PROSTATE CANCER UPDATE FOR CORRECTIONS

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NCCHC LAS VEGAS 2022

Disclosure

I DO NOT HAVE ANY RELEVANT FINANCIAL RELATIONSHIPS WITH ANY COMMERCIAL INTERESTS.”

I AM A FULL TIME EMPLOYEE OF YES CARE

EDUCATIONAL OBJECTIVES

Define patients appropriate for PSA screening

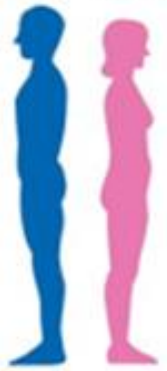
Review treatment options for patients with low, intermediate, and high-risk prostate cancer

Discuss the role of new hormonal and theranostic agents in diagnosis and treatment of prostate cancer

- **CANCER DEATHS**
- LUNG 142,500
- COLORECTAL 51,020
- BREAST 41,000
- PROSTATE 31,000

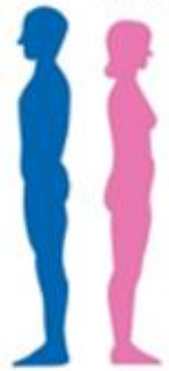
Estimated New Cases

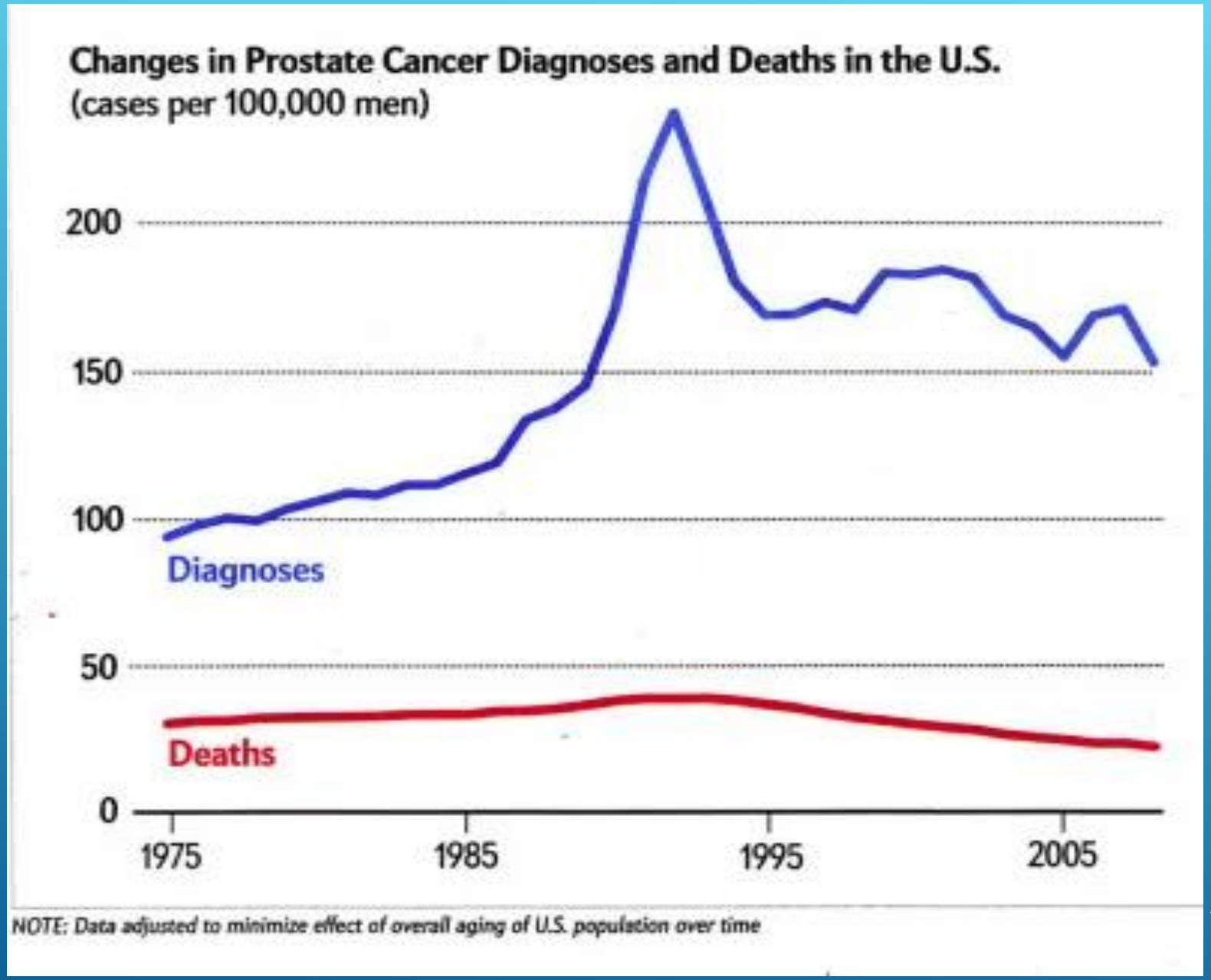
Males			Females		
Prostate	174,650	20%	Breast	268,600	30%
Lung & bronchus	116,440	13%	Lung & bronchus	111,710	13%
Colon & rectum	78,500	9%	Colon & rectum	67,100	8%
Urinary bladder	61,700	7%	Uterine corpus	61,880	7%
Melanoma of the skin	57,220	7%	Melanoma of the skin	39,260	4%
Kidney & renal pelvis	44,120	5%	Thyroid	37,810	4%
Non-Hodgkin lymphoma	41,090	5%	Non-Hodgkin lymphoma	33,110	4%
Oral cavity & pharynx	38,140	4%	Kidney & renal pelvis	29,700	3%
Leukemia	35,920	4%	Pancreas	26,830	3%
Pancreas	29,940	3%	Leukemia	25,860	3%
All Sites	**870,970**	**100%**	**All Sites**	**891,480**	**100%**



Estimated Deaths

Males			Females		
Lung & bronchus	76,650	24%	Lung & bronchus	66,020	23%
Prostate	31,620	10%	Breast	41,760	15%
Colon & rectum	27,640	9%	Colon & rectum	23,380	8%
Pancreas	23,800	7%	Pancreas	21,950	8%
Liver & intrahepatic bile duct	21,600	7%	Ovary	13,980	5%
Leukemia	13,150	4%	Uterine corpus	12,160	4%
Esophagus	13,020	4%	Liver & intrahepatic bile duct	10,180	4%
Urinary bladder	12,870	4%	Leukemia	9,690	3%
Non-Hodgkin lymphoma	11,510	4%	Non-Hodgkin lymphoma	8,460	3%
Brain & other nervous system	9,910	3%	Brain & other nervous system	7,850	3%
All Sites	**321,670**	**100%**	**All Sites**	**285,210**	**100%**




Changes in Prostate Cancer Diagnoses and Deaths in the U.S.
(cases per 100,000 men)
200
150
100
50
0
Diagnoses
Deaths
1975
1985
1995
2005
NOTE: Data adjusted to minimize effect of overall aging of U.S. population over time

- Overdiagnosis and Overtreatment of Prostate Cancer By M. Thompson Jr., MD

- 2012 by American Society of Clinical Oncology.

KEY POINTS

- Prostatc canccr is vcry common in thc aging U.S. male population and is most commonly a low-grade, low-volume tumor that poses a very low risk of progression and death.
- PSA testing and prostate biopsy have increasingly resulted in detection of low-risk tumors; nonetheless, these tumors are very often treated radically with surgery or radiation.
- It is possible, through the use of risk assessment tools, to identify men who are most likely to have high-risk cancer (for biopsy) and those who are most likely to have low-risk, potentially indolent cancer (to not have a biopsy).
- A range of novel biomarkers are in the process of validation and are predictive of high-risk prostate cancer.
- The future of prostate cancer detection will likely incorporate prostate-specific antigen and other bio-measures (e.g., digital rectal examination, age, body mass indcx), as wcll as rationally incorporatc novcl biomarkers associated with risk of high-grade cancer, to identify the man who is most likely to benefit from diagnosis and, ultimately, treatment of cancer.

PROSTATE CANCER PREVELENCE ON AUTOPSY

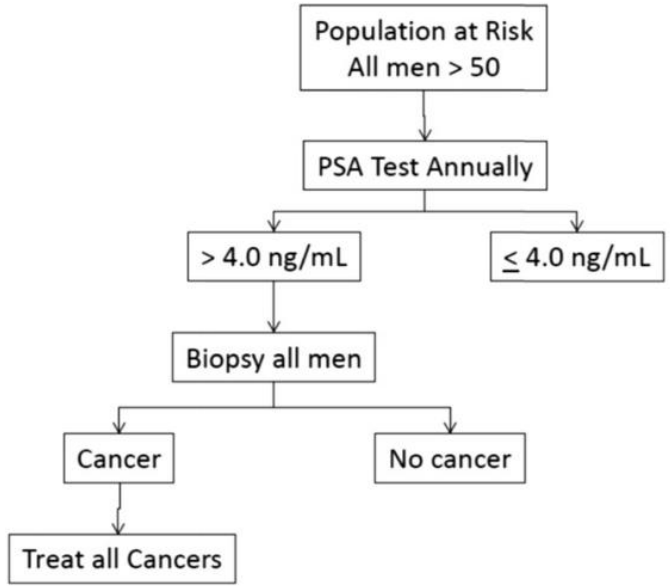
Table 1. Prevalence of Prostate Cancer at Autopsy[1]

Age (Years)	U.S. Prevalence–Whites (%)	U.S. Prevalence–Blacks (%)
41–50	37	43
51–60	44	46
61–70	65	70
71–80	83	81

Overdiagnosis and Overtreatment of Prostate Cancer By Ian M. Thompson Jr., MD
2012 by American Society of Clinical Oncology. 1092-9118/10/1-10

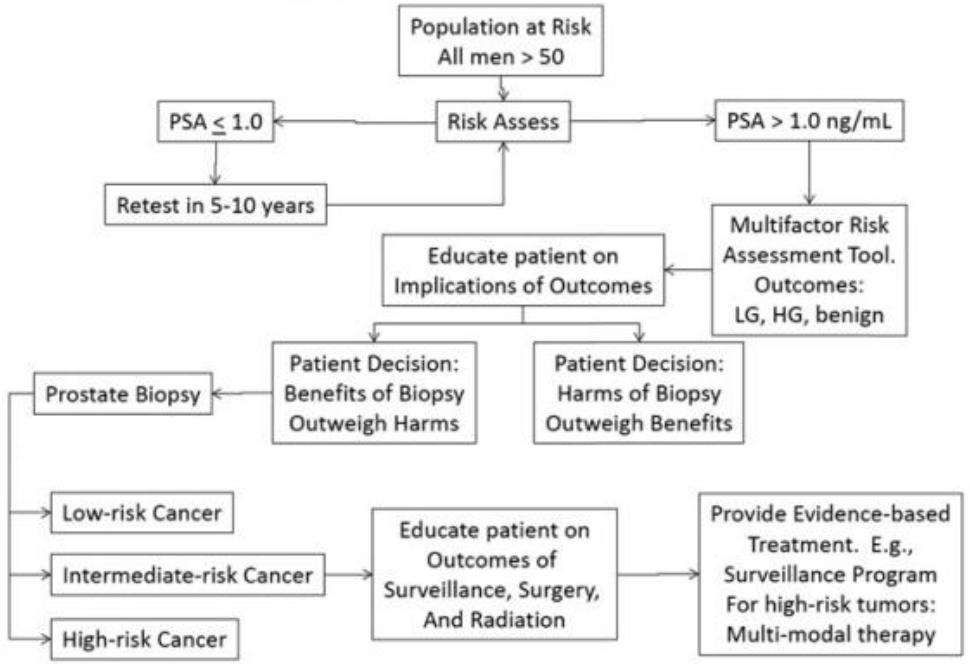
PROSTATE CANCER SCREENING

FIGURE 1. Early Approach to Prostate Cancer Screening and Treatment



Abbreviation: PSA, prostate-specific antigen.

FIGURE 3. Next-Generation Approach to Prostate Cancer Screening and Treatment



Abbreviations: HG, high grade; LG, low grade; PSA, prostate-specific antigen.

USPSTF GUIDELINES FOR PSA BASED PROSTATE CANCER SCREENING

Recommendation Summary

Population	Recommendation	Grade (What's This?)
Men aged 55 to 69 years	For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)–based screening for prostate cancer should be an individual one. Before deciding whether to be screened, men should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. However, many men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and erectile dysfunction. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening.	C
Men 70 years and older	The USPSTF recommends against PSA-based screening for prostate cancer in men 70 years and older.	D

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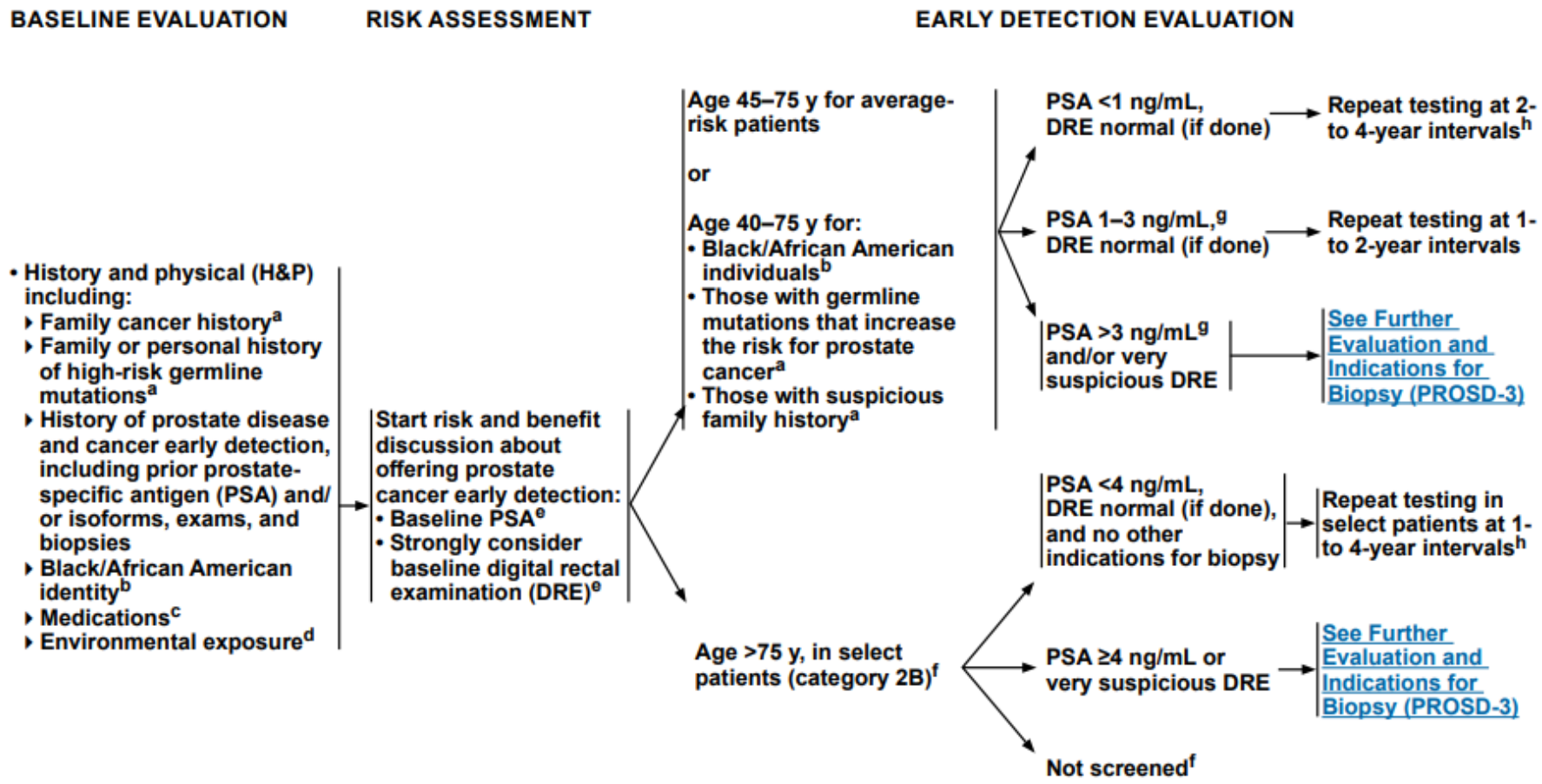
RISK

LIFE EXPECTANCY

PATIENT PREFERENCE



See footnotes on PROSD-2A.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

DRE- large gland vs small gland Nodular vs smooth

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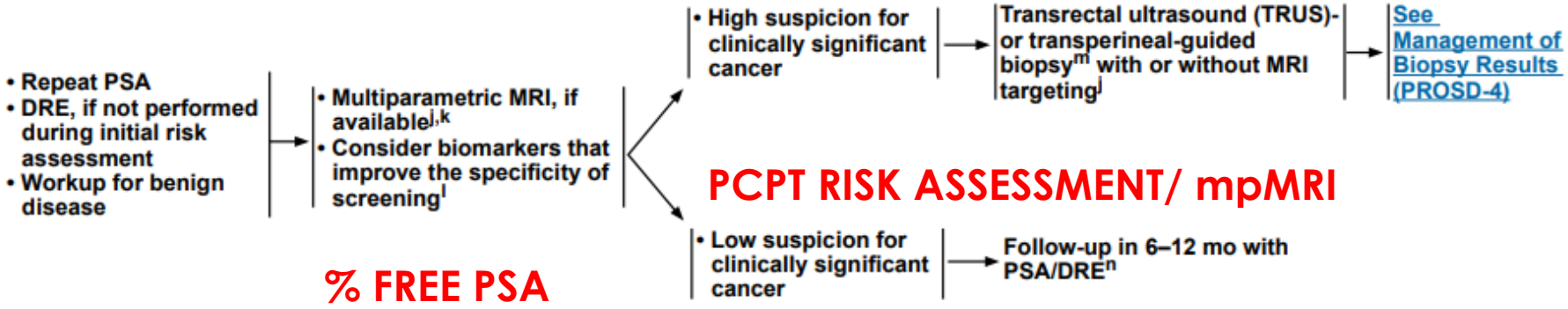
FURTHER EVALUATION AND INDICATIONS FOR BIOPSY[i]

MANAGEMENT



[i] The level of PSA correlates with the risk of prostate cancer. The Prostate Cancer Prevention Trial (PCPT) demonstrated that 15% of individuals with a PSA level ≤4.0 ng/mL and a normal DRE had prostate cancer diagnosed on end-of-study biopsies. Approximately 30% to 35% of those with serum PSA between 4 to 10 ng/mL will be found to have cancer. Total PSA levels >10 ng/mL confer a >67% likelihood of prostate cancer.

[j] In patients undergoing biopsy, targeting using MRI/ultrasound fusion significantly increases the detection of clinically significant, higher-risk (Grade Group ≥3) disease while lowering the detection of lower-risk (Grade Group 1 or lower-volume Grade Group 2) disease. It is recommended that MRI should precede biopsy and image-guided biopsy techniques be employed routinely. Although some advocate for excluding systematic biopsy in those undergoing MRI targeting, most advocate for a combined approach as some high-grade cancers are uniquely detected using the systematic approach. Siddiqui M, et al. JAMA 2015;313:390-397. Ahmed H, et al. Lancet 2017;389:815-822. Kasivisvanathan V, et al. N Engl J Med 2018;378;1767-1777. Drost FH, et al. Eur Urol 2020;77:78-94. Ahdoot M, et al. N Engl J Med 2020;382:917-928. Rouvière O, et al. Lancet Oncol 2019;20:100-109. van der Leest M, et al. Eur Urol 2019;75:570-578.

[k] A negative MRI does not exclude the possibility of cancer. Consider biomarkers and/or PSA density when deciding whether to avoid a biopsy in a man with a negative mpMRI result.

[l] Biomarkers that improve the specificity of detection are not, as yet, mandated as first-line screening tests in conjunction with serum PSA. However, there may be some patients who meet PSA standards for consideration of prostate biopsy, but for whom the patient and/or the physician wish to further define risk. Percent-free PSA may improve cancer detection. The probability of high-grade cancer (Gleason score ≥ 3+4, Grade Group 2 or higher) may be further defined utilizing the Prostate Health Index (PHI), SelectMDx, 4Kscore, ExoDx Prostate Test, MyProstateScore (MPS), and IsoPSA. Extent of validation of these tests across diverse populations is variable. It is not yet known how such tests could be applied in optimal combination with MRI.

[m] Transperineal biopsy is associated with a lower risk of sepsis and a reduced need for antibiotics compared to TRUS biopsy.

[n] Patients with a persistent and significant increase in PSA should be encouraged to undergo biopsy, including patients with a higher PSA density, even if they have a normal MRI.

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Characteristics

Race

African American

Age

66

PSA [ng/ml]

3.0

Family History of Prostate Cancer

Yes

Digital rectal examination

Normal

Prior biopsy

Never had a prior biopsy

☑ Percent free PSA available?

Percent free PSA

15

☐ PCA3 available?

☐ T2:ERG available?

Result | More Information

Risk of prostate cancer if biopsy were to be performed

Based on the provided risk factors a prostate biopsy performed would have a:

20% chance of high-grade prostate cancer,

28% chance of low-grade cancer,

52% chance that the biopsy is negative for cancer.

About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.

