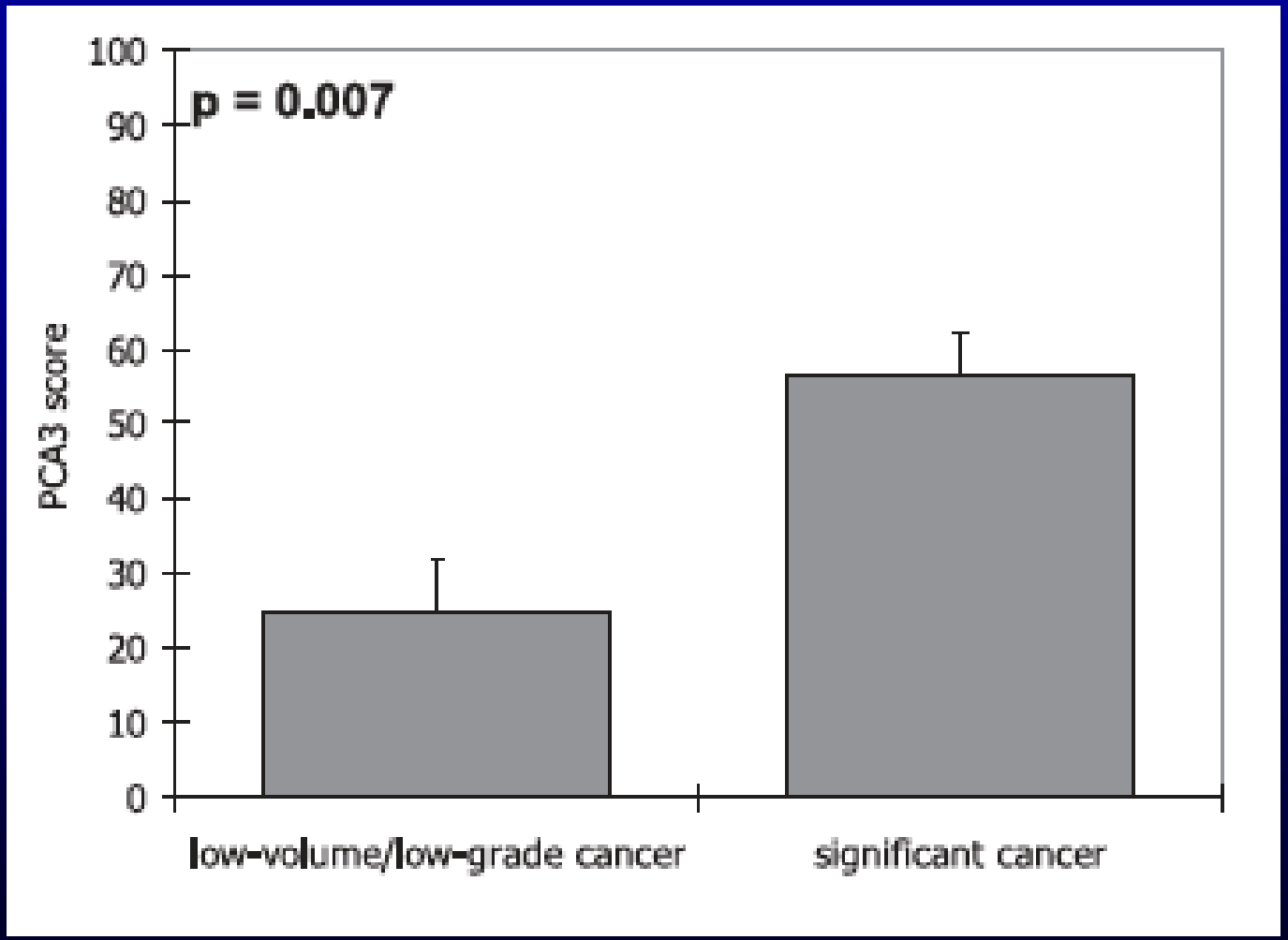
PCA3 – Gleason Grade



Nakanishi et al., J Urol 179:1804, 2008

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4Kscore (blood) test

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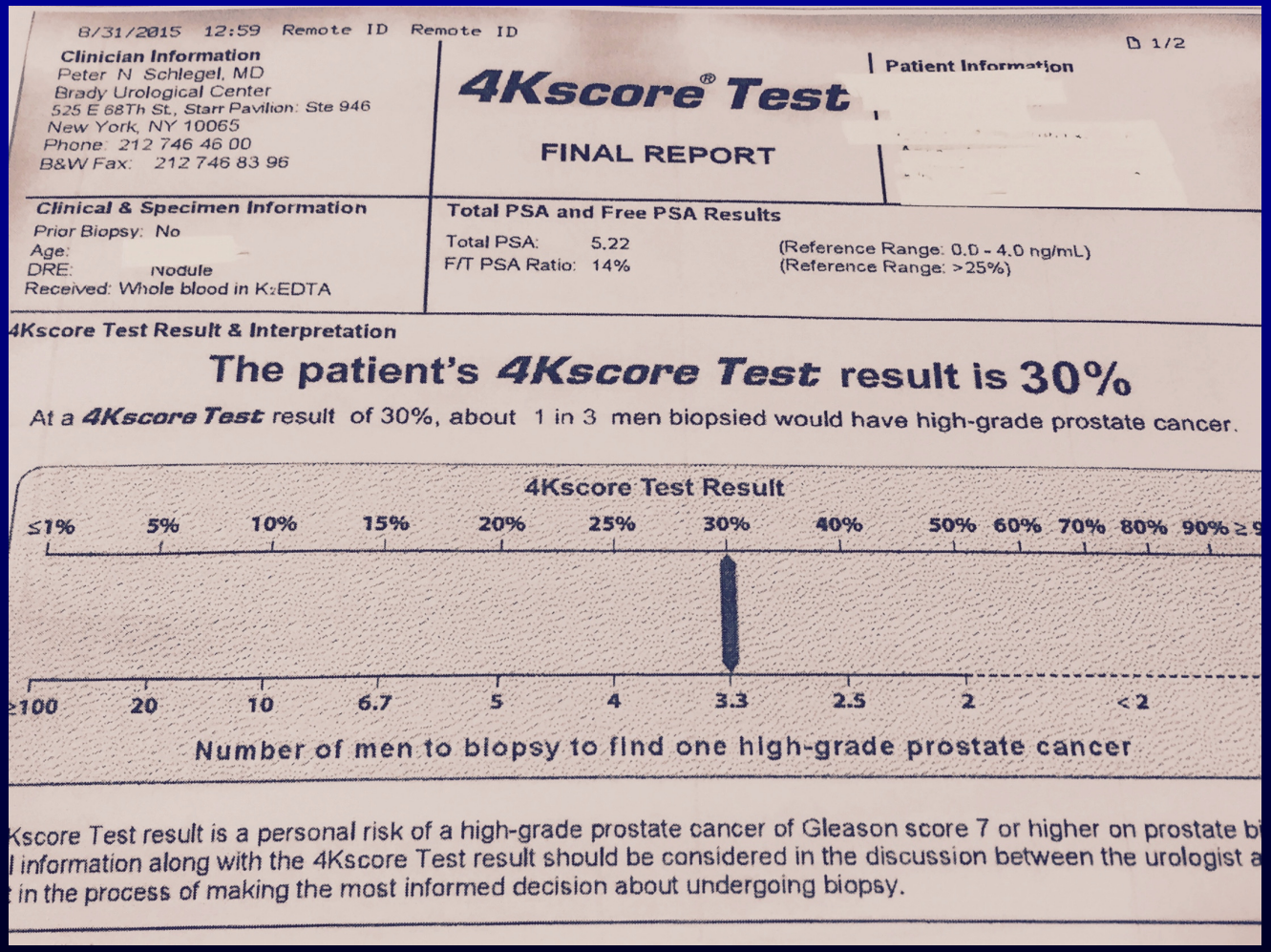
Result: 4KScore Test



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Clinician Information
Peter N Schlegel, MD
Brady Urological Center
525 E 68Th St., Starr Pavilion: Ste 946
New York, NY 10065
Phone: 212 746 46 00
B&W Fax: 212 746 83 96

4Kscore® Test

FINAL REPORT

Patient Information

Clinical & Specimen Information
Prior Biopsy: No
Age:
DRE: Nodule
Received: Whole blood in K2EDTA

Total PSA and Free PSA Results
Total PSA: 5.22 (Reference Range: 0.0 - 4.0 ng/mL)
F/T PSA Ratio: 14% (Reference Range: >25%)

4Kscore Test Result & Interpretation

The patient's *4Kscore Test* result is 30%

At a ***4Kscore Test*** result of 30%, about 1 in 3 men biopsied would have high-grade prostate cancer.

Kscore Test result is a personal risk of a high-grade prostate cancer of Gleason score 7 or higher on prostate bi
l information along with the 4Kscore Test result should be considered in the discussion between the urologist a
t in the process of making the most informed decision about undergoing biopsy.