Make a Gift to Support Prostate Cancer Research

Characteristics

Race

African American

Age

55

PSA [ng/ml]

3.0

Family History of Prostate Cancer

Yes

Digital rectal examination

Normal

Prior biopsy

Never had a prior biopsy

☑ Percent free PSA available?

Percent free PSA

15

☐ PCA3 available?

☐ T2:ERG available?

Result | More Information

Risk of prostate cancer if biopsy were to be performed

Based on the provided risk factors a prostate biopsy performed would have a:

13% chance of high-grade prostate cancer,

27% chance of low-grade cancer,

60% chance that the biopsy is negative for cancer.

About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.

Make a Gift to Support Prostate Cancer Research

Prostate Cancer Prevention Trial Risk Calculator Version 2.0

Characteristics

Race

Caucasian

Age

55

PSA [ng/ml]

3

Family History of Prostate Cancer

Yes

Digital rectal examination

Normal

Prior biopsy

Never had a prior biopsy

☑ Percent free PSA available?

Percent free PSA

10

☐ PCA3 available?

☐ T2:ERG available?

Result | More Information

Risk of prostate cancer if biopsy were to be performed

Based on the provided risk factors a prostate biopsy performed would have a:

12% chance of high-grade prostate cancer,

45% chance of low-grade cancer,

42% chance that the biopsy is negative for cancer.

About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.

If you are Caucasian, click here for a new update to the PCPTRC that incorporates detailed family history into a risk of prostate cancer calculation.

If you are Caucasian, click here for a research calculator that allows the incorporation of up to five single-nucleotide polymorphisms (SNP).

Characteristics

Race

Caucasian

Age

55

PSA [ng/ml]

3

Family History of Prostate Cancer

No

Digital rectal examination

Normal

Prior biopsy

Never had a prior biopsy

☑ Percent free PSA available?

Percent free PSA

15

☐ PCA3 available?

☐ T2:ERG available?

Result | More Information

Risk of prostate cancer if biopsy were to be performed

Based on the provided risk factors a prostate biopsy performed would have a:

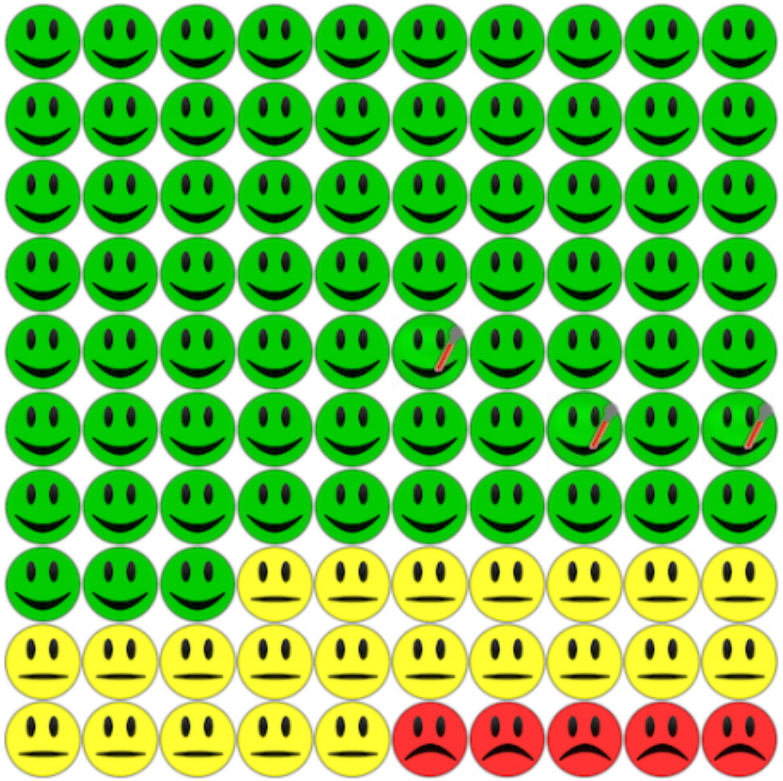
5% chance of high-grade prostate cancer,

22% chance of low-grade cancer,

73% chance that the biopsy is negative for cancer.

About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.



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Characteristics

Race

Caucasian

Age

55

PSA [ng/ml]

3

Family History of Prostate Cancer

No

Digital rectal examination

Normal

Prior biopsy

Never had a prior biopsy

☑ Percent free PSA available?

Percent free PSA

22

☐ PCA3 available?

☐ T2:ERG available?

Result | More Information

Risk of prostate cancer if biopsy were to be performed

Based on the provided risk factors a prostate biopsy performed would have a:


2% chance of high-grade prostate cancer,


14% chance of low-grade cancer,


84% chance that the biopsy is negative for cancer.


About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.

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FURTHER EVALUATION AND INDICATIONS FOR BIOPSY[i]

MANAGEMENT

- Repeat PSA
- DRE, if not performed during initial risk assessment
- Workup for benign disease

→

- Multiparametric MRI, if available[j,k]
- Consider biomarkers that improve the specificity of screening[l]

→

- High suspicion for clinically significant cancer → Transrectal ultrasound (TRUS)- or transperineal-guided biopsy[m] with or without MRI targeting[j] → See Management of Biopsy Results (PROSD-4)

PCPT RISK ASSESSMENT/ mpMRI

% FREE PSA

- Low suspicion for clinically significant cancer → Follow-up in 6–12 mo with PSA/DRE[n]

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PROSTATE MRI

- MULTIPARAMETRIC MRI mpMRI
  - Gadolinium contrast
  - 40 minutes
  - Replace TRUS and prostate Bx?
- BIPARAMETRIC MRI bpMRI PROSTAGRAM
  - No contrast
  - 15 minutes
  - Replace PSA?

PI-RADS score [redacted]

A PI-RADS v2 score is given according to each variable parameter. The scale is based on a score "Yes" or "No" for Dynamic Contrast-Enhanced (DCE) parameter, and from 1 to 5 for T2-weighted (T2W) and Diffusion-weighted imaging (DWI). The score is given for each lesion, with 1 being most probably benign and 5 being highly suspicious of malignancy:

- PI-RADS 1: very low (clinically significant cancer is highly unlikely to be present)
- PI-RADS 2: low (clinically significant cancer is unlikely to be present)
- PI-RADS 3: intermediate (the presence of clinically significant cancer is equivocal)
- PI-RADS 4: high (clinically significant cancer is likely to be present)
- PI-RADS 5: very high (clinically significant cancer is highly likely to be present)

PROSTATE CANCER DX

CLINICAL

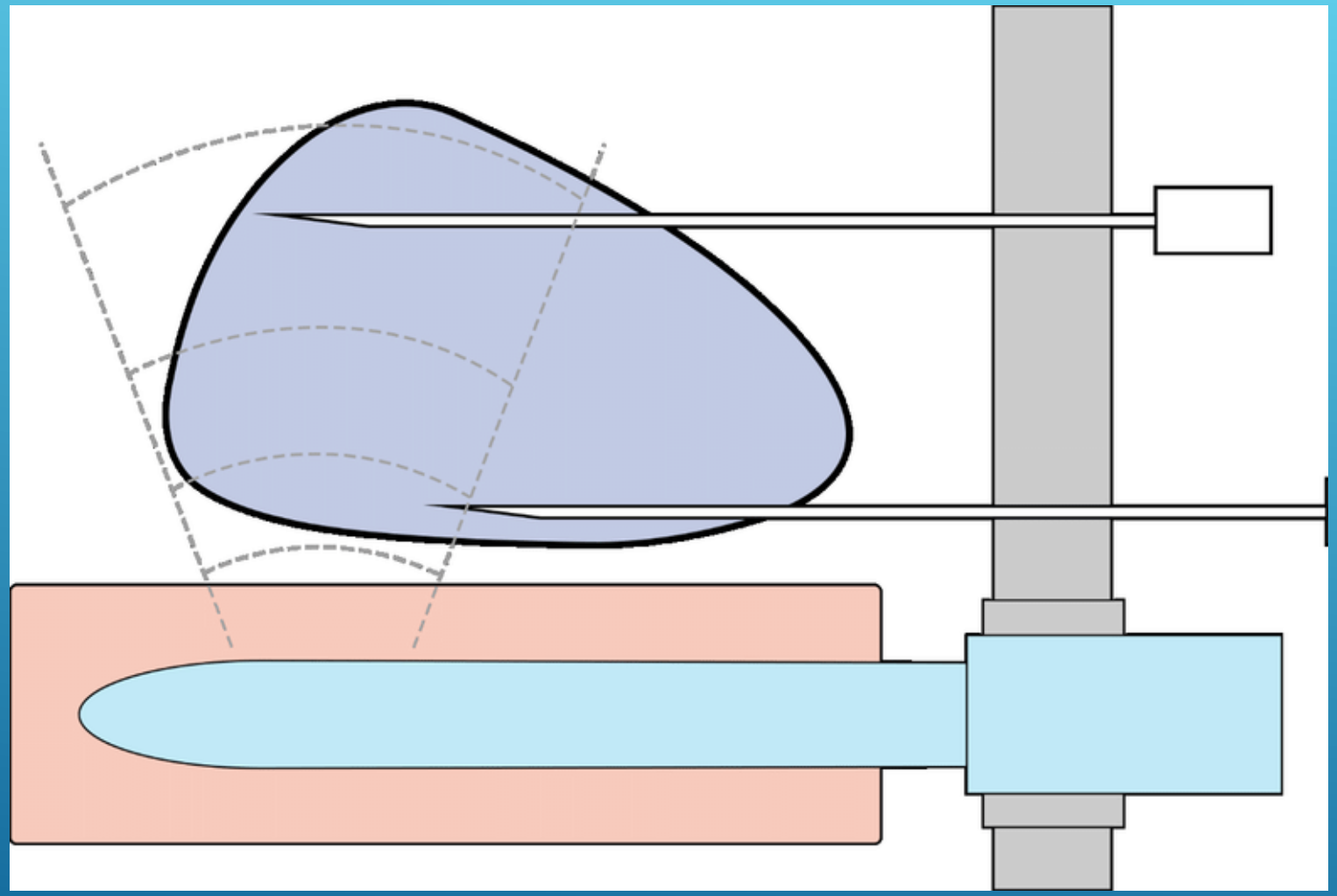
- EXTENDED PATTERN TRUS AND PROSTATE BX (AT LEAST 12 CORE SAMPLE)+ ANY PALPABLE LESIONS AND/OR RADIOGRAPHIC SUGGESTIVE AREAS

- TRANSPERINEAL PROSTATE BX

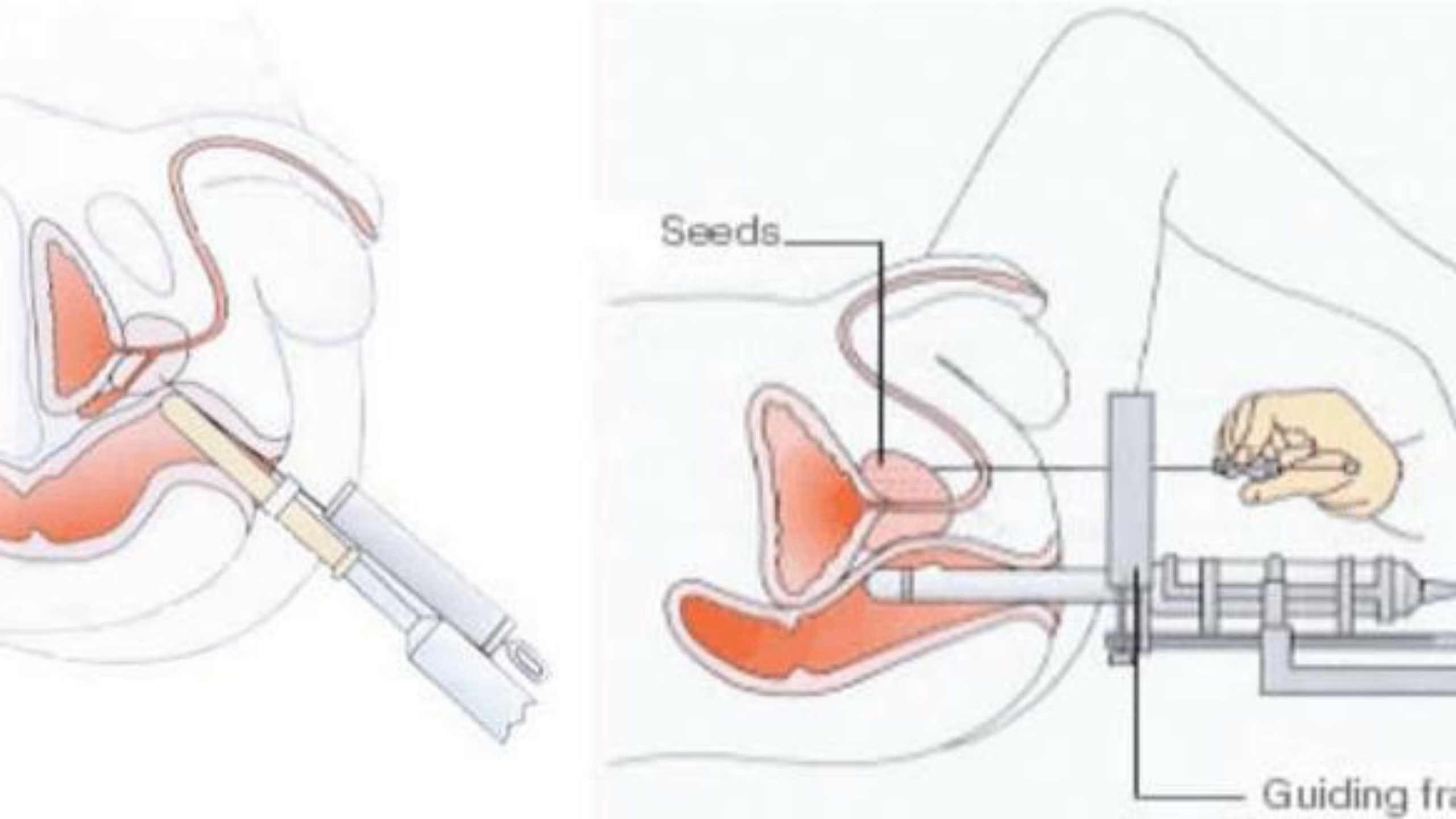
OPTIONS

- **IN UROLOGY OFFICE WITH LOCAL ANESTHESIA**
- IN HOSPITAL OUTPATIENT LOCAL ANESTHESIA
- IN HOSPITAL OUTPATIENT WITH GENERAL ANESTHESIA

GENERAL/SPINAL ANESTHESIA



TRANSPERINEAL PROSTATE BX


Seeds
Guiding fra

Guide 3
Prostate cancer stage by TNM score

Stage	Primary tumor (T)	Regional lymph nodes (N)	Distant metastasis (M)
Localized	**T1** Tumor cannot be felt during digital rectal exam and is not found on imaging tests, but cancer is present.	**N0** There is no cancer in nearby lymph nodes.	**M0** Cancer has not spread to other parts of the body.
	T2 Tumor is felt during digital rectal exam and is found only in the prostate.	**N0**	**M0**
	T3 Tumor has broken through outside layer of prostate. It may have grown into seminal vesicle(s).	**N0**	**M0**
	T4 Tumor has grown outside the prostate into nearby structures such as the bladder, rectum, pelvic muscles, and/or pelvic wall.	**N0**	**M0**
Regional	**Any T**	**N1** There is cancer (metastasis) in nearby lymph nodes.	**M0**
Metastatic	**Any T**	**Any N**	**M1** Cancer has spread to other parts of the body

GLEASON SCORING SYSTEM

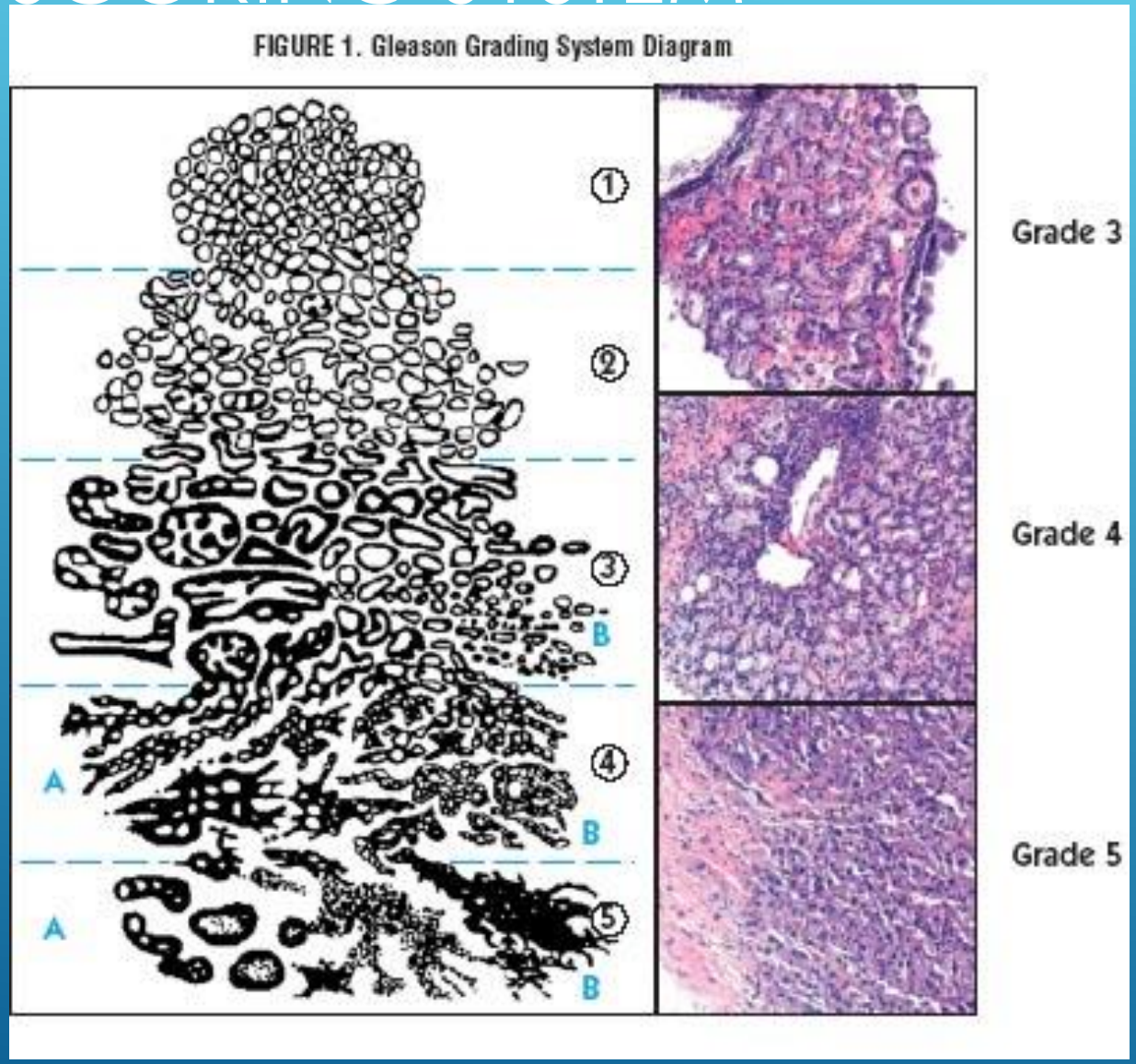


TABLE 2. Histologic Definition of the Updated Grading System

Grade Group	Gleason Score Equivalent	Characteristic Features
1	3 + 3 = 6	Only individual discrete well-formed glands
2	3 + 4 = 7	Predominantly well-formed glands with a lesser component of poorly formed/fused/cribriform glands
3	4 + 3 = 7	Predominantly poorly formed/fused/cribriform glands with a lesser component of well-formed glands*
4	8	Only poorly formed/fused/cribriform glands, predominantly well-formed glands and a lesser component lacking glands,† or predominantly lacking glands and a lesser component of well-formed glands†
5	9–10	Lack of gland formation (or necrosis) with or without poorly formed/fused/cribriform glands*

*For patients with greater than 95% poorly formed/fused/cribriform glands or lack of glands on a core or at RP, the component of less than 5% well-formed glands is not factored into the grade.
†Poorly formed/fused/cribriform glands can be a more minor component.

5 year biochemical DFS

96%

88%

63%

48%

26%

Guide 1 Gleason score summary	
6 or less	• The cancer is likely to grow and spread very slowly. • If the cancer is small, many years may pass before it becomes a problem. You may never need cancer treatment. • Also called **low grade.**
7	• The cancer is likely to grow and spread at a modest pace. • If the cancer is small, several years may pass before it becomes a problem. To prevent problems, treatment may be needed. • Also called **intermediate grade.**
8, 9, or 10	• The cancer is likely to grow and spread fast. • If the cancer is small, a few years may pass before the cancer becomes a problem. To prevent problems, treatment is needed now. • Also called **high grade.**

INITIAL RISK STRATIFICATION AND STAGING WORKUP FOR CLINICALLY LOCALIZED DISEASE[d]

Risk Group	Clinical/Pathologic Features See Staging (ST-1)			Additional Evaluation[g,h]	Initial Therapy
Very low[e]	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/mL • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core • PSA density <0.15 ng/mL/g			• Consider confirmatory mpMRI ± prostate biopsy if MRI not performed initially. All patients should undergo a confirmatory prostate biopsy within 1-2 years of their diagnostic biopsy.	See PROS-3
Low[e]	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL			• Consider confirmatory mpMRI ± prostate biopsy and/or molecular tumor analysis if MRI not performed inititally to establish candidacy for active surveillance. All patients should undergo a confirmatory prostate biopsy within 1-2 years of their diagnostic biopsy.	See PROS-4
Intermediate[e]	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): ▸ cT2b–cT2c ▸ Grade Group 2 or 3 ▸ PSA 10–20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)[f]	• Consider confirmatory mpMRI ± prostate biopsy and/or molecular tumor analysis if MRI not performed initially for those considering active surveillance. All patients should undergo a confirmatory prostate biopsy within 1-2 years of their diagnostic biopsy.	See PROS-5
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)[f]	Bone and soft tissue imaging[i,j] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-6
High	Has no very-high-risk features and has exactly one high-risk feature: • cT3a OR • Grade Group 4 or Grade Group 5 OR • PSA >20 ng/mL			Bone and soft tissue imaging[i,j] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7
Very high	Has at least one of the following: • cT3b–cT4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • >4 cores with Grade Group 4 or 5			Bone and soft tissue imaging[i,j] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7

See Footnotes for Initial Risk Stratification and Staging Workup for Clinically Localized Disease (PROS-2A).

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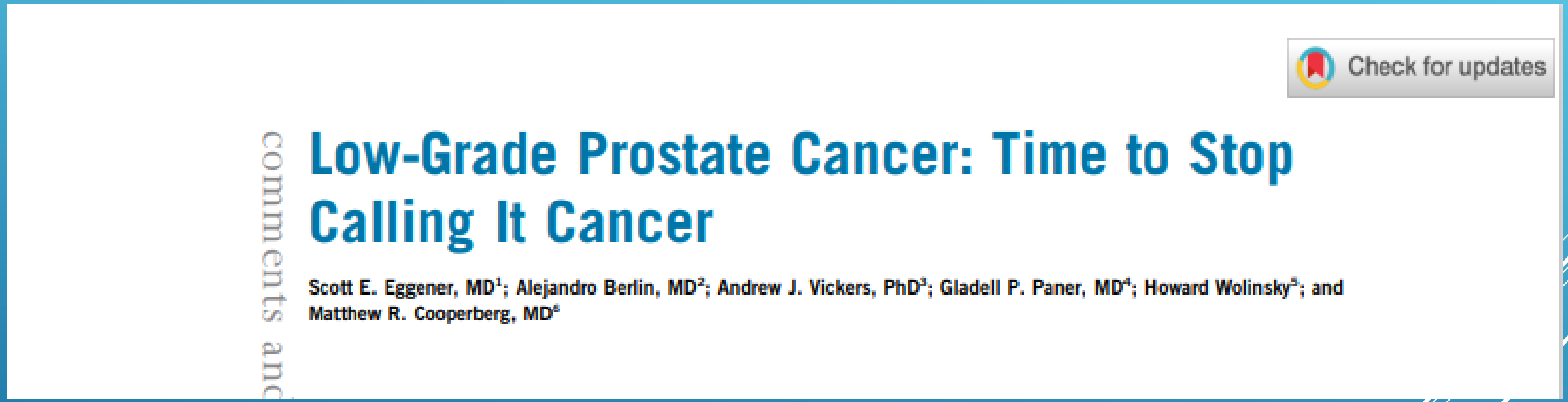


ascopubs.org/journal/ jco on April 18, 2022: DOI https://doi.org/10.1200/JCO.22.00123

comments and

Renaming Gleason Score 6 Prostate to Noncancer: A Flawed Idea Scientifically and for Patient Care

Jonathan I. Epstein, MD[1] and Adam S. Kibel, MD[2]

Unnecessary Diagnosis and Treatment

Worldwide, **hundreds of thousands of men** diagnosed annually with Gleason score 6 disease.

In the PSA era, millions of men are unnecessarily diagnosed and treated, costing billions of dollars.

> 50% Over 50% of men **over the age of 50 years** have histologic prostate cancer

50% **Up to 50%** of men with Gleason score 6 are treated with **radiation or surgery**

< 1% **15-year rates** of metastases or cancer-specific death are **less than 1%** in men with only GS 6

Smarter Screening

Selective screening based on risk, life expectancy, and patient preference
Increased use of serum, urine, and genetic biomarkers

Tailored Diagnosis and Management

Increase the clinical threshold to biopsy
MRI to minimize diagnosis of indolent disease and optimize biopsy quality
Appropriate utilization of surveillance strategies for early-stage disease

Nomenclature Change

Multidisciplinary discussion to modify the definition of prostate cancer

DOI: 10.1200/JCO.22.00123 *Journal of Clinical Oncology*

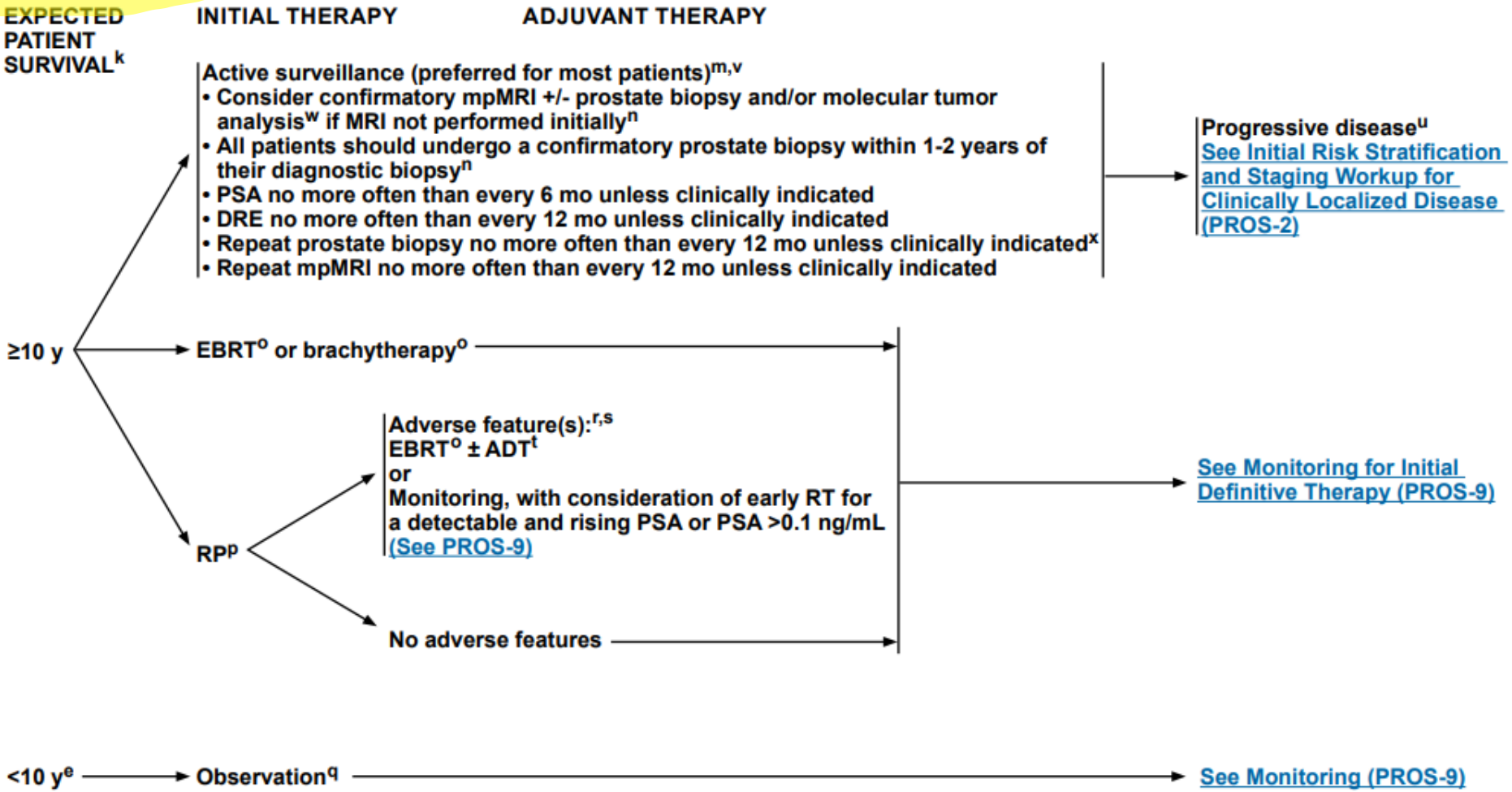
VERY-LOW-RISK GROUP

EXPECTED PATIENT SURVIVAL[k]	INITIAL THERAPY	ADJUVANT THERAPY
>20 y	Active surveillance (preferred)[m] • Consider confirmatory mpMRI +/- prostate biopsy if MRI not performed initially[n] • All patients should undergo a confirmatory prostate biopsy within 1-2 years of their diagnostic biopsy • PSA no more often than every 6 mo unless clinically indicated • DRE no more often than every 12 mo unless clinically indicated • Repeat prostate biopsy no more often than every 12 mo unless clinically indicated • Repeat mpMRI no more often than every 12 mo unless clinically indicated	Progressive disease[u] See Initial Risk Stratification and Staging Workup for Clinically Localized Disease (PROS-2)
	EBRT[o] or brachytherapy[o]	
	Radical prostatectomy (RP)[p] → Adverse feature(s):[r,s] EBRT[o] ± ADT[t] or Monitoring, with consideration of early RT for a detectable and rising PSA or PSA >0.1 ng/mL (See PROS-9)	See Monitoring for Initial Definitive Therapy (PROS-9)
	No adverse features	
10–20 y[l]	Active surveillance[m] • Consider confirmatory mpMRI +/- prostate biopsy if MRI not performed initially[n] • All patients should undergo a confirmatory prostate biopsy within 1-2 years of their diagnostic biopsy[n] • PSA no more often than every 6 mo unless clinically indicated • DRE no more often than every 12 mo unless clinically indicated • Repeat prostate biopsy no more often than every 12 mo unless clinically indicated • Repeat mpMRI no more often than every 12 mo unless clinically indicated	Progressive disease[u] See Initial Risk Stratification and Staging Workup for Clinically Localized Disease (PROS-2)
<10 y[e]	Observation[q]	See Monitoring (PROS-9)

See Footnotes for Risk Groups (PROS-8A).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

LOW-RISK GROUP



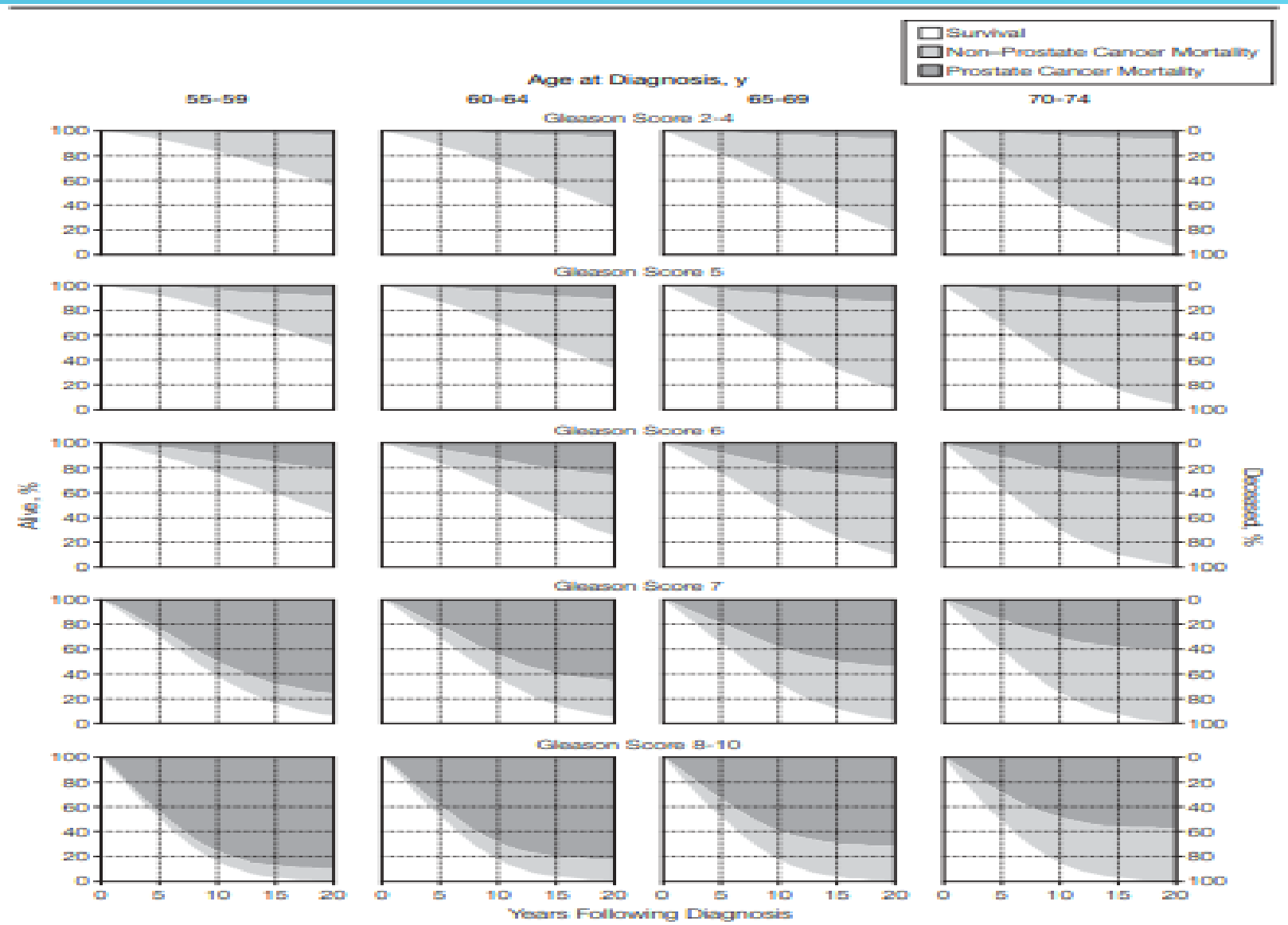
See Footnotes for Risk Groups (PROS-8A).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

- 1,643 patients
  - 545 active monitoring
  - 553 surgery
  - 545 xrt
- 10 year median f/u
  - 8 prostate cancer deaths in active monitoring group (3 Gleason 6, 5 Gleason 7)
  - 5 prostate cancer deaths in surgery group (3 Gleason 6, 2 Gleason 7)
  - 4 prostate cancer deaths in XRT group (2 Gleason 6, 2 Gleason 7)
  - **17 patients died of prostate cancer (Prostate Cancer Mortality 1%) /152 died of other causes(9.2%)**

PROTECT TRIAL (LOW RISK PROSTATE CANCER)

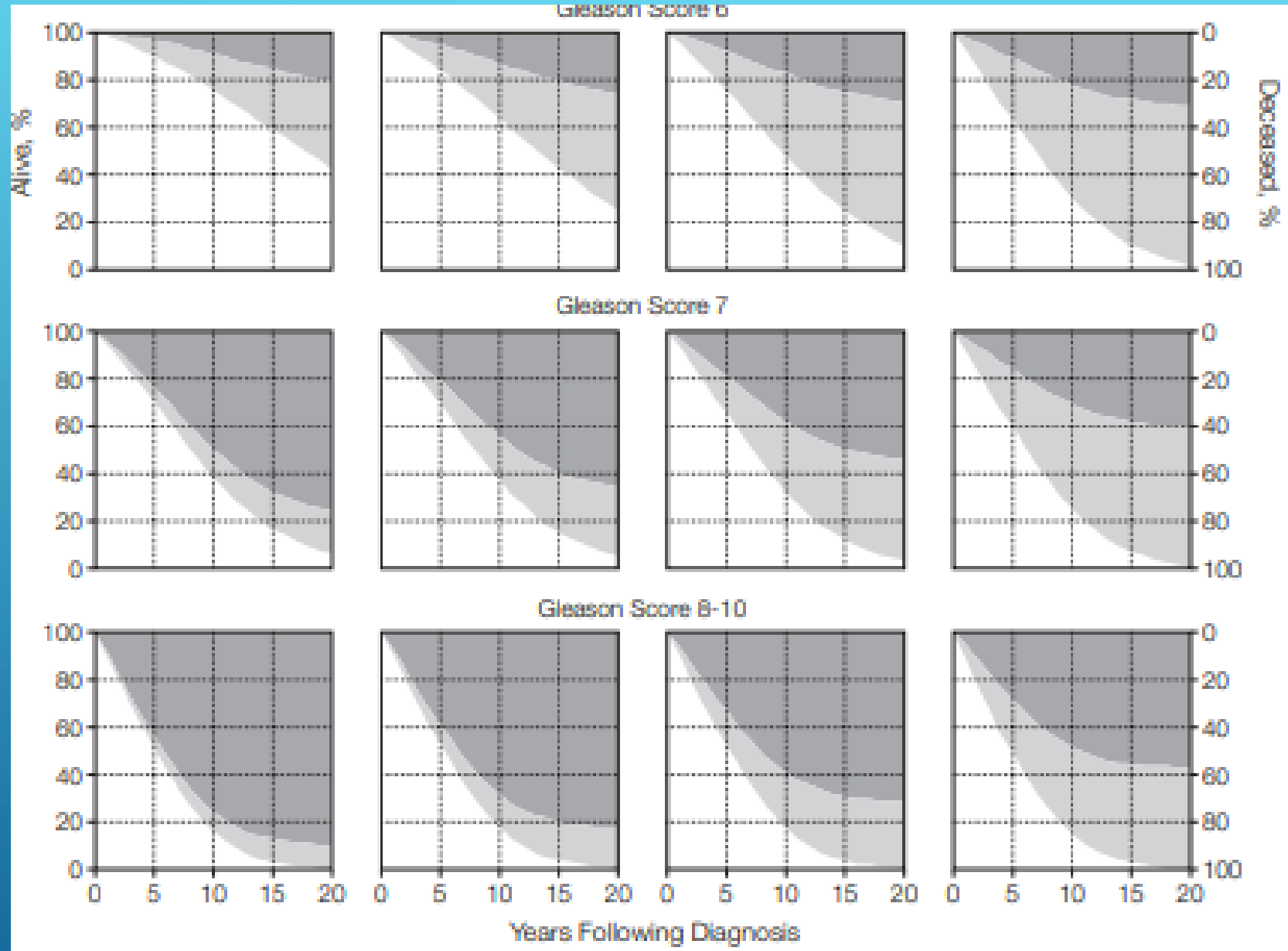
N ENGL J MED 375;15 NEJM.ORG OCTOBER 13, 2016



20-Year Outcomes Following Conservative Management of Clinically Localized Prostate Cancer

Peter C. Albertsen, MD, MS; James A. Hanley, PhD; Judith Fine, BA
Author Affiliations Article Information

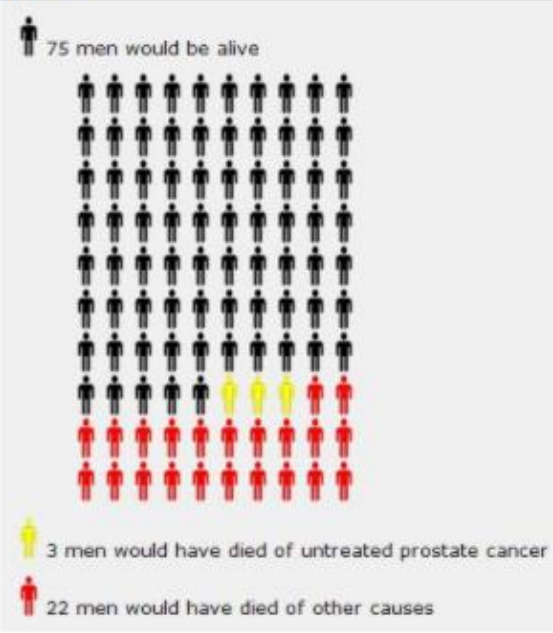
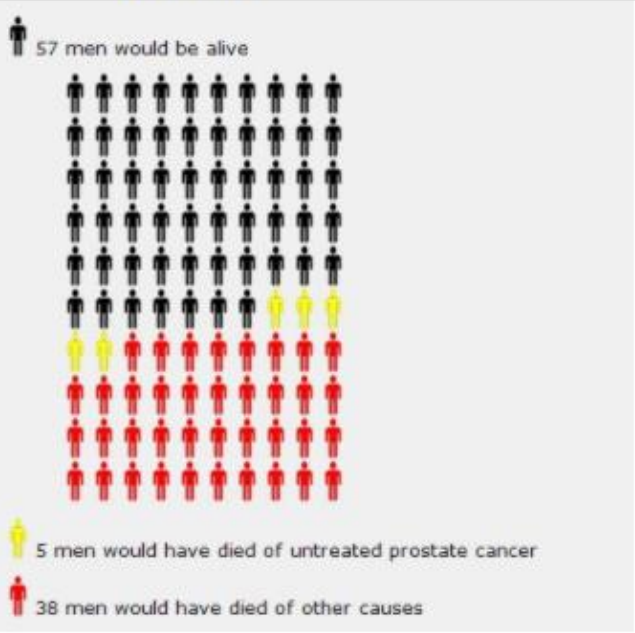
JAMA. 2005;293(17):2095-2101. doi:10.1001/jama.293.17.2095


Gleason Score 6
Gleason Score 7
Gleason Score 8-10
Alive, %
Deceased, %
0
20
40
60
80
100
0
5
10
15
20
Years Following Diagnosis