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4KScore Test

- Best performance characteristics of any test for detection of clinically important Pca

Includes:

- PSA
- %free PSA
- hK-2
- Pt exam, patient age
- Prior biopsy status

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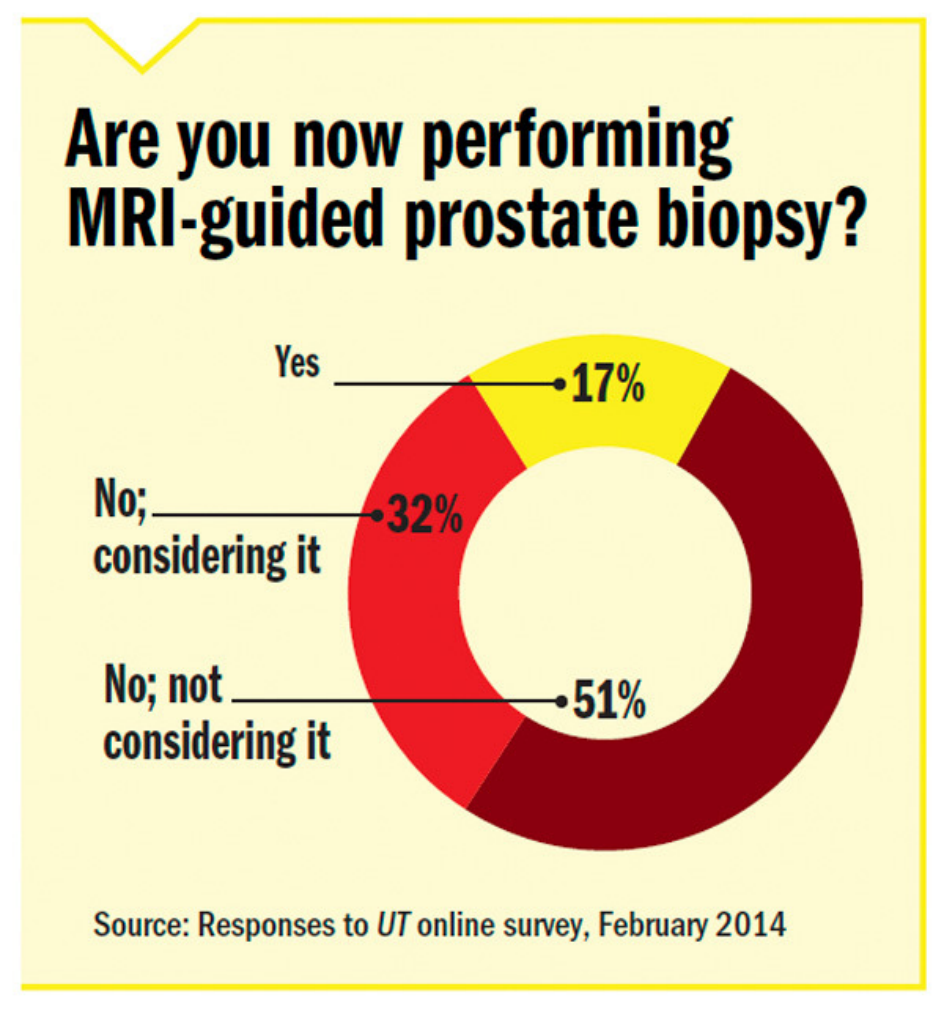
Imaging: Multiparametric MRI

- MRI (multiparametric technique)
  - T1, T2 images
  - Dynamic Contrast Enhancement (DCE)
  - Apparent Diffusion Coefficient (ADC)
  - Diffusion Weighted Imaging
  - Can identify larger/more aggressive cancers
  - May identify “lesions” that are not cancer

How commonly is MR used?