WebCore

Male Life Expectancy Survey

Imagine that there were 100 men like you: the same age and overall health, and the same prostate cancer in terms of stage, grade and PSA. If none of these men received treatment intended to cure their cancer, this is what we would expect to happen:

At 10 Years	At 15 Years
	

75/78=96%

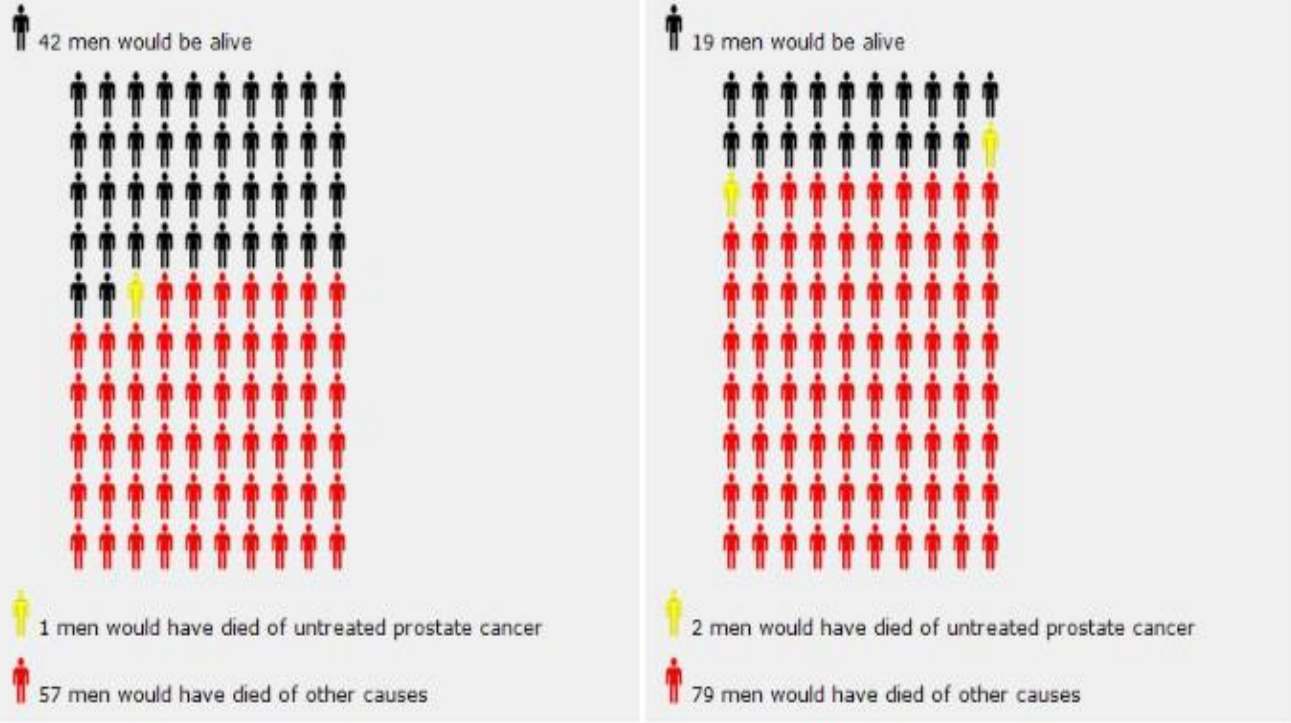
The graph above has taken account the following information that you have reported:

Prostate Cancer Characteristics

Age:	67.
T Stage:	T1C.
Gleason Grade:	6.
PSA:	6.

- **The Memorial Sloan Kettering Male Life Expectancy tool** (https://webcore.mskcc.org/survey/surveyform.aspx?preview=true&excelsurveylistid=4).

42/43=97%



The graph above has taken account the following information that you have reported:

Health Conditions: Asthma; COPD; Smoked more than 100 cigarettes; Low HDL cholesterol; Diabetes.

Prostate Cancer Characteristics

Age:	67.
T Stage:	T1C.
Gleason Grade:	6.
PSA:	6.

HOW MANY RADIATION TREATMENTS ARE NEEDED TO TREAT PROSTATE CANCER?

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NCCN Guidelines Version 4.2022
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PRINCIPLES OF RADIATION THERAPY

Table 1: Below are examples of regimens that have shown acceptable efficacy and toxicity. The optimal regimen for an individual patient warrants evaluation of comorbid conditions, voiding symptoms and toxicity of therapy. Additional fractionation schemes may be used as long as sound oncologic principles and appropriate estimate of BED are considered.

See PROS-3, PROS-4, PROS-5, PROS-6, PROS-7, PROS-8, PROS-12, and PROS-H for other recommendations, including recommendations for neoadjuvant/concomitant/adjuvant ADT.

Regimen	Preferred Dose/Fractionation	NCCN Risk Group (✓ indicates an appropriate regimen option if radiation therapy is given)					
		Very Low and Low	Favorable Intermediate	Unfavorable Intermediate	High and Very High	Regional N1	Low Volume M1[a]
EBRT							
Moderate Hypofractionation (Preferred)	3 Gy x 20 fx 2.7 Gy x 26 fx 2.5 Gy x 28 fx	✓	✓	✓	✓	✓	
	2.75 Gy x 20 fx						✓
Conventional Fractionation	1.8–2 Gy x 37–45 fx	✓	✓	✓	✓	✓	
Ultra-Hypofractionation	7.25–8 Gy x 5 fx 6.1 Gy x 7 fx	✓	✓	✓	✓		
	6 Gy x 6 fx						✓

N Engl J Med 2012;367:203-13.

Table 2. Patient-Reported Urinary, Erectile, and Bowel Dysfunction at 2 Years, According to Study Group.*

Dysfunction	Radical Prostatectomy	Observation	P Value
	no./total no. (%)		
Urinary incontinence†	49/287 (17.1)	18/284 (6.3)	<0.001
Erectile dysfunction‡	231/285 (81.1)	124/281 (44.1)	<0.001
Bowel dysfunction§	35/286 (12.2)	32/282 (11.3)	0.74

* The values reported are the number of men reporting the dysfunction and the total number of men who responded to the question.
† Urinary incontinence was defined by patient reports ("have a lot of problems with urinary dribbling," "lose larger amounts of urine than dribbling but not all day," "have no control over urine," or "have an indwelling catheter").
‡ Erectile dysfunction was defined as the inability to have an erection or an erection sufficient for vaginal penetration.
§ Bowel dysfunction was defined by patient reports that it was a "moderate" or "big" problem.

ACTIVE SURVEILLANCE

- Active surveillance (preferred for most patients)
- • Consider confirmatory mpMRI +/- prostate biopsy and/or molecular tumor analysis if MRI not performed initially
- • All patients should undergo a confirmatory prostate biopsy within 1-2 years of their diagnostic biopsy
- • PSA no more often than every 6 m unless clinically indicated
- • DRE no more often than every 12 m unless clinically indicated
- • Repeat prostate biopsy no more often than every 12 m unless clinically indicated
- • Repeat mpMRI no more often than every 12 m unless clinically indicated

- **ACTIVE SURVEILLANCE ON SITE PROTOCOL**
- **NO NEED FOR ROUTINE UROLOGY F/U FOR ACTIVE SURVEILLANCE**

CLINICAL

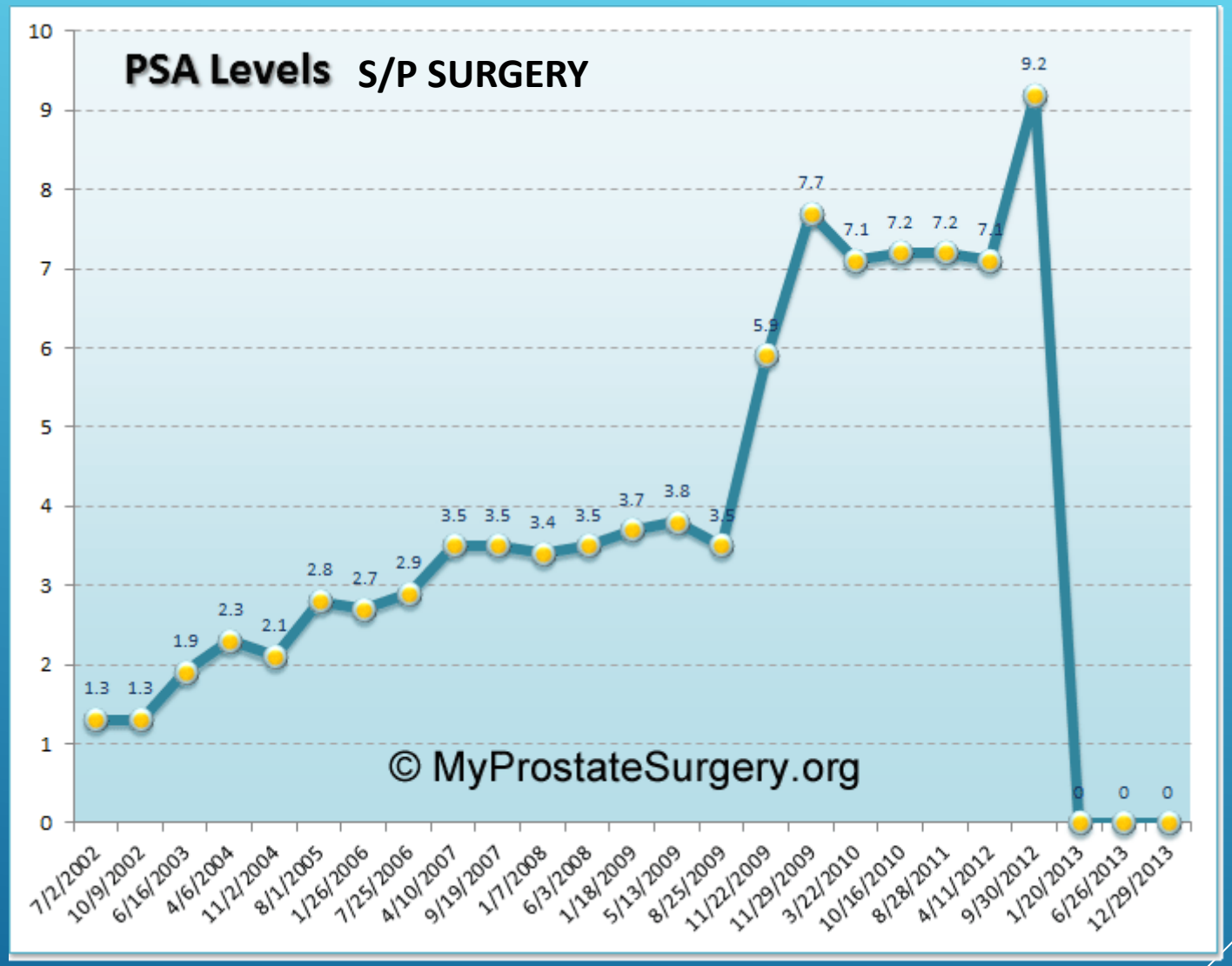
- DRE yearly
- PSA Q 6 months

OPTIONS

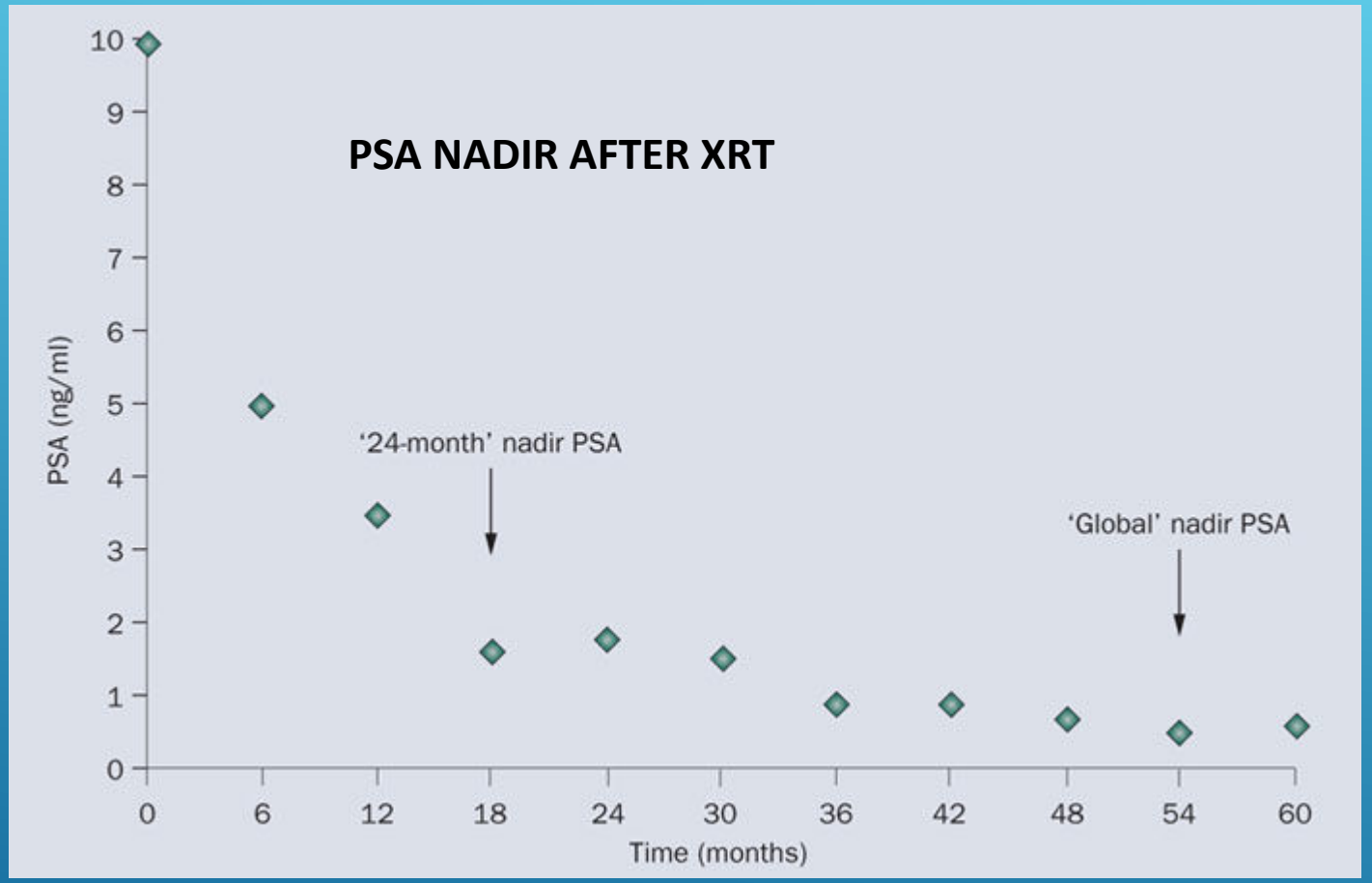
- **DRE ON SITE/PSA ON SITE**
- DRE AT UROLOGY/XRT
- PSA AT UROLOGY/XRT

PROSTATE CANCER SURVEILLANCE

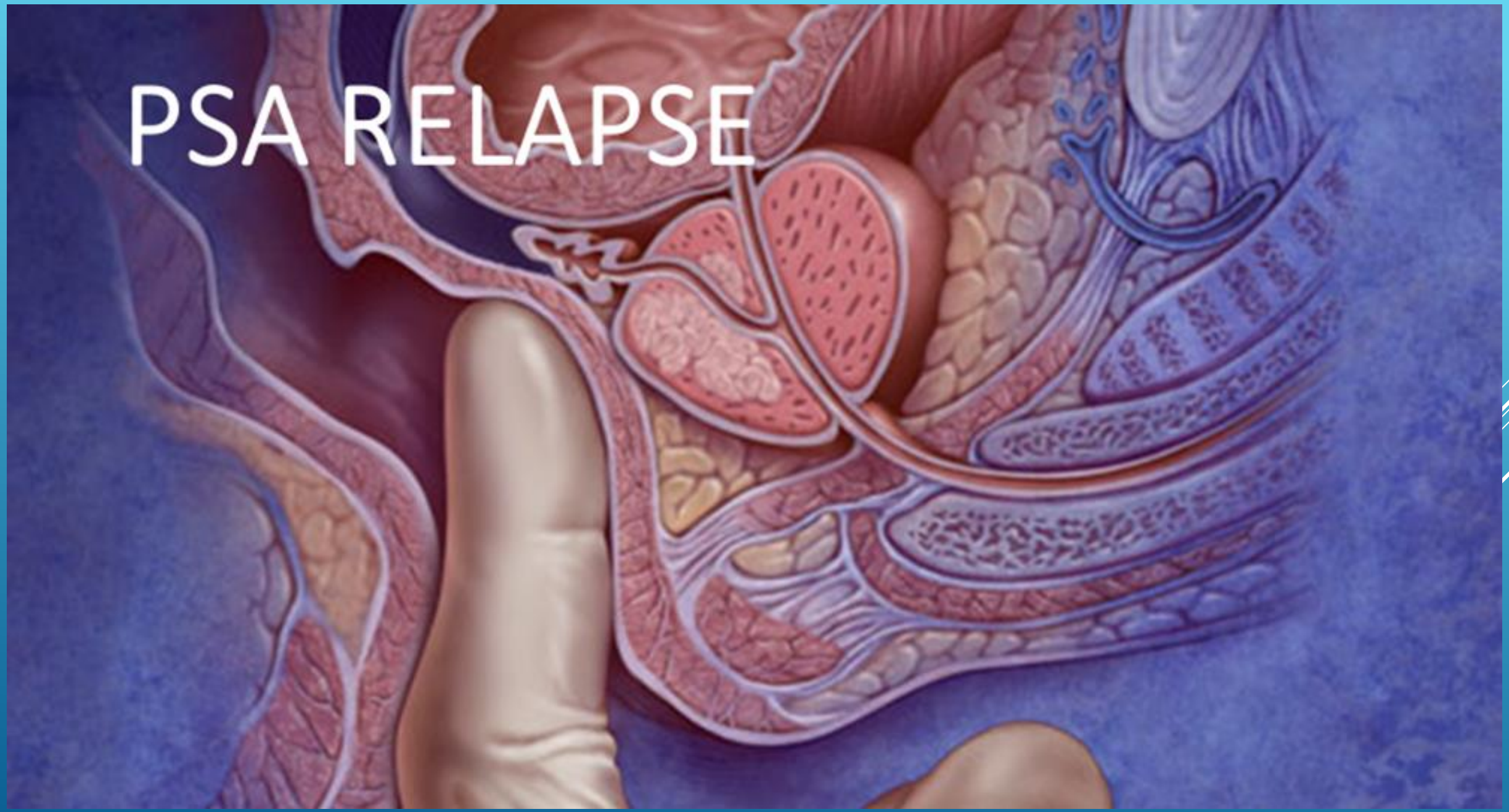
PROSTATE CANCER SURVEILLANCE CAN BE PERFORMED ON SITE BY A PRIMARY CARE PROVIDER


PSA Levels S/P SURGERY
© MyProstateSurgery.org
10
9
8
7
6
5
4
3
2
1
0
1.3
1.3
1.9
2.3
2.1
2.8
2.7
2.9
3.5
3.5
3.4
3.5
3.7
3.8
3.5
5.9
7.7
7.1
7.2
7.2
7.1
9.2
0
0
0
7/2/2002
10/9/2002
6/16/2003
4/6/2004
11/2/2004
8/1/2005
1/26/2006
7/25/2006
4/10/2007
9/19/2007
1/7/2008
6/3/2008
1/18/2009
5/13/2009
8/25/2009
11/22/2009
11/29/2009
3/22/2010
10/16/2010
8/28/2011
4/11/2012
9/30/2012
1/20/2013
6/26/2013
12/29/2013

PSA NADIR AFTER XRT



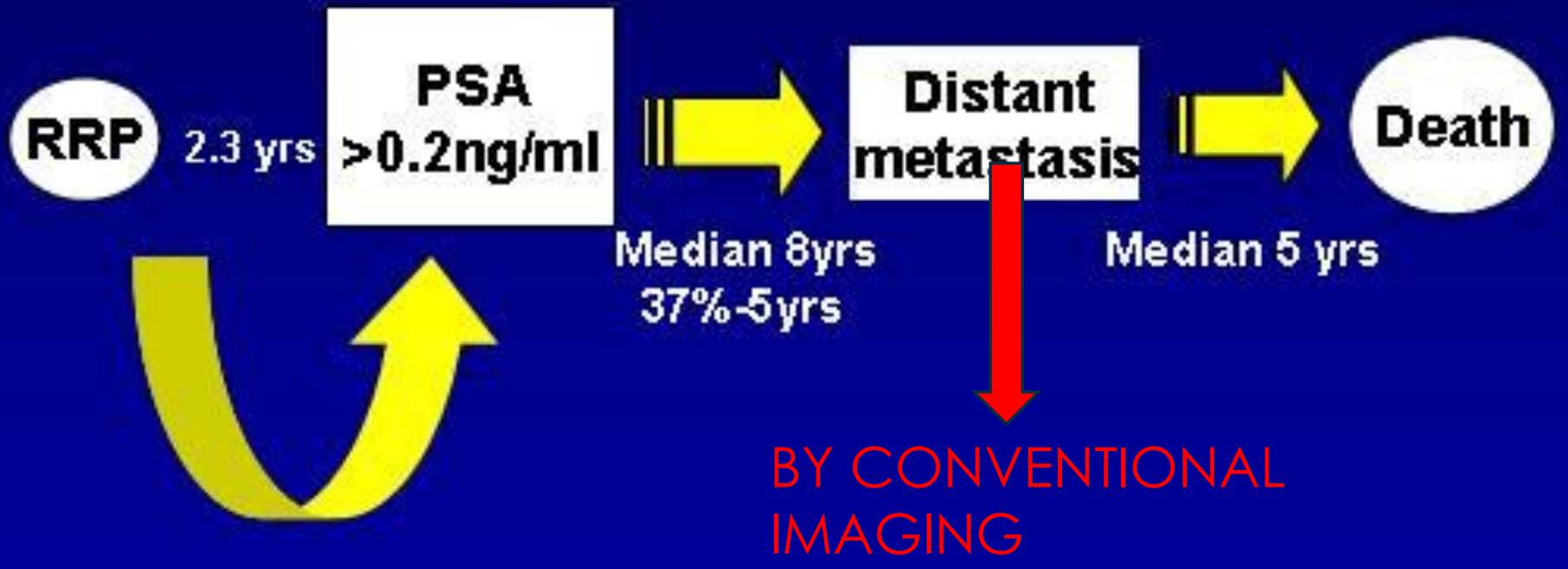
PSA RELAPSE



Defining Biochemical Recurrence

INITIAL THERAPY	PSA VALUES
Radical Prostatectomy	PSA level of 0.2 ng/ml or more
Radiation Therapy or Brachytherapy	PSA rise of 2 ng/ml or more above post Radiation nadir PSA

The natural history of progression following PSA recurrence after radical prostatectomy*



*Pound CP, et al. 1999 JAMA 281, 1591-1597.