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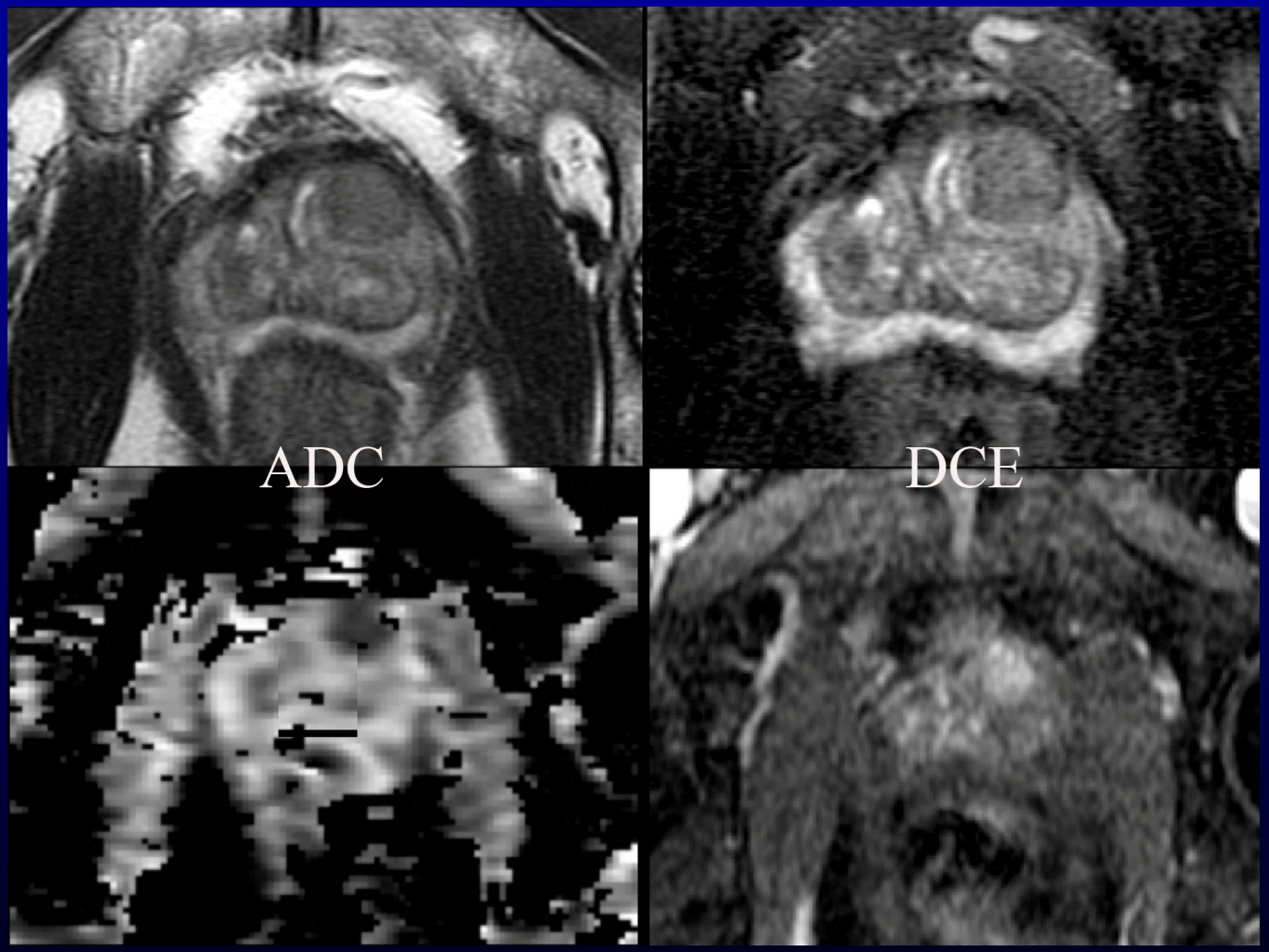
MRI Imaging of PCa



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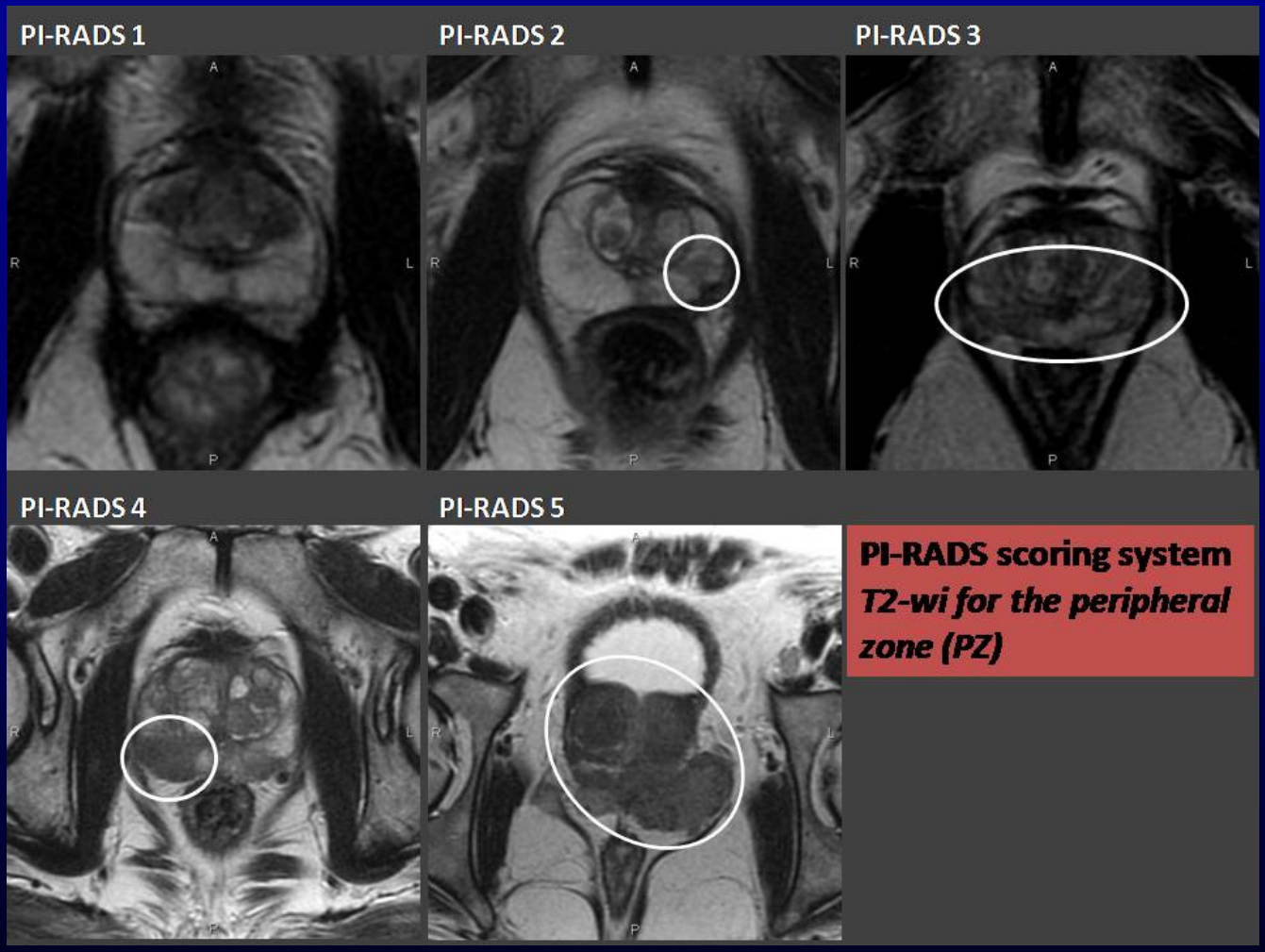
Risk-assessment of MR lesion



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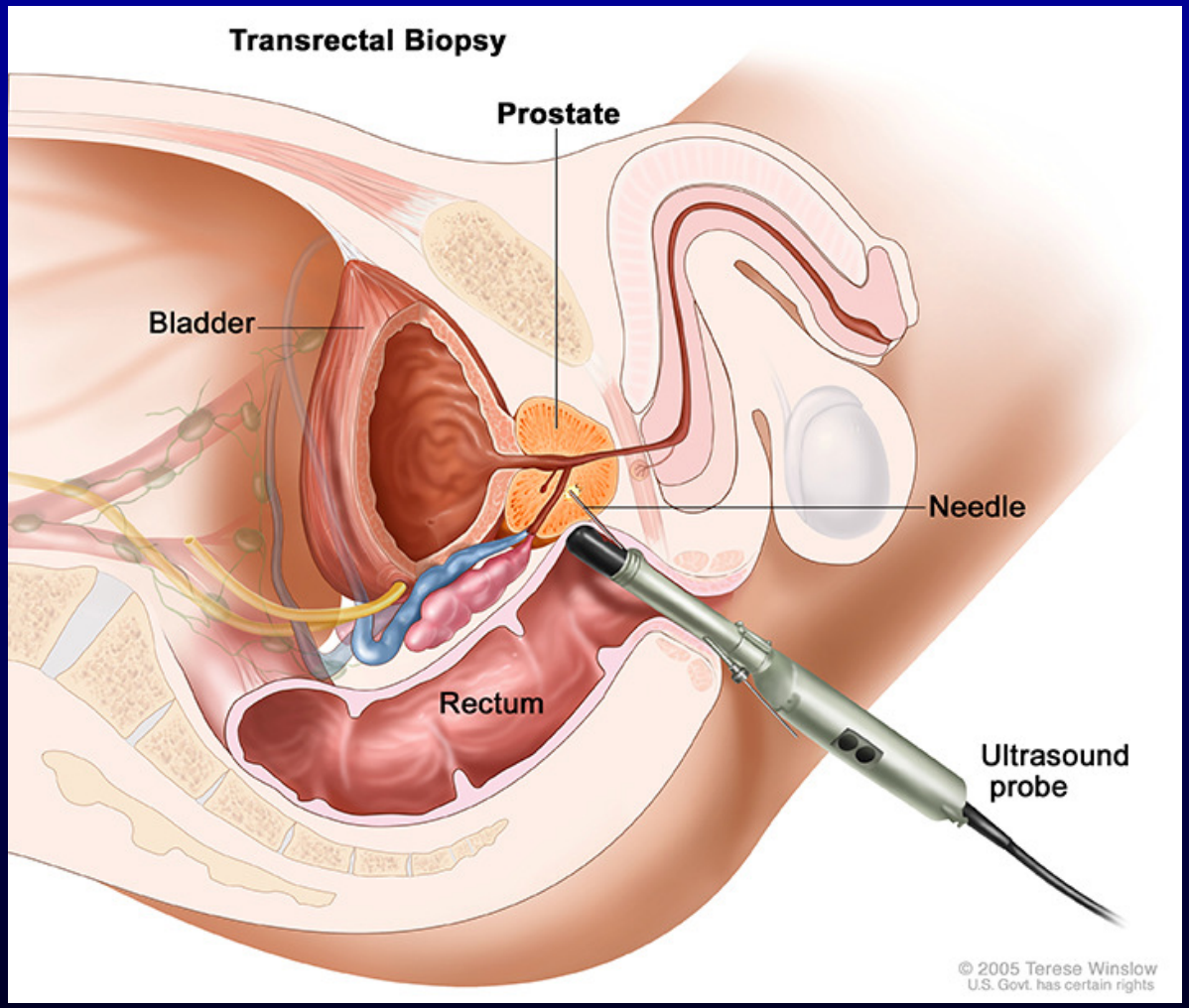
MRI Imaging of PCa