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RADICAL PROSTATECTOMY PSA PERSISTENCE/RECURRENCE

PSA persistence/ recurrence[aa]

- Risk stratification[mm]
  - PSADT

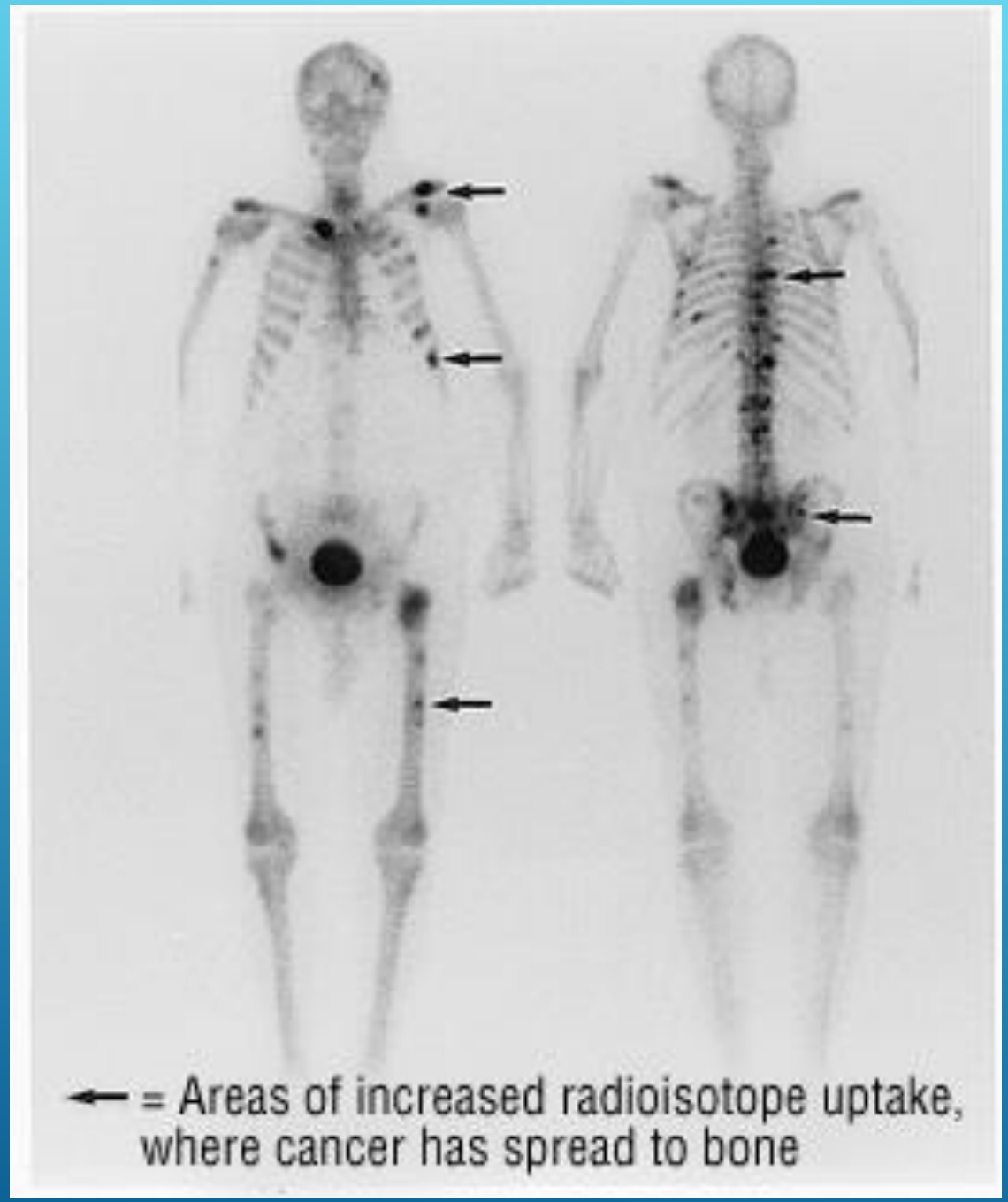
Consider:

- Bone and soft tissue imaging[i,j]
- Prostate bed biopsy (especially if imaging suggests local recurrence)

PSMA PET or bone scan and ct abd/pelvis

Studies negative for distant metastases or imaging not performed → EBRT[o] ± ADT[t] or Observation[q] → Progression[j,kk] → See Systemic Therapy for Castration-Naïve Disease (PROS-12)

Studies positive for distant metastases → See Systemic Therapy for Castration-Naïve Disease (PROS-12)


← = Areas of increased radioisotope uptake,
where cancer has spread to bone

ANDROGEN DEPRIVATION THERAPY

- ADT AS A RADIATION SENSITIZER
  - 4-6 MONTHS WITH XRT FOR INTERMEDIATE RISK PROSTATE CANCER
  - 2-3 YEARS WITH XRT FOR HIGH RISK PROSTATE CANCER
- ADT AS THERAPY FOR METASTATIC DISEASE

TIMING AND INTENSITY OF ANDROGEN DEPRIVATION THERAPY IN BIOCHEMICAL RECURRENCE

- IMMEDIATE (WITHIN 3 MONTHS) VS DELAYED ADT (AT TIME OF METS BY CONVENTIONAL IMAGING)
- NO DIFFERENCE IN OVERAL SURVIVAL OR PROSTATE CANCER SPECIFIC SURVIVAL
- TOAD TRIAL--immediate ADT delayed local and distant progression; however, there was no clear benefit for overall survival or prostate cancer–specific mortality in the PSA recurrent population.

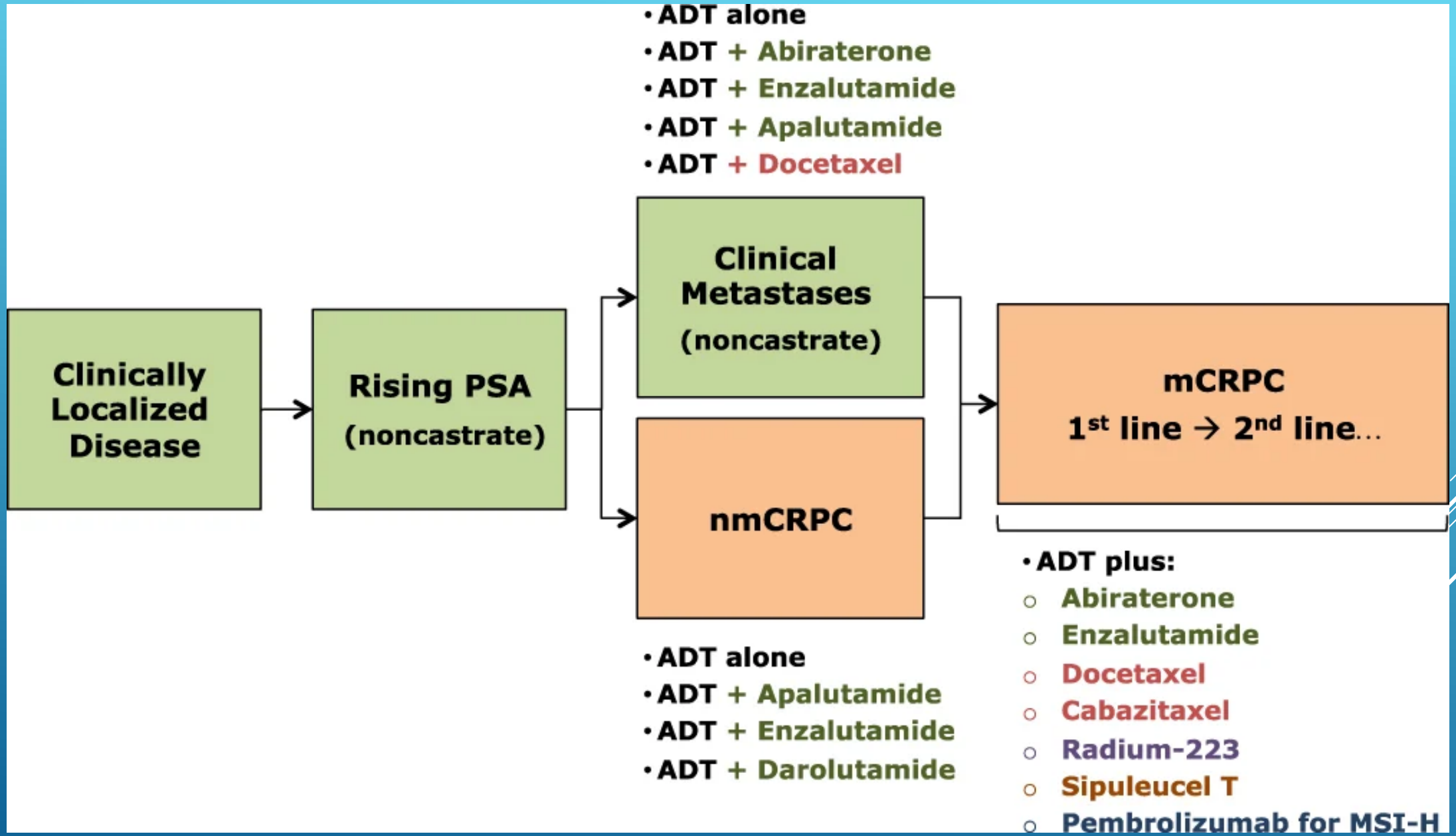
LHRH Products for Hormonal Treatment of Prostate Cancer

Injectable LHRH Agonists		
Generic Name	**Brand Name**	**Manufacturer**
Leuprolide	Lupron Depot®	TAP
Goserelin	Zoladex®	AstraZeneca
Buserelin	Suprefact®	Hoechst Pharmaceuticals
Nafarelin acetate	Synarel®	Searle Pharmaceuticals
Leuprolide	Viadur®	Bayer
Triptorelin	Trelstar Depot™ & LA™	Pharmacia & Upjohn
Leuprolide	Eligard™	Atrix/Sanofi-Synthelabo

Information obtained from respective package inserts.

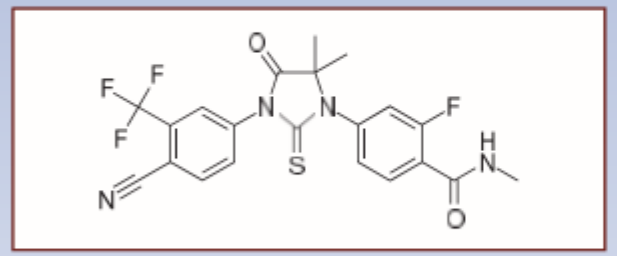
- ASCVD
- DIABETES
- OSTEOPOROSIS
- LOSS OF LEAN MUSCLE MASS
- COGNITIVE IMPAIRMENT
- HOT FLASHES
- BREAST TENDERNESS
- LOSS OF INTEREST IN SEX

HORMONAL TOXICITY


Clinically Localized Disease
Rising PSA (noncastrate)
Clinical Metastases (noncastrate)
nmCRPC
mCRPC 1st line → 2nd line…
• ADT alone
• ADT + Abiraterone
• ADT + Enzalutamide
• ADT + Apalutamide
• ADT + Docetaxel
• ADT alone
• ADT + Apalutamide
• ADT + Enzalutamide
• ADT + Darolutamide
• ADT plus:
Abiraterone
Enzalutamide
Docetaxel
Cabazitaxel
Radium-223
Sipuleucel T
Pembrolizumab for MSI-H

Indications, Dosing, and AEs in AR-Targeted Agents for Prostate Cancer

Enzalutamide[1]

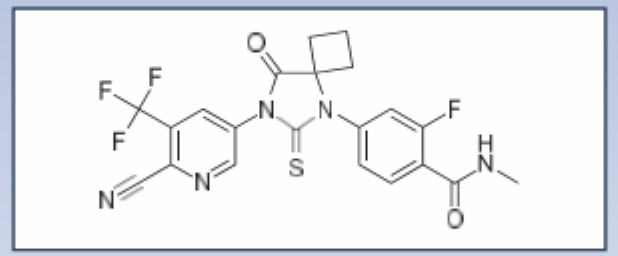


Indication
- Patients with CRPC and mCSPC

Dosing
- 160 mg orally once daily; swallow whole with or without food
- Should also receive a GnRH analog concurrently or have had a bilateral orchiectomy

AEs in ≥10% of Patients
- Asthenia/fatigue, back pain, hot flush, constipation, arthralgia, decreased appetite, diarrhea, and hypertension

Apalutamide[2]

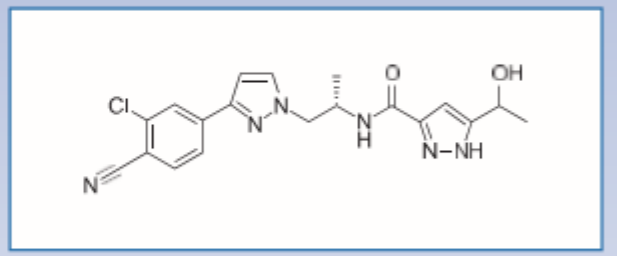


Indication
- Patients with mCSPC and nmCRPC

Dosing
- 240 mg orally once daily; swallow whole with or without food
- Should also receive a GnRH analog concurrently or have had a bilateral orchiectomy

AEs in ≥10% of Patients
- Fatigue, arthralgia, rash, decreased appetite, falls, weight decrease, hypertension, hot flush, diarrhea, and fracture

Darolutamide[3]



Indication
- Patients with nmCRPC

Dosing
- Two 300-mg tablets administered orally twice daily; taken with food
- Should also receive a GnRH analog concurrently or have had a bilateral orchiectomy

AEs in ≥2% of Patients
- Fatigue, pain in extremity, and rash

PRACTICE AID

AR-Targeted Agents in Prostate Cancer

Full abbreviations, accreditation, and disclosure information available at **PeerView.com/ProstateCancer2021**

PeerView Oncology

Us TOO

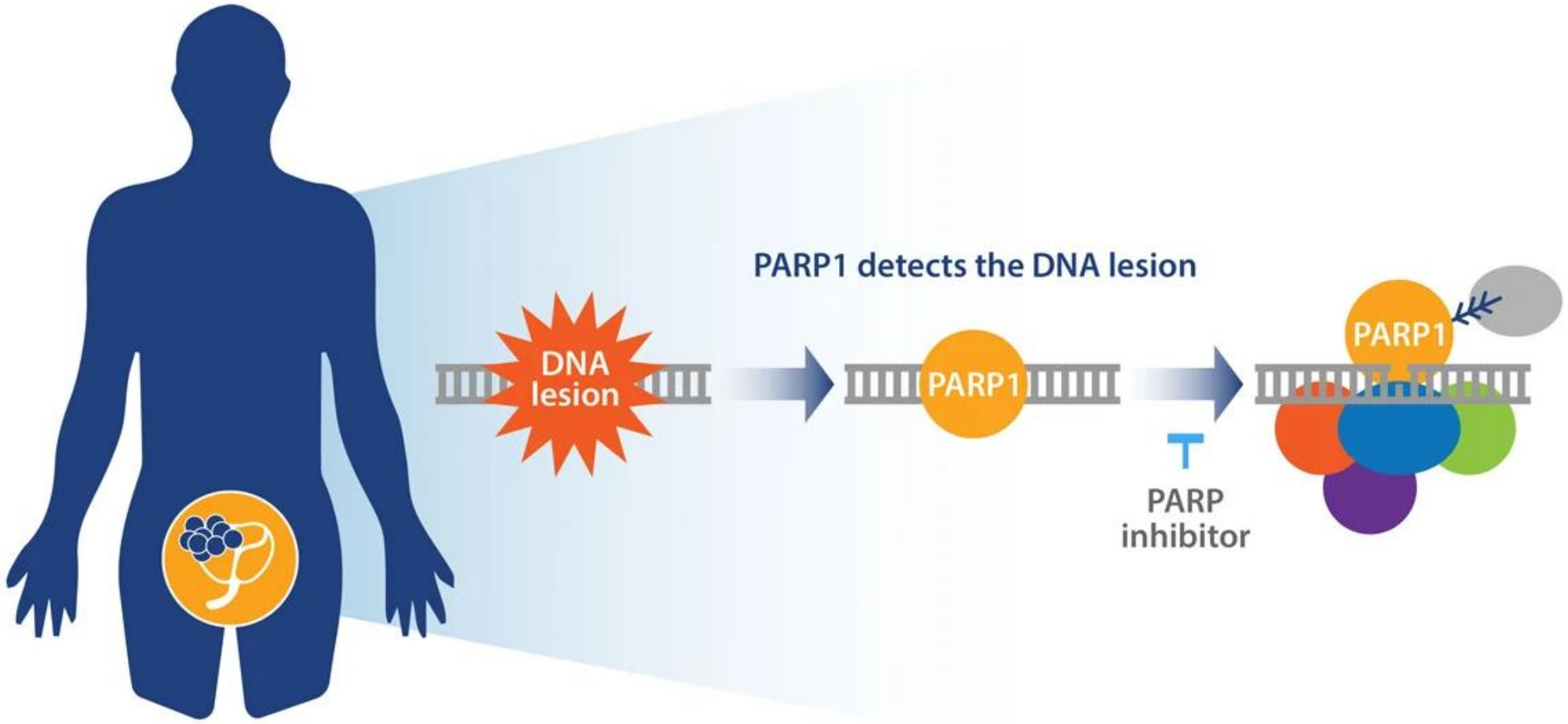
Level 1 Evidence for Improved OS in mHSPC[1-10]

Clinical Trial(s)	Intervention	Control	Comments
STAMPEDE-H	Prostate radiation + ADT (+/- docetaxel)	ADT (+/- docetaxel)	Benefit in low-volume subgroup
GETUG-15 CHAARTED STAMPEDE-C	Docetaxel + ADT	ADT	Benefit in high-volume subgroup
LATITUDE STAMPEDE-G	Abiraterone + ADT	ADT	Similar benefits by risk group
ARCHES ENZAMET	Enzalutamide + ADT	ADT	Similar benefits by risk group
TITAN	Apalutamide + ADT	ADT	Similar benefits by risk group
ARASENS	Darolutamide + ADT + docetaxel	ADT + docetaxel	Similar benefits for recurrent and de novo metastatic disease
PEACE-1	Abiraterone + ADT + docetaxel (+/- prostate radiation)	ADT + docetaxel (+/- prostate radiation)	rPFS benefit for all; OS benefit in high-volume

1. Parker CC et al. *Lancet*. 2018;392:2353-2366. 2. Armstrong AJ et al. *J Clin Oncol. 2022;40:1616-1622*. 3. Davis ID et al. *N Engl J Med*. 2019;381:121-131.
4. James N et al. *Lancet*. 2016;387:1163-1177. 5. Sweeney CJ et al. *N Engl J Med*. 2015;373:737-746. 6. Chi KN et al. *N Engl J Med*. 2019;381:13-24.
7. Fizazi K et al. *N Engl J Med*. 2017;377:352-360. 8. James ND et al. *N Engl J Med*. 2017;377:338-351. 9. Smith MR et al. *N Engl J Med*. 2022;386:1132-1142.
10. Fizazi K et al. *Lancet*. 2022;399:1695-1707.

PARPi for Prostate Cancer

CrownBio
CONNECTING SCIENCE TO PATIENTS



PARP Inhibitor	ClinicalTrials.gov Identifier	Population	DNA Repair Genes	Treatment
Niraparib	NCT02854436 Galahad	mCRPC	*BRCA1/2, ATM, FANCA, PALB2, CHEK2, BRIP1,* or *HDAC2*	Niraparib (single-arm study)
Olaparib	NCT03432897 BrUOG 337	LAPC	*BRCA1, BRCA 2, ATM, CHEK1, CHEK2, FANCONIS ANEMIA (FANCL), HDAC2, PALB2, BARD1, BRIP1, CDK12, PPP2R2A, RAD51B, RAD51C, RAD51D, RAD54L*	Olaparib prior to prostatectomy (single-arm study)
	NCT03012321	mCRPC	*ATM, BRCA1, BRCA2, FANCA, PALB2, RAD51, ERCC3, MRE11, NBN, MLH3, CDK12, CHEK2, HDAC2, ATR, PMS2, GEN1, MSH2, MSH6, BRIP1,* or *FAM175A*	Abiraterone/Prednisone, Olaparib or Abiraterone/Prednisone + Olaparib
	NCT03047135	rPC	*ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D*	Olaparib following prostatectomy (single-arm study)
Rucaparib	NCT03413995 TRIUMPH	mHSPC	*BRCA1, BRCA2, ATM, CHEK2, NBN, RAD50, RAD51C, RAD51D, PALB2, MRE11, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM*	Rucaparib (single-arm study)
	NCT02952534 TRITON2	mCRPC	*BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12 CHEK2, FANCA, NBN PALB2, RAD51, RAD51B RAD51C, RAD51D, RAD54L*	Rucaparib (single-arm study)
	NCT02975934 TRITON3	mCRPC	*BRCA1, BRCA2, ATM*	Rucaparib vs abiraterone, enzalutamide or docetaxel
	NCT03533946 ROAR	nmCRPC	*ATM, ATR, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, ERCC3, FAM175A, FANCA, FANCL, GEN1, HDAC2, MLH1, MRE11, NBN, PALB2, PPP2R2A, RAD51, RAD54L*	Rucaparib (single-arm study)
Talazoparib	NCT03148795	mCRPC	*BRCA1, BRCA2*	Talazoparib (single-arm study)

mCRPC: Metastatic Castration-Resistant Prostate Cancer, LAPC: Locally Advanced Prostate Cancer, rPC: Recurrent Prostate Cancer, mHSPC: Metastatic Hormone-Sensitive Prostate Cancer, nmCRPC: Non Metastatic Castration-Resistant Prostate Cancer.

PETS

PETS

- FDG PET
- NAF-18 PET
- C-11 CHOLINE PET/CT
- C-11 ACETATE
- F-FLUCUCLOVINE PET "AXUMIN" FACBC
- **PSMA PET** (^{68}Ga-PSMA-11 PET or PIFLUFOSTAT F-18)

- IF PSA > 0.2 42% positive PSMA PET
- IF PSA > 2.0 95% positive PSMA PET
- Relapse in pelvic nodes
- Relapse in bones
- Relapse in pelvic nodes and bones

USE OF PSMA PET FOR PSA RELAPSE WITH NEGATIVE BONE SCAN

PSA RELAPSE- BIOCHEMICAL FAILURE

- POST XRT
  - PSA INCREASE OF AT LEAST 2.0 NG/ML ABOVE NADIR
  - PSA NADIR AFTER XRT MAY TAKE 12-18 MONTHS
  - TX OPTIONS OF OBSERVATION VS ADT
- S/P PROSTATECTOMY
  - PSA PERSISTANCE -ADD POST OPERATIVE XRT TO PROSTATE BED
  - PSA RELAPSE (INITIALLY UNDETECTABLE WITH SUBSEQUENT DETECTABLE PSA THAT INCREASES ON TWO OR MORE DETERMINATIONS)
  - OBTAIN PSMA PET
  - TREAT LYMPH NODES WITH XRT/ TREAT FOR ADVANCED DISEASE?

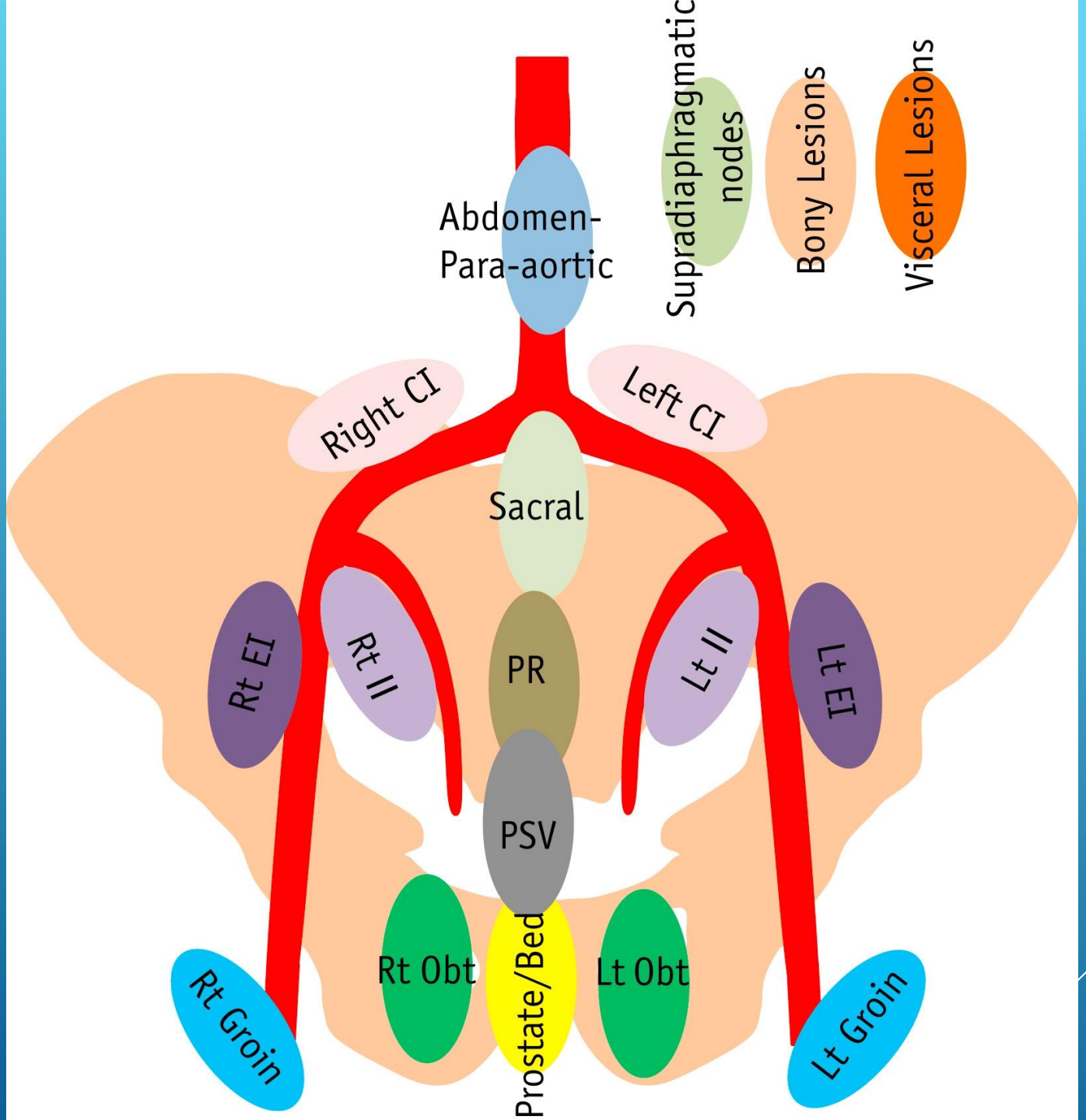
BIOCHEMICAL RECURRENCE (-CONVENTIONAL IMAGING)

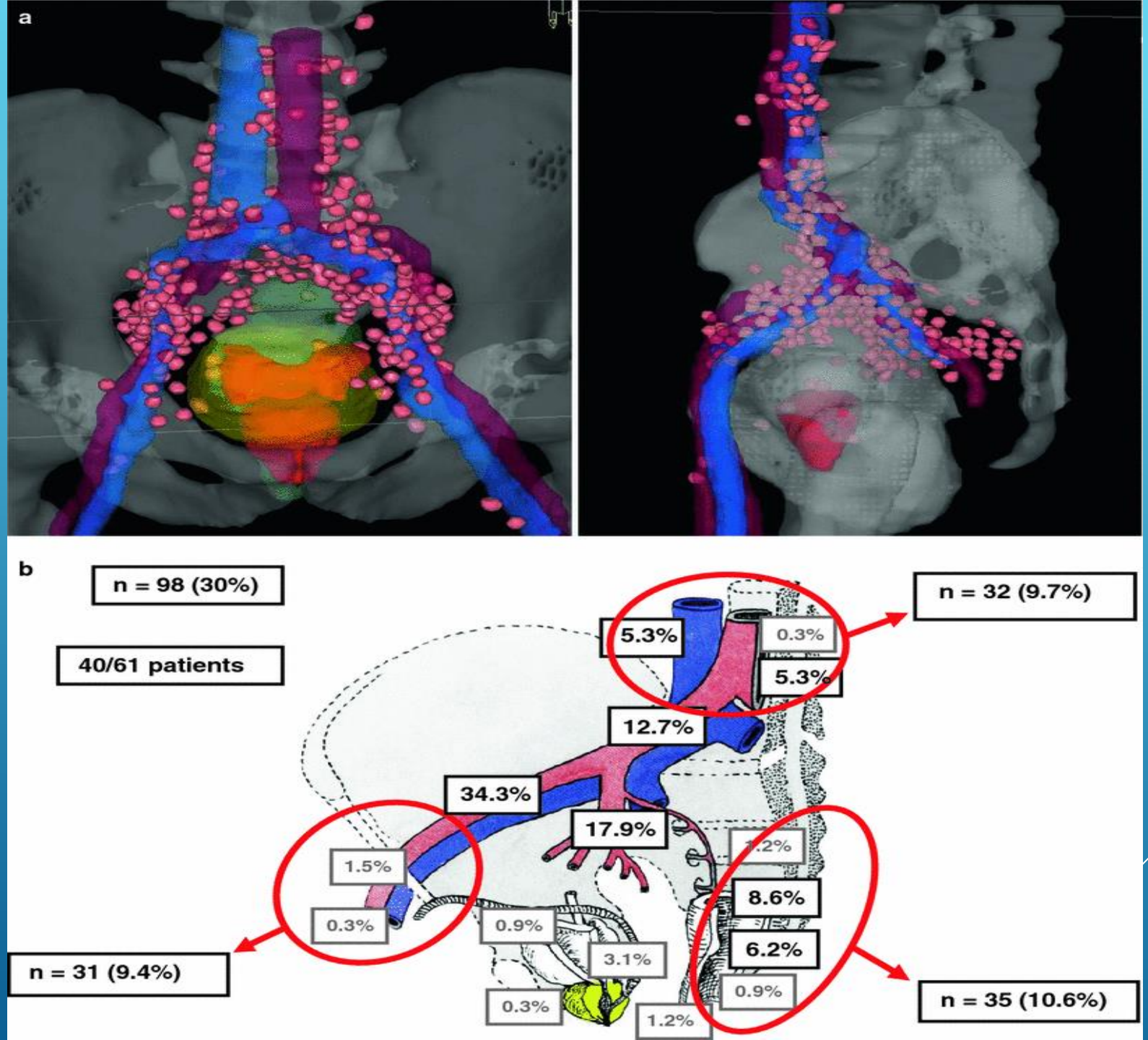
S/P RADICAL PROSTATECTOMY

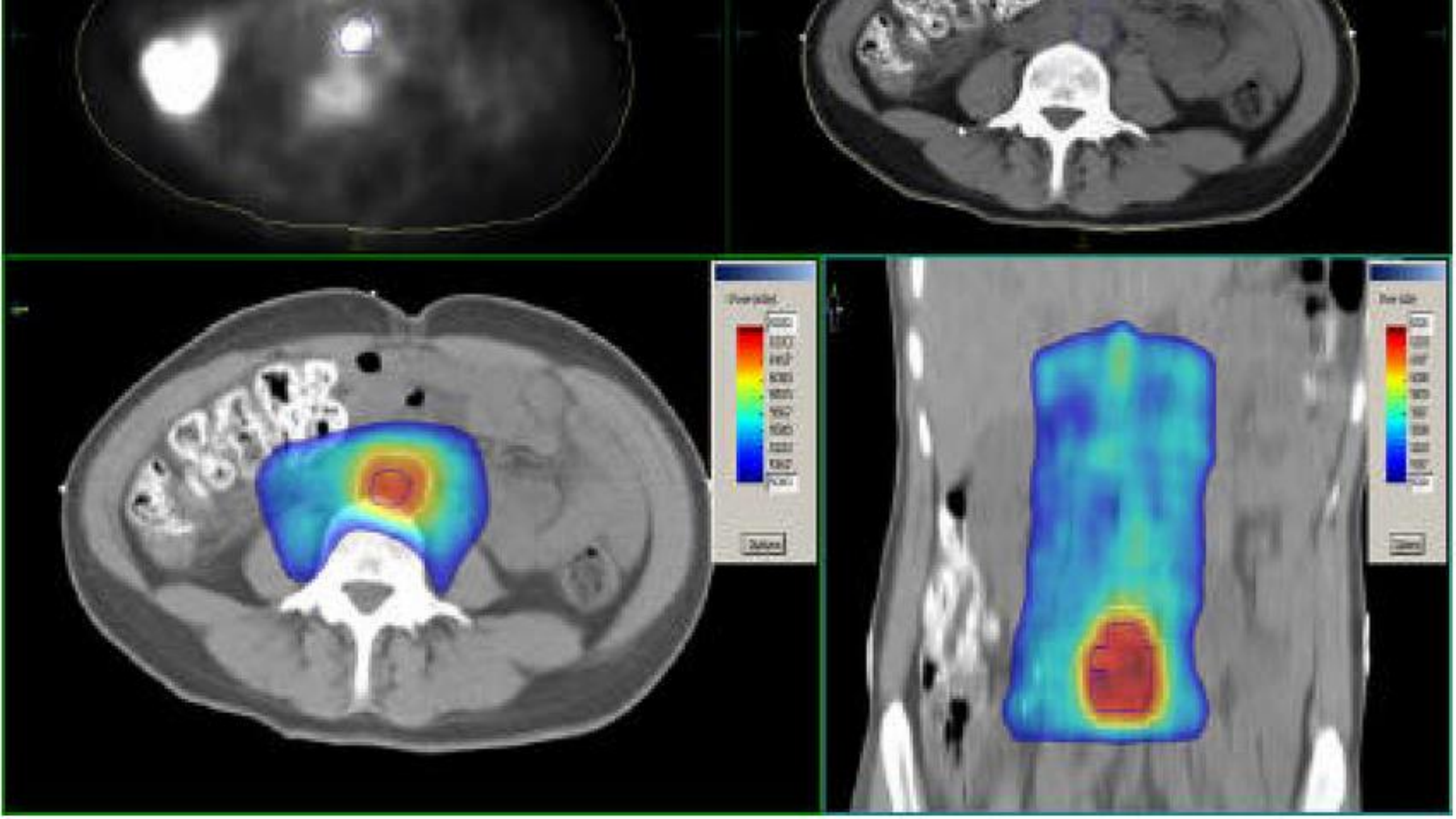
- XRT TO PROSTATE BED +/- REGIONAL NODES

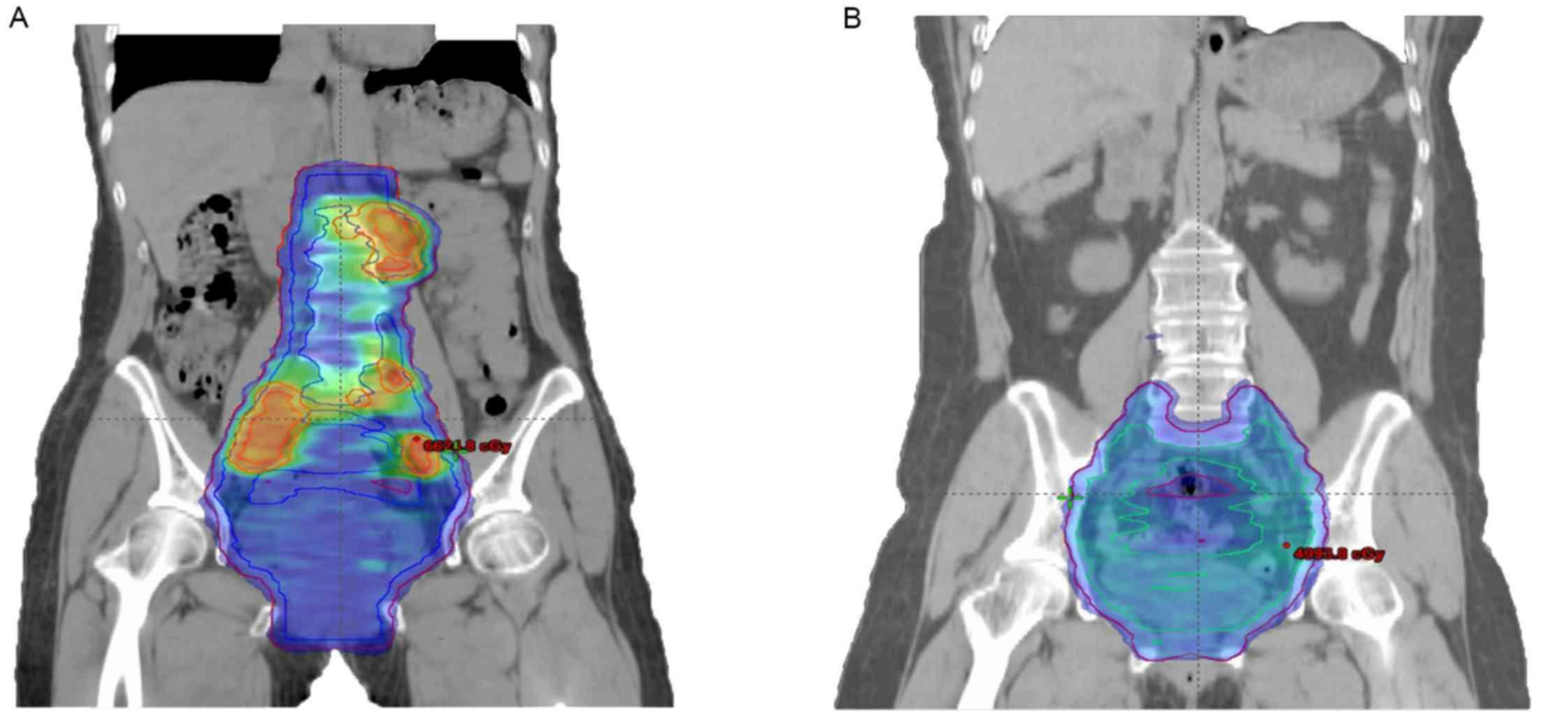
S/P XRT

- OBSERVATION
- ADT


Abdomen-
Para-aortic
Supradiaphragmatic
nodes
Bony Lesions
Visceral Lesions
Right CI
Left CI
Sacral
Rt EI
Rt II
PR
Lt II
Lt EI
PSV
Rt Obt
Prostate/Bed
Lt Obt
Rt Groin
Lt Groin


a
b
n = 98 (30%)
40/61 patients
n = 32 (9.7%)
n = 31 (9.4%)
n = 35 (10.6%)
5.3%
0.3%
5.3%
12.7%
34.3%
17.9%
1.5%
0.3%
0.9%
3.1%
0.3%
1.2%
8.6%
6.2%
0.9%
1.2%




A
B

BIOCHEMICAL RECURRENCE

DOI: 10.1200/EDBK_351033 *American Society of Clinical Oncology Educational Book* 42 (May 3, 2022) 352-359

PRACTICAL APPLICATIONS

- Salvage radiation to the prostate bed and pelvic lymph nodes is the standard approach to treating biochemical recurrence.
- The concurrent use of antiandrogen therapy with radiation therapy has also demonstrated improved overall survival.
- Prostate-specific membrane antigen PET scans have the ability to detect recurrent disease at lower prostate-specific antigen levels and improve progression-free survival when these lesions are covered in the radiation treatment plan.
- The decision to initiate androgen deprivation factors depends on multiple factors, including Gleason score, initial prostate-specific antigen, prostate-specific antigen doubling time, and patient preference.
- If androgen deprivation therapy is initiated, intermittent therapy is preferable to continuous therapy.