- Can the MR image help guide detection?
  - In-gantry biopsy
  - Fusion of MR with ultrasound (TRUS Fusion)

- Can MR guide treatment
  - Surgery
  - Radiation
  - Focal therapy

Prostate biopsies



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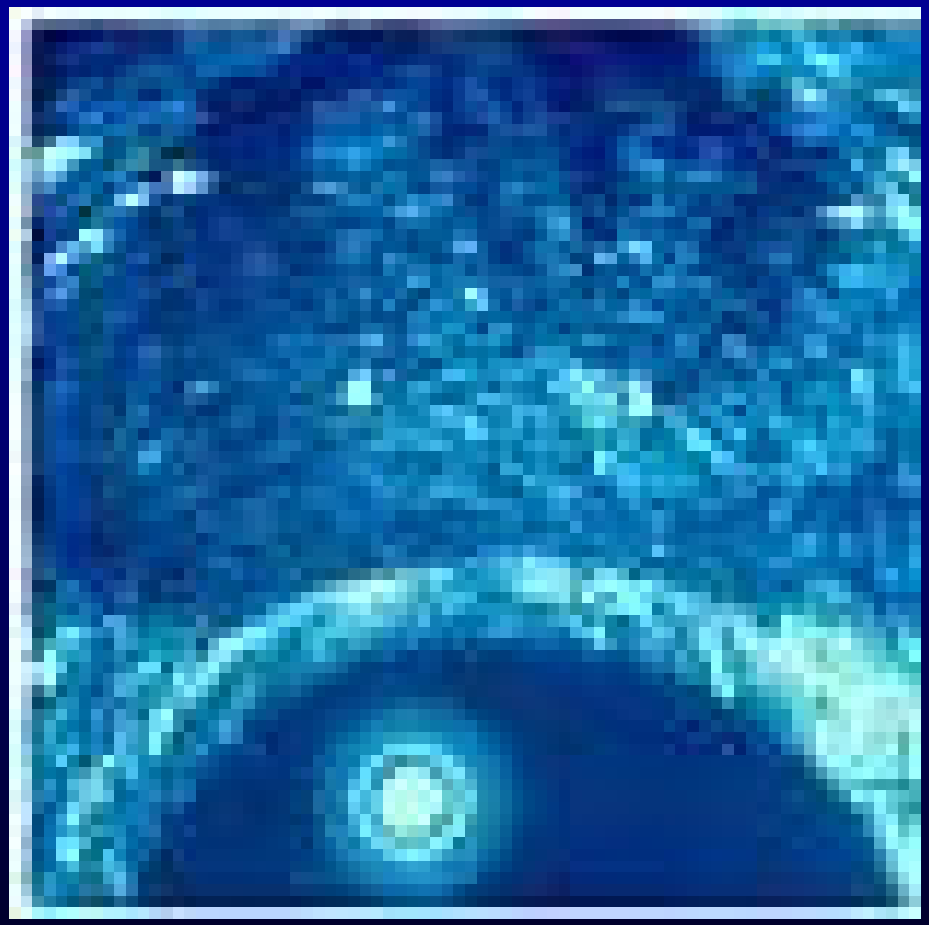
Prostate biopsies