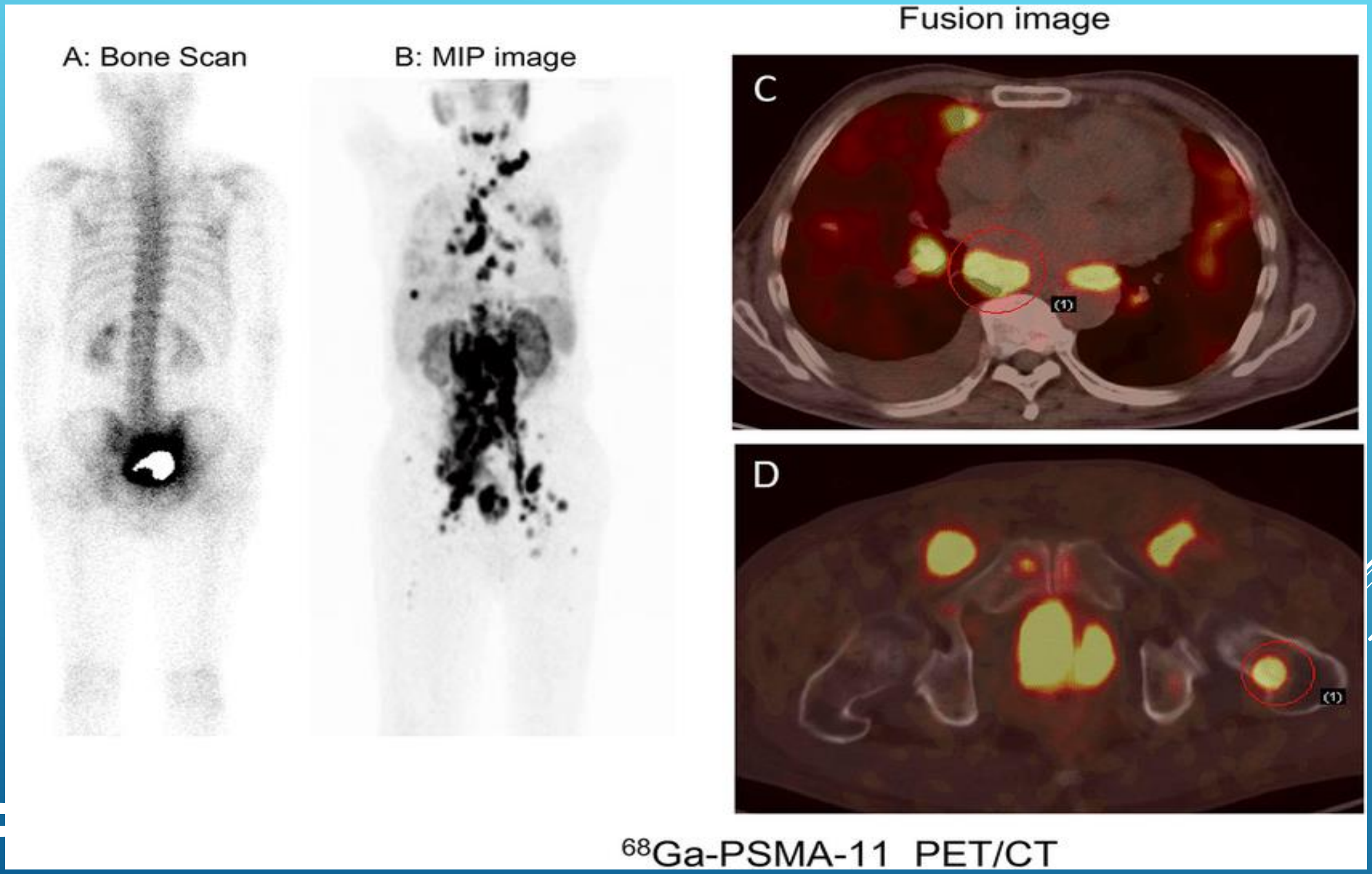
BIOCHEMICAL RECURRENCE

S/P RADICAL PROSTATECTOMY

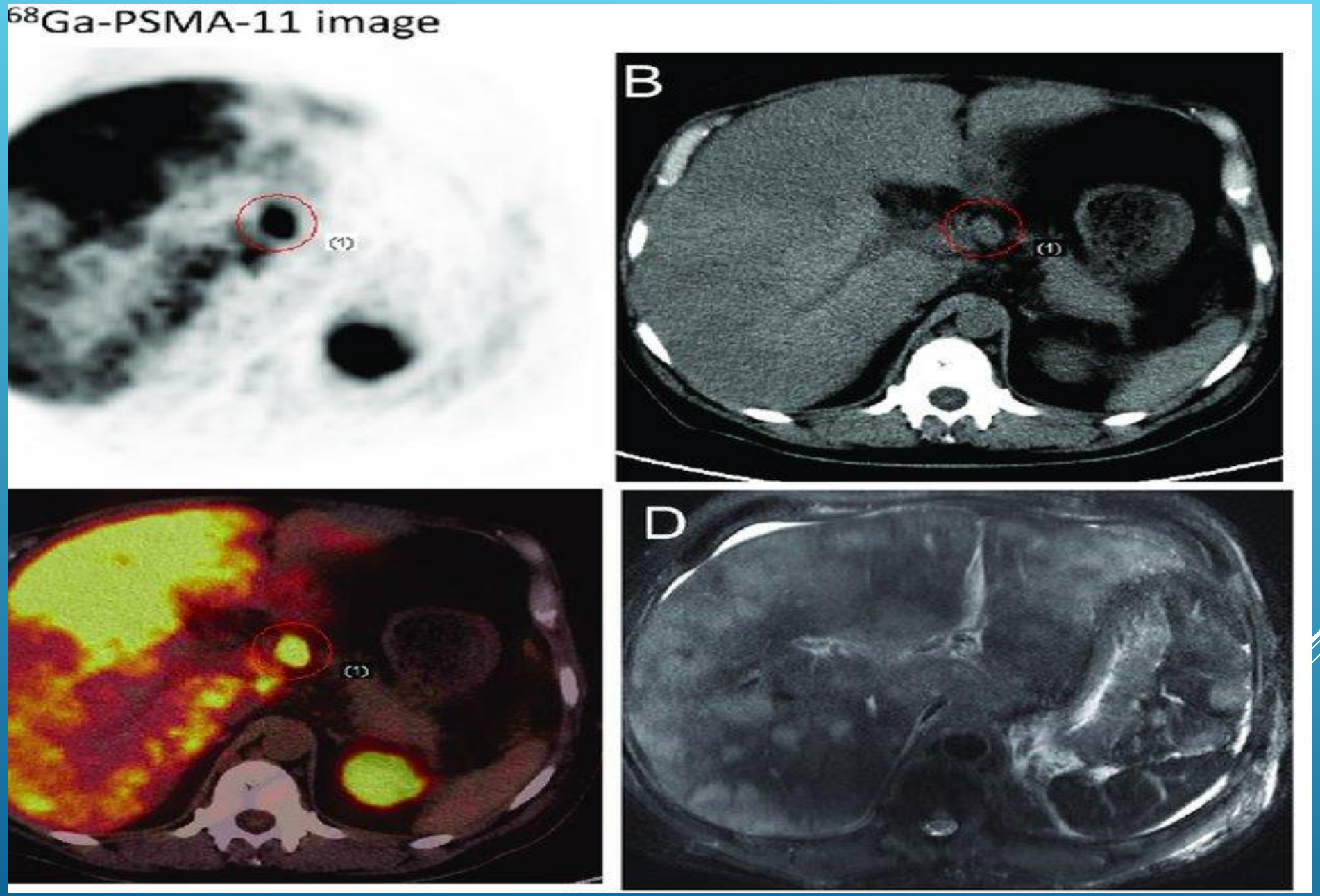
- XRT TO PROSTATE BED +/- REGIONAL NODES

S/P XRT

- **OBSERVATION**
- **ADT**



^{68}Ga-PSMA-11 PET/CT


^{68}Ga-PSMA-11 image
B
D
(1)
(1)
(1)

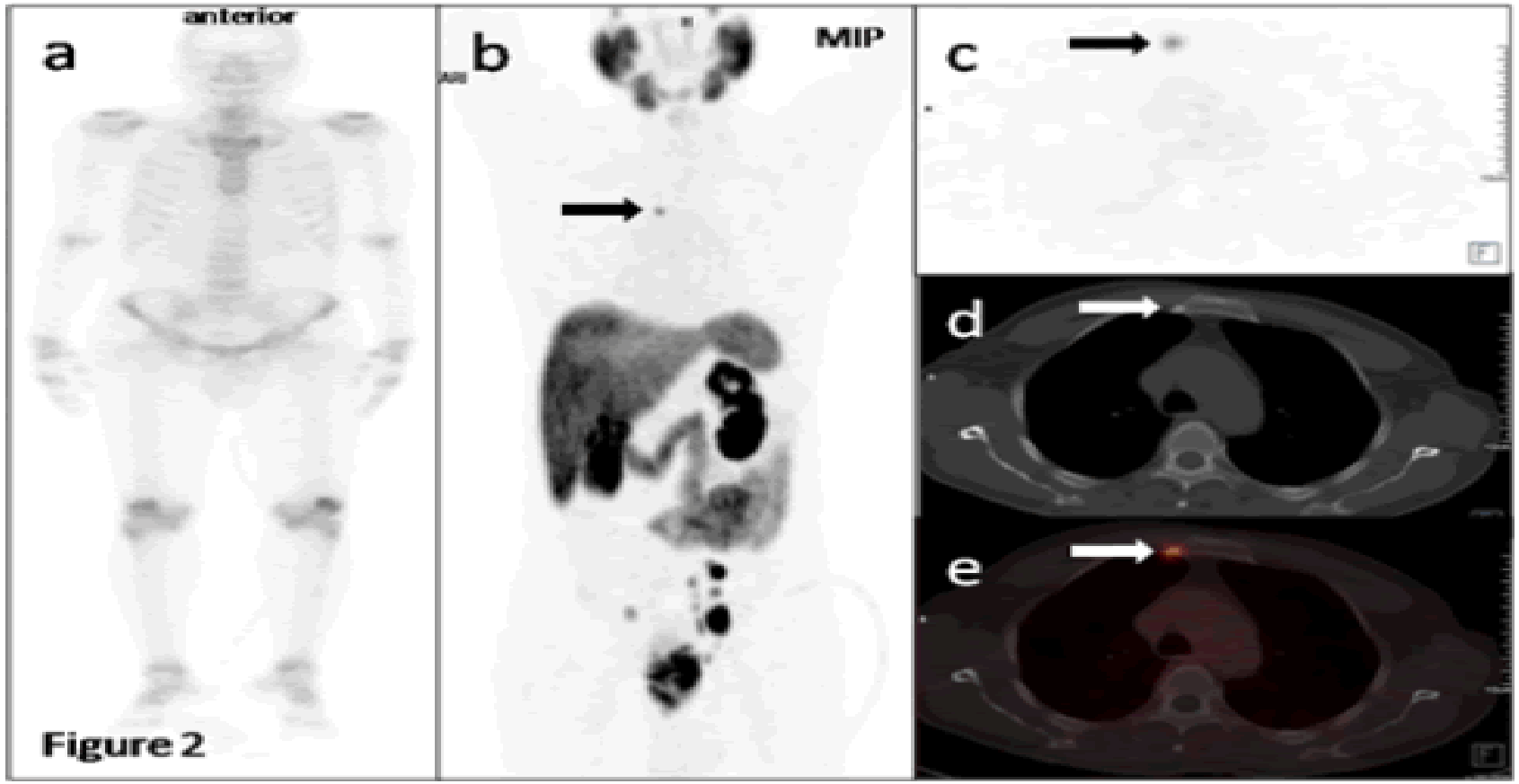


Figure 2: 62 Years male with adenocarcinoma prostate, gleason score 5+4, PSA 17.5 ng/ml underwent MDP bone scan (image a) and 68GaPSMA PET-CT (image b, c, d, e). MDP bone scan was reported normal while PSMA PET-CT showed locally infiltrating prostate lesion with pelvic lymphnodes and a solitary bony lesion in sternum (block arrows).

PSMA IMAGING

PRACTICAL APPLICATIONS

- PSMA imaging has high sensitivity for detecting the location of prostate cancer recurrence in the setting of increasing prostate-specific antigen after definitive management (biochemical recurrence). The impact on decision-making for salvage radiation remains to be defined.
- More accurate identification of patients with oligometastatic disease using PSMA imaging could pave the way for metastasis-directed surgical or radiation therapy.
- Change in uptake (standardized uptake value) of PSMA is being explored for assessment of response to systemic therapy, but additional work is needed to establish the meaning of such changes with established outcome parameters.
- Radiolabeled PSMA conjugates are being studied in phase II and III trials as theranostics—selecting patients with expression for treatment—and have yielded objective responses.

INDICATIONS FOR PSMA PET

Clinical Scenarios for Prostate Cancer

Scenario #	Description	Appropriateness	Score
1	Patients with suspected prostate cancer (e.g., high/rising PSA levels, abnormal digital rectal examination results) evaluated for targeted biopsy and detection of intraprostatic tumor	Rarely Appropriate	3
2	Patients with very low, low, and favorable intermediate-risk prostate cancer	Rarely Appropriate	2
3	Newly diagnosed unfavorable intermediate, high-risk, or very high-risk prostate cancer	Appropriate	8
4	Newly diagnosed unfavorable intermediate, high-risk, or very high-risk prostate cancer with negative/equivocal or oligometastatic disease on conventional imaging	Appropriate	8
5	Newly diagnosed prostate cancer with widespread metastatic disease on conventional imaging	May be Appropriate	4
6	PSA persistence or PSA rise from undetectable level after radical prostatectomy	Appropriate	9
7	PSA rise above nadir after definitive radiotherapy	Appropriate	9
8	PSA rise after focal therapy of the primary tumor	May be Appropriate	5
9	nmCRPC (M0) on conventional imaging	Appropriate	7
10	Post-treatment PSA rise in the mCRPC setting in a patient not being considered for PSMA-targeted radioligand therapy	May be Appropriate	6
11	Evaluation of eligibility for patients being considered for PSMA-targeted radioligand therapy	Appropriate	9
12	Evaluation of response to therapy	May be Appropriate	5

WILL ROGERS EFFECT

- When the Okies left Oklahoma and moved to California, they raised the average intelligence level in both states.
- The **Will Rogers phenomenon** is encountered in many disciplines but is particularly relevant to radiology in the setting of staging scans and is due to reclassifying borderline individuals also known as **stage migration** [1].
- The most common example in medicine is upstaging certain patients with malignancy by changes in criteria or technique, resulting in the worst patients in the lower stage becoming the best patients in the higher stage. The end result is that both lower and higher stage improve their outcome when viewed as separate cohorts without any individual patient or the whole patient group improving.

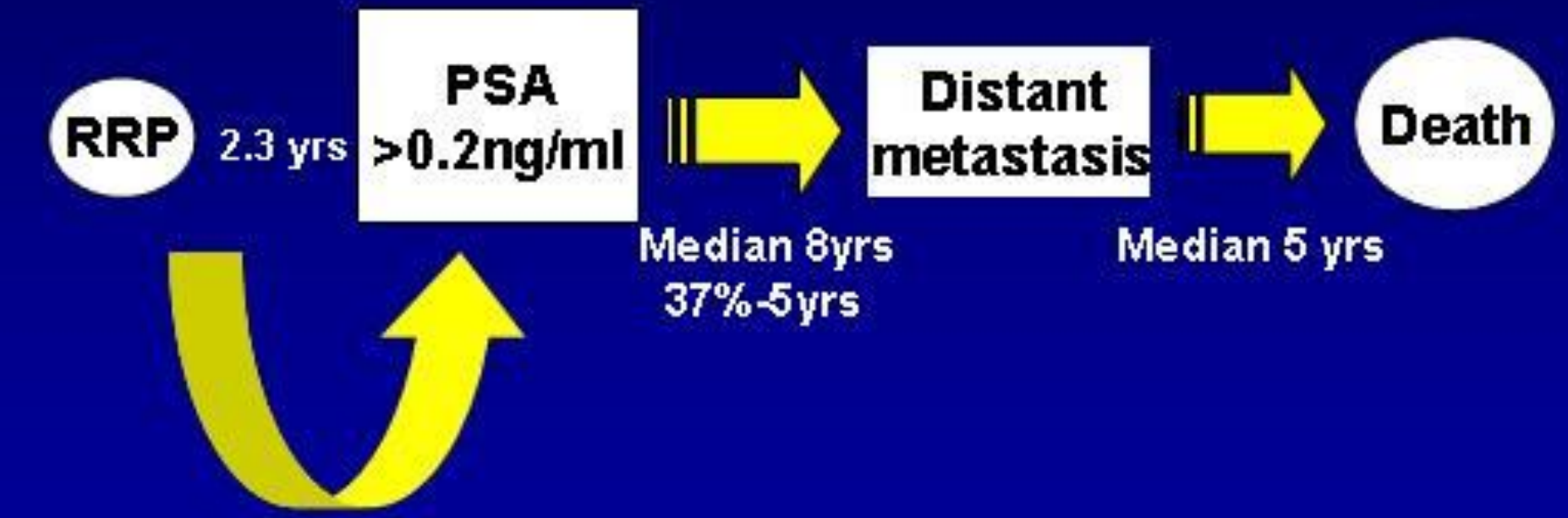
WILL ROGERS EFFECT

- When the worst prognosis patients from one risk group move to the higher risk group, the average outcome of both risk groups will improve even if treatment has no impact on disease. This phenomenon is known as the Will Rogers effect, in which the improved outcomes of both groups could be falsely attributed to improvement in treatment, but would be due only to improved risk group assignment. As an example, F-18 sodium fluoride PET/ CT may categorize some patients as M1b who would have been categorized previously as M0 using a bone scan (stage migration). Absent any change in the effectiveness of therapy, the overall survival of both M1b and M0 groups would improve. The definition of M0 and M1 disease for randomized clinical trials that added docetaxel or abiraterone to ADT was based on CT and conventional radionuclide bone scans. Results suggest that overall survival of M1 disease is improved, whereas progression-free but not overall survival of M0 disease is improved. Therefore, a subset of patients now diagnosed with M1 disease using F-18 sodium fluoride PET/ CT might not benefit from the more intensive therapy used in these trials and could achieve equivalent overall survival from less intensive therapy aimed at M0 disease. Carefully designed clinical trials using proper staging will be necessary to prove therapeutic benefit, rather than making assumptions compromised by stage migration.

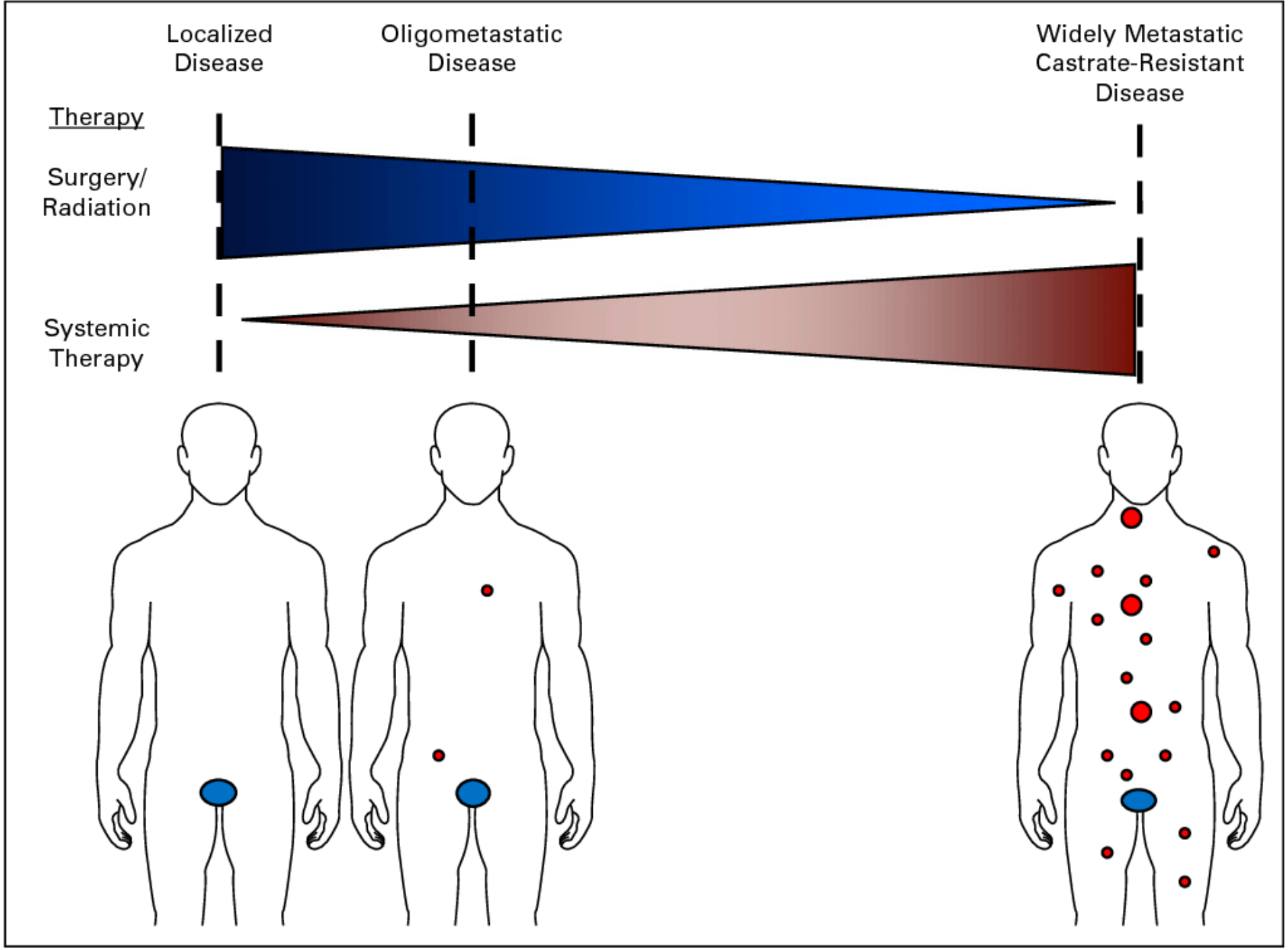
Next-Generation Imaging: Clinical Implications

- All of the FDA-approved agents and level 1 evidence from therapeutic prostate cancer trials utilized conventional CT/bone scans
- Earlier detection may not mean that earlier therapeutic intervention is beneficial but it may result in this approach
- Earlier detection may result in “aborting” planned curative intent therapies without supporting data
- Adoption of next-generation imaging will occur over time and be admixed with curative intent

The natural history of progression following PSA recurrence after radical prostatectomy*



*Pound CP, et al. 1999 JAMA 281, 1591-1597.


Localized Disease
Oligometastatic Disease
Widely Metastatic Castrate-Resistant Disease
Therapy
Surgery/ Radiation
Systemic Therapy

FALSE POSITIVE PSMA-PET

- PRESACRAL AND PARAAORTIC GANGLION
- LOW UPTAKE SOLITARY RIB LESIONS
- PAGETS DISEASE
- FIBROUS DYSPLASIA
- HEMANGIOMAS

OLIGOMETASTATIC DISEASE

OI https://doi.org/ 10.1200/EDBK_ 239041

PRACTICAL APPLICATIONS

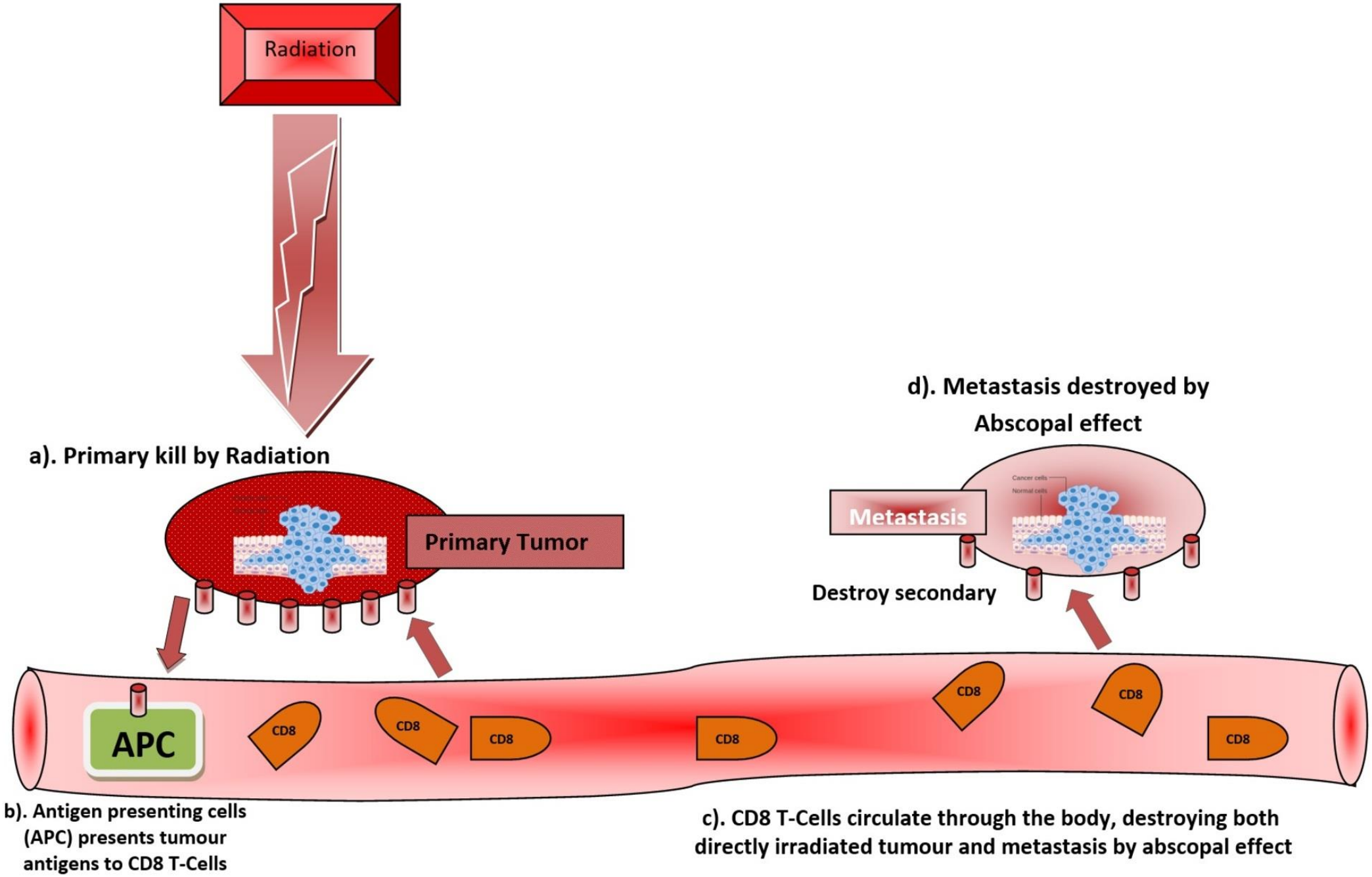
- OMPC, generally defined by the presence of five or fewer metastatic sites on imaging, represents a transitional state between localized and widespread metastatic disease and encompasses a wide spectrum of disease biologies and clinical behaviors.
- A growing body of evidence suggests that a subset of patients with OMPC may achieve a deep and prolonged response with multimodality therapy—combination surgery/radiation and systemic therapy—with improvement in disease-specific outcomes, such as time to castration resistance, PFS, and OS.
- Local cytoreductive therapies, such as radical prostatectomy with or without pelvic LN dissection and RT, seem to be well tolerated in patients with OMPC.
- Pelvic RT has been demonstrated to improve outcomes in patients with high-volume metastatic prostate cancer receiving abiraterone plus aDT.
- Participation in clinical trials or institutional registries is strongly encouraged for patients with OMPC who opt for an aggressive multimodality approach.

Rationale for Metastases Directed Therapy

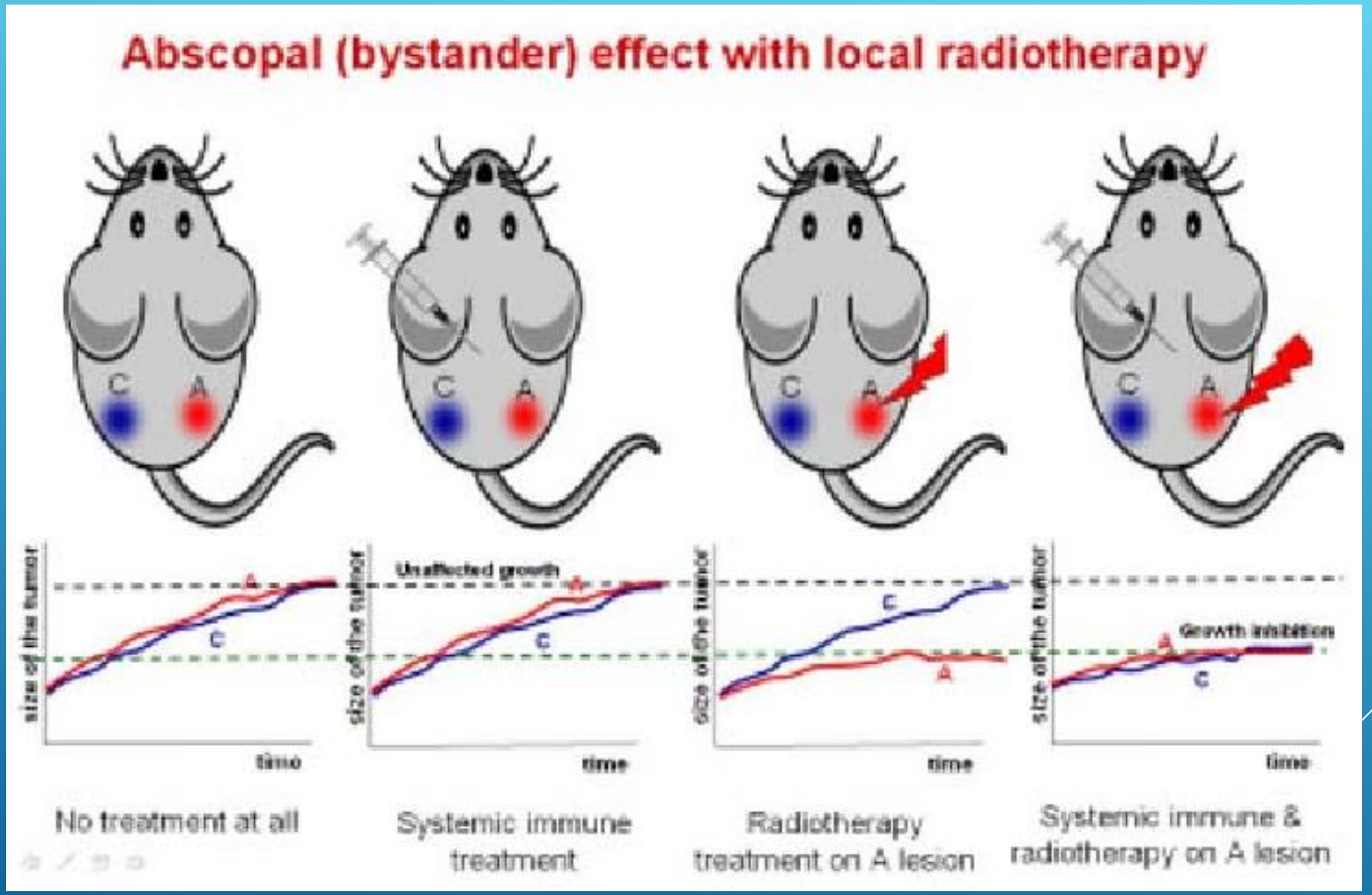
- Early ablation of metastatic lesions may reduce the risk of skeletal events or other complications from disease progression.
- Metastatic lesions may have differing molecular phenotype = systemic therapy resistance. Targeting may delay/defer castrate resistance and/or systemic therapy augmentation
- Improve Oncologic Outcome

International guideline recommendations for MDT in oligorecurrent disease [1-2]

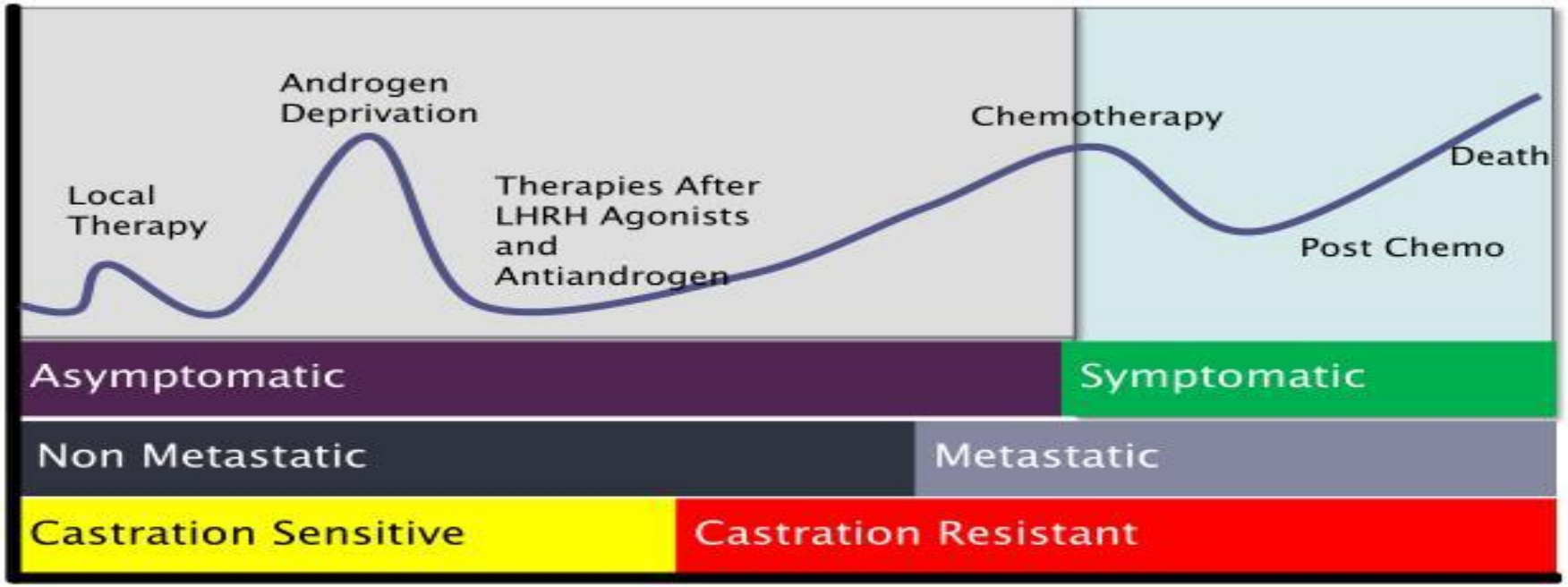
Guideline	Recommendations	
EAU	• Recommend to offer immediate ADT to M1 patients asymptomatic from their tumour	• Strength rating: weak
	• Recommend to discuss deferred ADT with well-informed M1 patients asymptomatic from their tumour since it lowers the treatment-related side effects, provided the patient is closely monitored	• Strength rating: weak
	• Recommend to discuss combination therapy including ADT plus systemic therapy with all M1 patients	• Strength rating: strong
	• Recommend to only offer metastasis-directed therapy to M1 patients within a clinical trial or well-designed prospective cohort study	• Strength rating: strong
NCCN	• SBRT to metastases can be considered in patients with oligometastatic progression where progression-free survival is the goal	
	• ADT alone is not a preferred regimen	• Category 2A


Radiation
a). Primary kill by Radiation
Primary Tumor
APC
CD8
CD8
CD8
CD8
CD8
CD8
CD8
b). Antigen presenting cells (APC) presents tumour antigens to CD8 T-Cells
c). CD8 T-Cells circulate through the body, destroying both directly irradiated tumour and metastasis by abscopal effect
d). Metastasis destroyed by Abscopal effect
Metastasis
Destroy secondary

Abscopal (bystander) effect with local radiotherapy



Natural History of Prostate Cancer



- Typical presentation of patients as they move through the different stages.
  The line represents level burden of disease. Time is not proportional

Abbreviation: LHRH=luteinizing hormone–releasing hormone.

N Engl J Med 2021;385:1091-103

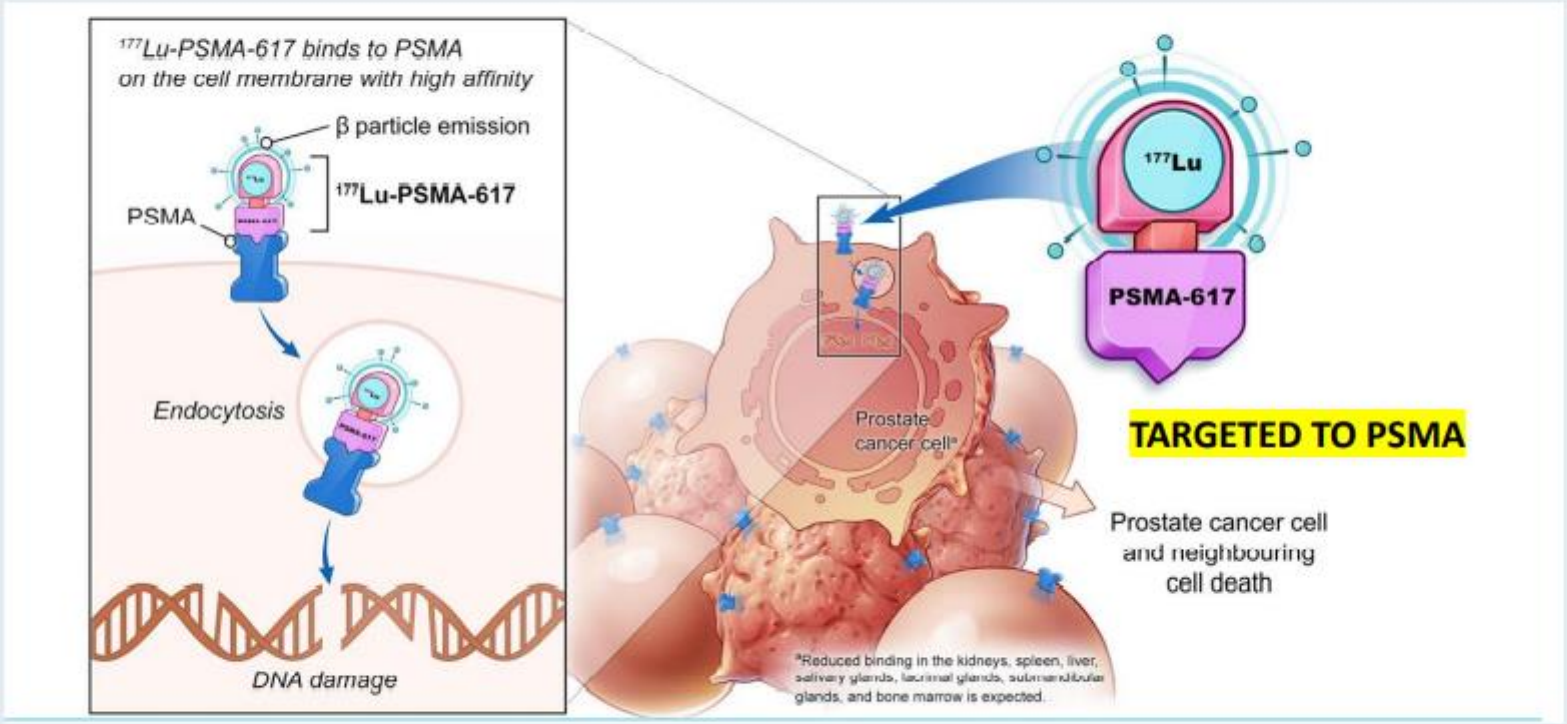
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

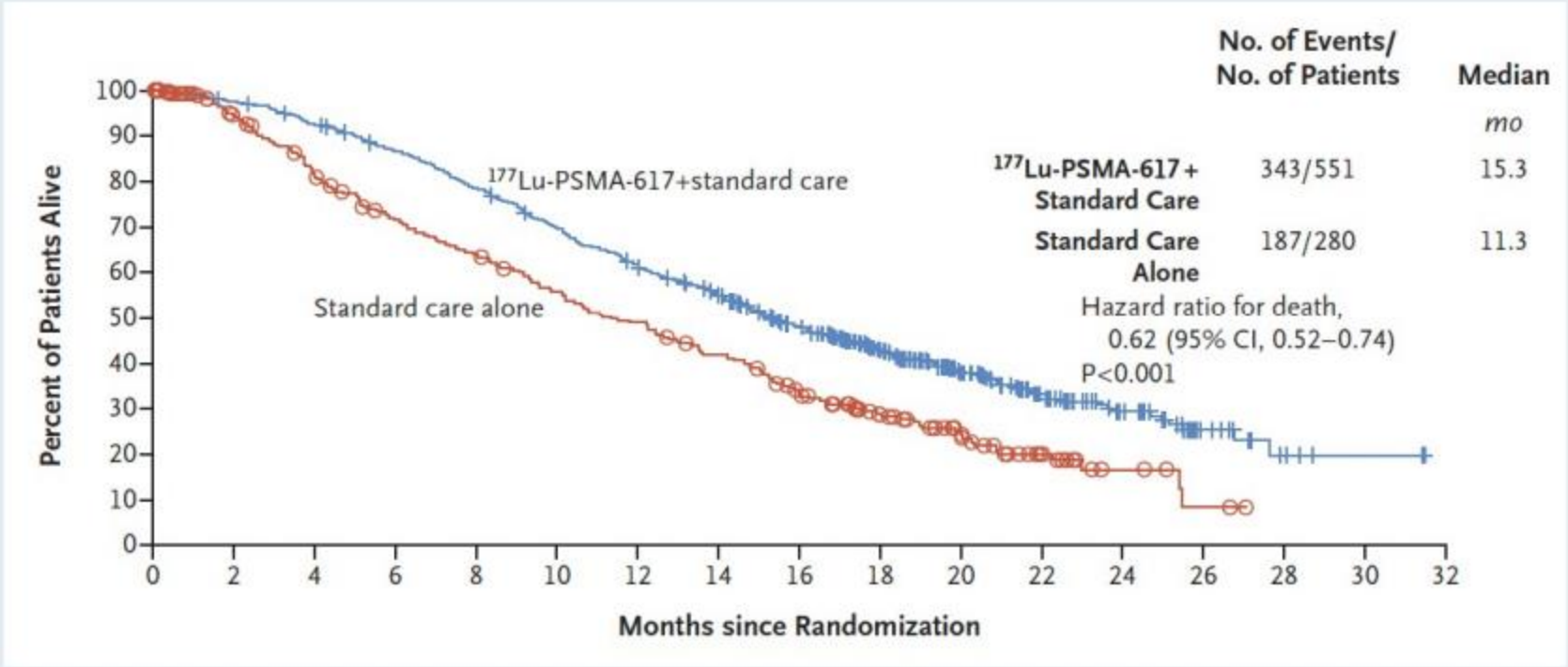
^{177}Lu-PSMA-617: Mechanism of Action



Morris MJ et al. ASCO 2021;Abstract LBA4.

RTP RESEARCH TO PRACTICE

VISION: Overall Survival



Sartor O et al. *N Engl J Med* 2021;385:1091-103.

TAKE HOME POINTS

- Perform risk assessment
- mpMRI prior to biopsy
- Active surveillance instead of surgery/xrt for low risk
- On site surveillance- watch for PSA recurrence/biochemical failure
- Role of PSMA pet
- Treatment of advanced disease incorporating new imaging data

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- Low-Grade Prostate Cancer: Time to Stop Calling It Cancer *Journal of Clinical Oncology* 40, no. 27 (September 20, 2022) 3110-3114.
- Peter C. Albertsen, MD, *JAMA.* 2005;293(17):2095-2101. doi:10.1001/jama.293.17.2095