- DRE era: Digitally directed
- TRUS
  - Initially: detection of large lesions
  - Subsequently: Adequate mapping of prostate
  - 6 cores/prostate (seeking 1 cm tumor in 4 cm)
  - Additional biopsies of other regions

TRUS guidance for biopsy



Fusion TRUS/MRI

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Fusion TRUS/MRI

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Future imaging: PET-MR

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The Future of Prostate Cancer

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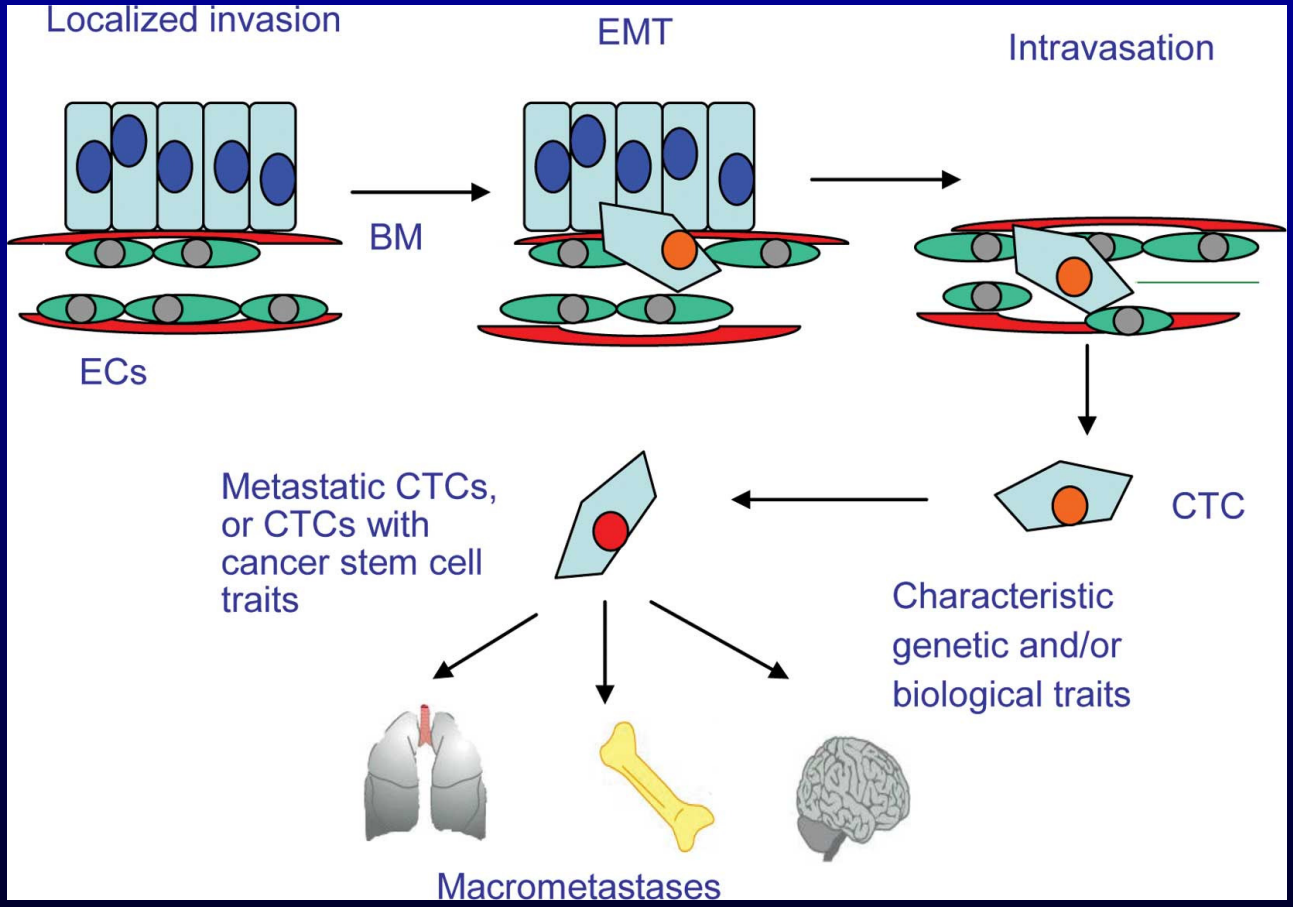
“Liquid biopsy” CTCs



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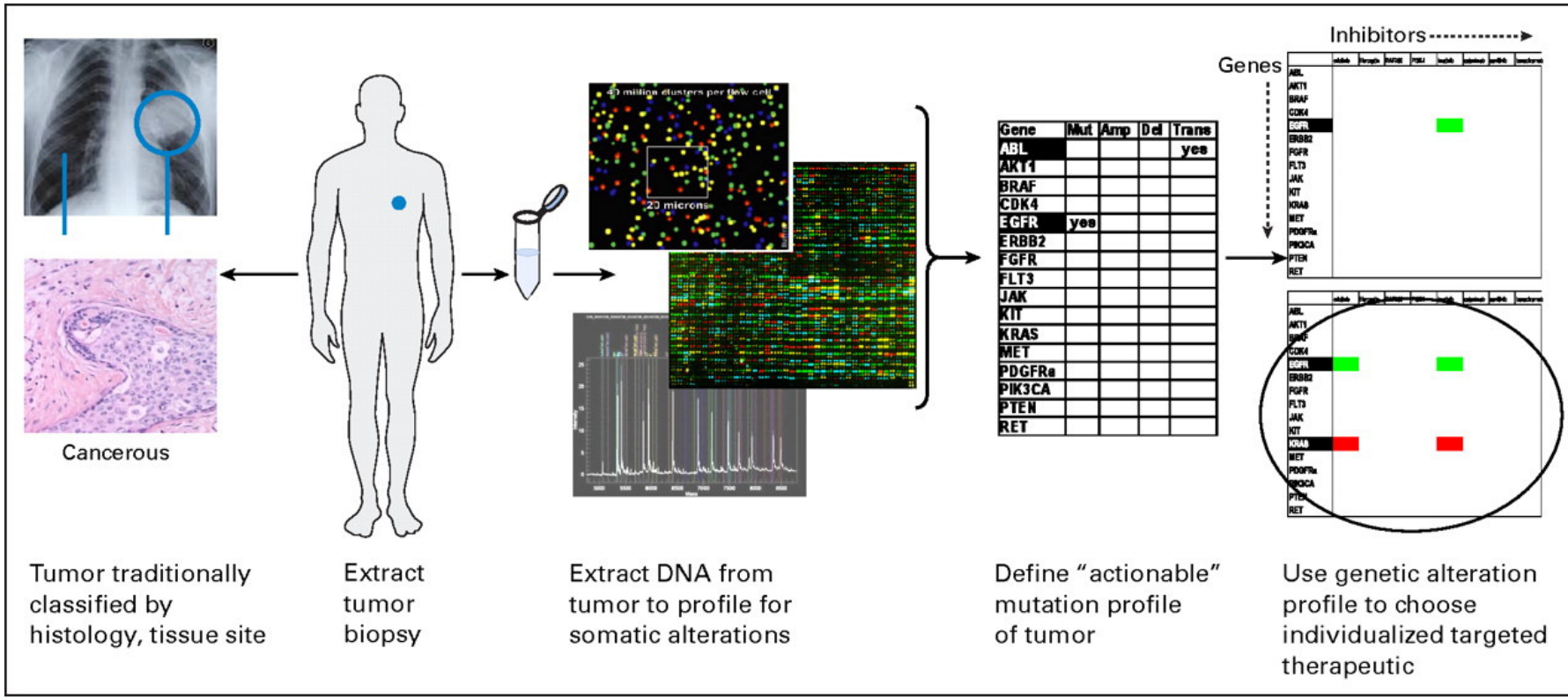
Molecular Classification of Prostate Cancer



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Gene mutations ➔ Treatment

	Frequency	Therapy
Ets gene fusion	50-60%	PARP inhibitor
PTEN/MAGI2	25-40%	PI3K inhibitor
BRAC2/ATM	20%	PARP inhibitor
Spink1	10-15%	EGFr inhibitor
Aurora kinase A	5-40%	AURK inhibitor
SPOP	10%	?
BRaf fusion	1%	Raf inhibitor

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- Support for prostate cancer research/treatment
  - EDRN staff, support
  - Collaboration, support for Pathology/researchers
  - Newest technology and applications
  - Key collaboration with Med Onc, Rad Onc, IR
- Key physicians within Urology
  - Dr. Doug Scherr
  - Dr. Christopher Barbieri
  - Dr. Jim Hu
  - Dr. Neil Bander

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